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Facile synthesis of ethyl 2-arylpropenoates by cross-coupling reaction using electrogenerated highly reactive zinc

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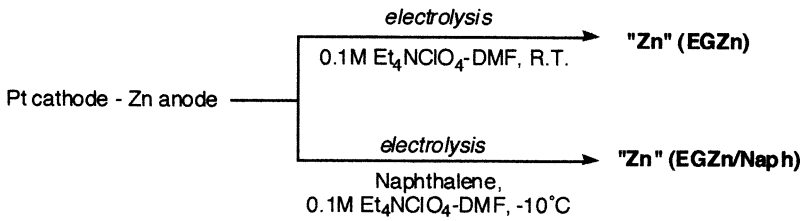
Abstract—Highly reactive zinc metal was prepared by electrolysis of a DMF solution containing naphthalene and a supporting electrolyte in a one-compartment cell fitted with a platinum cathode and a zinc anode. This reactive zinc was used for efficient transformation of ethyl 2-bromoacrylate into the corresponding organozinc compound, which was reacted with various aryl iodides or bromides in the presence of 5 mol% $Pd(P(o\text{-}Tol)_3)_2Cl_2$ to give the corresponding cross-coupling products in high yields. These cross-coupling reactions were successfully applied to a synthesis of the precursor of naproxen and cicloprofen, non-steroidal anti-inflammatory agent.

1. Introduction

Organozinc compounds are very useful organometallic compounds for the forming reaction of carbon–carbon bonds.[1] Organozinc halides can usually be prepared by direct insertion of zinc metal into organic halides,[1b] but commercially available zinc metal is generally poorly reactive. Therefore, activation of the metal is necessary for preparation of organozinc halides. Various methods of zinc activation, such as the reduction of zinc halide with alkaline metal or alkali metal naphthalenide, have been reported.[2] These methods, however, require high temperature and long reaction times, or vigorous stirring during the reaction.

We have already reported a new method for the preparation of reactive zinc by electrolysis and its use in facile isoprenylation[3] and allylation[4,5] of aldehydes and ketones. It was shown that this electrogenerated reactive zinc (EGZn) was an aggregation of very fine crystalline zinc particles with a large surface area.[4] We have also reported a facile preparation of organozinc compounds from functionalized alkyl iodides by using EGZn and their cross-couplings with aryl halides.[6] However, organozinc bromides were rarely obtained or were only obtained in very low yields from the corresponding organic bromides, even if the reactive EGZn was used. Recently, we developed a new electrochemical method for preparation of more highly reactive zinc (EGZn/Naph) by using naphthalene as a mediator (Scheme 1).[7] The reaction of EGZn/Naph with ethyl 2-bromoacrylate gave efficiently the corresponding organozinc bromide and subsequent cross-coupling reaction with various aryl iodides in the presence of palladium catalyst proceeded efficiently to give ethyl 2-arylpropenoates in high yields.[7] However, no cross-coupling reaction occurred under these conditions when aryl bromide was used as one of the coupling components. We examined various reaction conditions and found that the cross-coupling using aryl bromides could undergo when THF, instead of DMF, was used as a solvent.

In this paper, we report a facile synthesis of ethyl



Scheme 1.

Keywords: electrolysis; reactive zinc; coupling reactions; palladium catalyst; anti-inflammatory agent.

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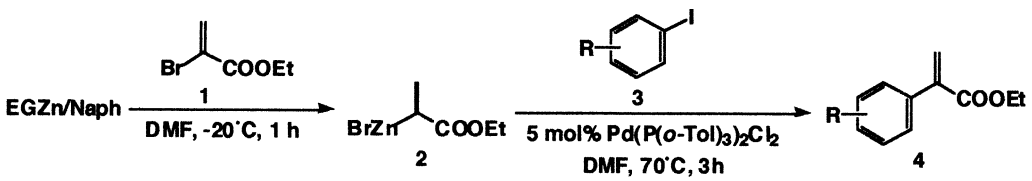


Scheme 2.

Table 1. Cross-coupling reaction of organozinc bromide **2** with iodobenzene (**3a**) using various zinc metals

Entry	Type of zinc	Yield of **4a** (%)[a]
1	Zn powder[b]	0
2	Zn–Cu couple	11
3	EGZn	19
4	EGZn/Naph	98

Organozinc bromide **2**, prepared from ethyl 2-bromoacrylate (**1**) (3 mmol) and zinc (6 mmol), was reacted in DMF at 70°C for 3 h with iodobenzene (2 mmol) in the presence of 5 mol% of $Pd(P(o\text{-}Tol)_3)_2Cl_2$.

[a] Isolated yields.

[b] Commercially available zinc from Kanto Chemical Co. Inc. was activated according to Ref. 8.

2-arylpropenoates by cross-coupling reaction of organozinc bromide derived from ethyl 2-bromoacrylate with various aryl bromides and iodides. Application of these cross-coupling reactions to a synthesis of the precursor of non-steroidal anti-inflammatory agents such as naproxene and cicloprofen was also reported.

2. Results and discussion

2.1. Electrochemical preparation of highly reactive zinc (EGZn/Naph)

Highly reactive zinc was readily prepared by electrolysis of a DMF solution containing 0.1 M Et_4NClO_4 in the presence of naphthalene in a one-compartment cell fitted with a platinum plate cathode (2×2 cm^2) and a zinc plate anode (2×2 cm^2). Electrolysis was carried out at a constant current of 60 mA cm^{-2} at −10°C under a nitrogen atmosphere. At the cathode, a one-electron reduction of naphthalene molecule readily occurred to give naphthalene radical anion preferentially. The formation of the naphthalene radical anions was shown by the dark green color appeared on the surface of the cathode. On the other hand, at the anode, dissolution of the zinc metal occurred to give zinc ions, which were reduced by the naphthalene radical anions to give zero-valence highly reactive zinc, EGZn/Naph (Scheme 1). The EGZn/Naph was an aggregation of very

Table 2. Synthesis of ethyl 2-arylpropenoates (**4**) by palladium catalyzed cross-coupling of aryl iodides (**3**) with organozinc bromide **2**

Entry	ArI	Product	Yield (%)[a]
1	C_6H_5I (**3a**)	$C_6H_5C(=CH_2)CO_2Et$ (**4a**)	98
2	4-$CH_3OC_6H_4I$ (**3b**)	4-$CH_3OC_6H_4C(=CH_2)CO_2Et$ (**4b**)	98
3	4-$CH_3C_6H_4I$ (**3c**)	4-$CH_3C_6H_4C(=CH_2)CO_2Et$ (**4c**)	98
4	3-$CH_3C_6H_4I$ (**3d**)	3-$CH_3C_6H_4C(=CH_2)CO_2Et$ (**4d**)	96
5	2-$CH_3C_6H_4I$ (**3e**)	2-$CH_3C_6H_4C(=CH_2)CO_2Et$ (**4e**)	84
6	4-NCC_6H_4I (**3f**)	4-$NCC_6H_4C(=CH_2)CO_2Et$ (**4f**)	97
7	4-$CH_3OOCC_6H_4I$ (**3g**)	4-$CH_3OOCC_6H_4C(=CH_2)CO_2Et$ (**4g**)	98
8	2-$CH_3OOCC_6H_4I$ (**3h**)	2-$CH_3OOCC_6H_4C(=CH_2)CO_2Et$ (**4h**)	51
9	4-BrC_6H_4I (**3i**)	4-$BrC_6H_4C(=CH_2)CO_2Et$ (**4i**)	96

Organozinc bromide **2**, prepared from ethyl 2-bromoacrylate (**1**) (3 mmol) and EGZn/Naph (6 mmol), in DMF was reacted at 70°C for 3 h with aryl iodides **3** (2 mmol) in the presence of 5 mol% of $Pd(P(o\text{-}Tol)_3)_2Cl_2$.

[a] Isolated yields. The yields are based on aryl iodides **3** employed.

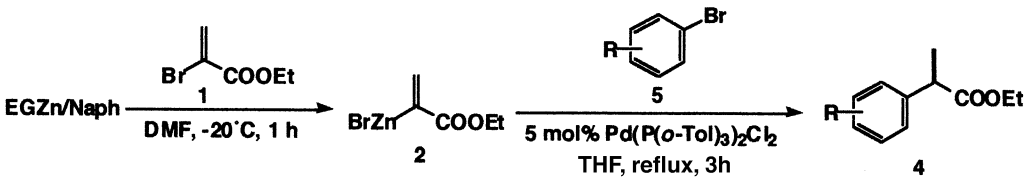
fine zinc particles with much smaller sizes than those of EGZn[6] and was dispersed in the DMF solution. Although the nature and structure of EGZn/Naph are not clear at the present stage, it was found to be very reactive towards an oxidative addition to organic bromides.

The high reactivity of EGZn/Naph was shown from the transforming reaction of ethyl 2-bromoacrylate (**1**) into the corresponding organozinc bromide **2** followed by its cross-coupling with iodobenzene (**3a**; R=H) to give ethyl 2-phenylpropenoate (**4a**; R=H) (Scheme 2). When activated zinc powder[8] or zinc–copper couple was used in this reaction, the cross-coupling product **4a** was not obtained or obtained in a very low yield. Even when EGZn was used, the product **4a** was obtained only in 19% yield. However, when EGZn/Naph was used for preparation of **2**, the product **4a** was obtained in 98% yield (Table 1).

2.2. Synthesis of ethyl 2-arylpropenoates (4) by cross-coupling of organozinc compound 2 with aryl iodides

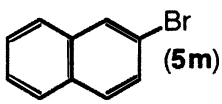
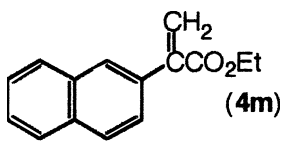
The cross-coupling of **2**, derived from ethyl 2-bromoacrylate (**1**) and EGZn/Naph, with aryl iodides was examined under various conditions. It was found that the temperature in the forming step of **2** and the kind of metal complex in the cross-coupling step are the most effective factors in this reaction. The reaction of ethyl 2-bromoacrylate (**1**) with EGZn/Naph at 80, 0, or −20°C and the following cross-coupling reaction with iodobenzene (**3a**) using 5 mol% $Pd(P(o\text{-}Tol)_3)_2Cl_2$ gave ethyl 2-phenylacrylate (**4a**) in 72, 84, or 98% yield, respectively. A palladium complex of $Pd(PPh_3)_2Cl_2$ could also be used in the same way as $Pd(P(o\text{-}Tol)_3)_2Cl_2$, but the use of $Ni(PPh_3)_2Cl_2$ gave **4a** in a low yield.

Electrochemical preparation of EGZn/Naph in DMF and the subsequent reaction with ethyl 2-bromoacrylate at −20°C for 1 h gave efficiently the corresponding organozinc bromide **2**. Subsequent one-pot reactions of a DMF solution containing **2** with various iodobenzenes (**3a**–**3i**) in the presence of 5 mol% $Pd(P(o\text{-}Tol)_3)_2Cl_2$ at 70°C for 3 h gave the corresponding cross-coupled products, ethyl 2-arylpropenoates (**4a**–**4i**), in high yields (Scheme 2). The results are summarized in Table 2. The use of iodobenzene itself



Scheme 3.

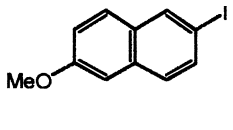
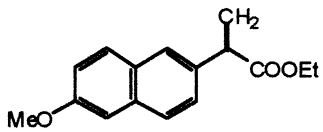
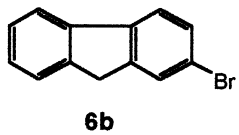
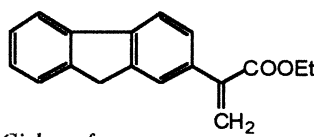
Table 3. Synthesis of ethyl 2-arylpropenoates (**4**) by palladium catalyzed cross-coupling of aryl bromides (**5**) with organozinc bromide **2**

Entry	ArBr	Product	Yield (%)[a]
1	C_6H_5Br (**5a**)	$C_6H_5C(=CH_2)CO_2Et$ (**4a**)	47
2	$4\text{-}CH_3OC_6H_4Br$ (**5b**)	$4\text{-}CH_3OC_6H_4C(=CH_2)CO_2Et$ (**4b**)	98
3	$4\text{-}CH_3C_6H_4Br$ (**5c**)	$4\text{-}CH_3C_6H_4C(=CH_2)CO_2Et$ (**4c**)	98
4	$4\text{-}NCC_6H_4Br$ (**5f**)	$4\text{-}NCC_6H_4C(=CH_2)CO_2Et$ (**4f**)	96
5	$4\text{-}CH_3COC_6H_4Br$ (**5j**)	$4\text{-}CH_3COC_6H_4C(=CH_2)CO_2Et$ (**4j**)	93
6	$4\text{-}O_2NC_6H_4Br$ (**5k**)	$4\text{-}O_2NC_6H_4C(=CH_2)CO_2Et$ (**4k**)	67
7	$4\text{-}BrC_6H_4Br$ (**5l**)	$4\text{-}BrC_6H_4C(=CH_2)CO_2Et$ (**4i**)	40
8	 (**5m**)	 (**4m**)	92

A mixture of organozinc bromide **2**, prepared from ethyl 2-bromoacrylate (**1**) (3 mmol) and EGZn/Naph (6 mmol), was reacted under reflux in THF for 3 h with aryl bromides **5** (2 mmol) and 5 mol% of $Pd(P(o\text{-}Tol)_3)_2Cl_2$.

[a] Isolated yields. The yields are based on aryl bromides **5** employed.

Table 4. Synthesis of the precursor of naproxen (**7a**) and cicloprofen (**7b**)

Entry	ArX	Product	Yield (%)[a]
1[b]	 **6a**	 *Naproxen precursor* **7a**	95
2[c]	 **6b**	 *Cicloprofen precursor* **7b**	97

[a] Isolated yields.
[b] Organozinc bromide **2** was prepared from ethyl 2-bromoacrylate (**1**) (3 mmol) and EGZn/Naph (6 mmol). Organozinc bromide **2** was reacted in DMF at 70°C for 3 h with aryl iodides **6a** (2 mmol) in the presence of 5 mol% of $Pd(P(o\text{-}Tol)_3)_2Cl_2$.
[c] Organozinc bromide **2** was reacted under reflux in THF for 3 h with aryl bromides **6b** (2 mmol) and 5 mol% of $Pd(P(o\text{-}Tol)_3)_2Cl_2$.

(**3a**) and substituted iodobenzenes carrying an electron-donating (**3b**, **3c**, or **3d**) or an electron-withdrawing group (**3f** or **3g**) gave the corresponding products **4** in almost quantitative yields. Iodobenzenes carrying *ortho*-substituents (**3e** and **3h**) gave **4e** and **4h** in lower yields, probably due to their steric hindrances. Cross-coupling of **2** with 4-bromo-iodobenzene **3i** also took place efficiently to give the product **4i** in 96% yield.

2.3. Synthesis of ethyl 2-arylpropenoates (4) by cross-coupling of organozinc compound 2 with aryl bromides

Cross-coupling reactions of organozinc bromide **2** with aryl iodides took place efficiently to give the products **4** in high yields. However, no products were obtained when aryl bromides, instead of aryl iodides, were used under these conditions. After examination of several reaction conditions, we found that the expected cross-coupling reaction took place to give **4** in high yields when THF, instead of DMF, was used as a solvent in the reaction step of **2** with aryl bromides (**5**) (Scheme 3).

Results are summarized in Table 3. Cross-coupling reactions with bromobenzenes carrying an electron-donating (**5b** and **5c**) or an electron-withdrawing groups (**5f** and **5j**) gave the corresponding cross-coupled products **4** in excellent yields. Lower yields were observed from the reaction of 4-nitro-bromobenzene (**5k**) (entry 6). In the case of 1,4-dibromobenzene (**5l**) there are two reaction sites and, therefore, the expected cross-coupling product (**4i**) was obtained in a 40% yield together with 23% of 1,4-bis(1-ethoxycarbonylvinyl)benzene. A reason of the low yield of **4a** in the reaction of bromobenzene (**5a**) is not clear at the present stage. Cross-coupling with 2-bromonaphthalene proceeded efficiently to give the corresponding product **4m** in 92% yield (entry 8).

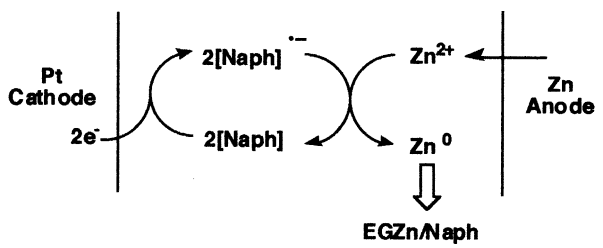
2.4. Application to a synthesis of the precursor of anti-inflammatory agents

It appeared that the cross-coupling reaction of organozinc bromide **2**, readily prepared from ethyl 2-bromoacrylate and EGZn/Naph, with aryl iodides or bromides gave ethyl 2-arylpropenoates **4** in excellent yields. Therefore we attempted to apply this cross-coupling reaction to a synthesis of the precursor of anti-inflammatory agents. Reaction of organozinc bromide **2** with 2-iodo-6-methoxy-naphthalene (**6a**) and 2-bromofluorene (**6b**) gave the precursor of naproxen (**7a**) and cicloprofen (**7b**) in 95 and 97% yield, respectively (Table 4). Enantioselective hydrogenation of **7a** and **7b** would give ethyl esters of (*S*)-naproxen and (*S*)-cicloprofen in high yields and in high enantioselectivities, since hydrogenation of α,β-unsaturated acids with Ru-(*S*)-BINAP catalyst has been reported to give (*S*)-alkanoic acids in a high enantioselective manner.[9]

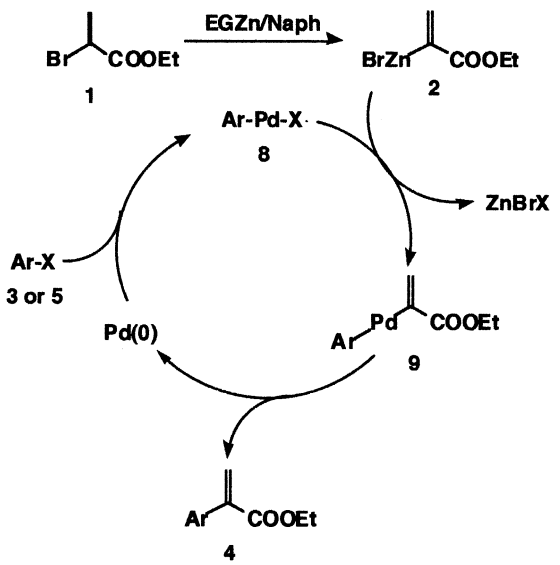
2.5. Reaction pathways

Probable reaction pathways of the preparation of EGZn/Naph are shown in Scheme 4. Electrolysis of a DMF solution with a platinum cathode and a zinc anode results in anodic dissolution of zinc metal to give zinc ions. On the other hand, at the cathode, a one-electron reduction of naphthalene molecule occurs to give radical anion of naphthalene, which was shown by appearance of the dark green color on the surface of the cathode. Reduction of zinc ion with naphthalene radical anion would give zero-valent reactive zinc (EGZn/Naph).

Probable reaction pathways of the present cross-couplings are shown in Scheme 5. Oxidative addition of Pd(0) to aryl



Scheme 4.



Scheme 5.

halides would give Ar–Pd–X (**8**), which undergoes metal exchange reaction with organozinc bromide **2** to give an intermediate **9**. Reductive elimination of **9** would give the cross-coupling product, ethyl 2-arylpropenoates **4**.

3. Conclusion

We developed a new electrochemical method for preparation of highly reactive zinc (EGZn/Naph) by using naphthalene as mediator in the electrolysis. The corresponding organozinc bromide could readily be prepared under mild conditions by the reaction of ethyl 2-bromoacrylate with EGZn/Naph. Subsequent cross-coupling reaction of the organozinc bromide with various aryl halides readily took place in the presence of a palladium catalyst to give the corresponding cross-coupled products, ethyl 2-arylpropenoates, in high yields. It was also found that this cross-coupling reaction could be applied to a synthesis of the precursor of anti-inflammatory agents such as naproxen and cicloprofen.

4. Experimental

4.1. General methods

IR spectra were recorded on a JASCO IR-810 infrared spectrometer (neat between NaCl plates). ^{1}H NMR spectra were recorded on a JEOL JNM-EX270 FT-NMR spectrometer operated at 270 MHz (solvent $CDCl_3$). Proton-decoupled ^{13}C spectra were recorded at 67.8 MHz on a JEOL JNM-EX270 spectrometer. ^{1}H and ^{13}C chemical shifts are reported in ppm (δ) using $SiMe_4$ as an internal standard. High and low resolution mass spectra were determined with a JEOL JMS-AX500 or JEOL JMS-SX102A spectrometer. Thin-layer chromatography and column chromatography were carried out on a Merck Kieselgel 60 PF_{254}.

4.2. Solvent and reagents

Commercially available anhydrous *N*,*N*-dimethylformamide (DMF) and tetrahydrofuran (THF) packed under a nitrogen atmosphere (Kanto Chemical) were used without further purification. Tetraethylammonium perchlorate was prepared according to the previous reported method.[6] The zinc metal plate (Nilaco) is commercially available in more than 99.9% purities, and was washed with 2N HCl, methanol, acetone and dried before electrolysis. Commercially available naphthalene (Junsei Chemical, 99%) was used after recrystallization from methanol. Most of aryl iodides and aryl bromides are commercially available and they were purified by distillation prior to use. Ethyl 2-bromoacrylate[10] and 4-iodoanisole[11] were prepared according to the procedure reported in the literatures. 2-Iodo-6-methoxynaphthalene and 4-iodobenzonitrile was prepared from the corresponding bromide according to the reported method.[12]

4.2.1. Ethyl 2-bromoacrylate (1).[10] 82%; bp 80°C/69 mm Hg; IR (neat) 1725, 1605, 1259, 1102 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.96 (1H, d, J=1.7 Hz), 6.27 (1H, d, J=1.7 Hz), 4.29 (2H, q, J=7.3 Hz), 1.34 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 161.72, 130.26, 121.47, 62.57, 13.93; EIMS *m*/*z* (relative intensity) 180 (18), 178 (18), 150 (19), 133 (40), 105 (49), 99 (65), 45 (100); HRMS Calcd for $C_5H_7BrO_2$ *m*/*z* 177.9629. Found *m*/*z* 177.9622.

4.2.2. 4-Iodoanisole (3b).[11] 55%; mp 51–52°C (lit:[11] 52°C); ^{1}H NMR ($CDCl_3$) δ 7.56 (2H, dd, J=2.3, 6.9 Hz), 6.68 (2H, dd, J=2.3, 6.9 Hz), 3.78 (3H, s).

4.2.3. 4-Iodobenzonitrile (3f). 70%; IR (nujol) 2226, 1579, 1475, 1393 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.85 (2H, dd, J=1.7, 6.6 Hz), 7.37 (2H, dd, J=1.7, 6.6 Hz).

4.2.4. Methyl 4-iodobenzoate (3g).[13] A mixture of 4-iodobenzoic acid (2.48 g, 10 mmol), chlorotrimethylsilane (3.18 ml, 25 mmol), methanol (53 ml), and THF (17.4 ml) was stirred for 36 h at room temperature. Extraction of the reaction mixture was carried out with dichloromethane (30 ml×3). After evaporation of dichloromethane, the crude product was recrystallized from ether and ethanol. 95%; IR (nujol) 1716, 1586, 1454, 1378 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82–7.79 (2H, dd, J=2.0, 8.6 Hz), 7.75–7.72 (2H, dd, J=2.0, 8.6 Hz), 3.91 (3H, s).

4.2.5. Methyl 2-iodobenzoate (3h). Esterification of 2-iodobenzoic acid according to the preparation of **3g** afforded the crude product. Distillation of the crude product gave a colorless oil.[13] 49%; bp 144°C/20 mm Hg; ^{1}H NMR ($CDCl_3$) δ 8.00 (1H, d, J=7.6 Hz), 7.81 (1H, d, J=7.6 Hz), 7.41 (1H, t, J=7.6 Hz), 7.16 (1H, t, J=7.6 Hz), 3.94 (3H, s).

4.2.6. 2-Iodo-6-methoxynaphthalene (6a).[12] 38%; mp 145–146°C (lit.[12] mp 146–147°C); ^{1}H NMR ($CDCl_3$) δ 8.14 (s, 1H), 7.68–7.46 (m, 3H), 7.25–7.07 (m, 2H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 157.93, 136.19, 134.68, 133.30, 130.55, 128.34, 128.30, 119.52, 105.63, 88.05, 55.28.

4.3. Preparation of electrogenerated highly reactive zinc (EGZn/Naph)

A normal one-compartment cell equipped with a magnetic stirrer and a serum cap was used. Electrogenerated highly reactive EGZn/Naph (6 mmol) was prepared by the electrolysis of a DMF solution (10 ml) containing 0.1 M Et_4NClO_4 (230 mg) and naphthalene (12 mmol) in a one-compartment cell fitted with a platinum plate cathode (2×2 cm^2) and a zinc plate anode (2×2 cm^2). Electrolysis was carried out at −10°C at a constant current of 60 mA/cm^2 under nitrogen atmosphere. The quantity of electricity passed was 0.012 F, which corresponded to 2 F per mol of zinc metal. The amount of EGZn/Naph was calculated from the weight of dissolved zinc anode metal. A solution containing EGZn/Naph was directly used for the preparation of organozinc compounds after the zinc anode was removed from the electrolysis cell.

4.4. General procedure for cross-coupling reaction using EGZn/Naph

Cross-coupling using aryl iodides. To the DMF solution containing EGZn/Naph was added ethyl 2-bromoacrylate (**1**) (3 mmol) and the mixture was stirred at −20°C under nitrogen atmosphere for 1 h. DMF solution (5 ml) of aryl iodide (2 mmol) and $Pd(P(o\text{-}Tol)_3)_2Cl_2$ (0.11 mmol) was added, and the reaction mixture was stirred at 70°C for 3 h. The resulting mixture was quenched with HCl solution and filtered. The filtrate was extracted with diethyl ether (50 ml×3) and the combined organic layers were washed with water (100 ml×3), saturated $Na_2S_2O_3$ solution (100 ml×1) and saturated NaCl solution (100 ml×1) and dried over $MgSO_4$. After evaporation of diethyl ether, the crude product was purified by column chromatography on silica gel with ethyl acetate–hexane (1:5) to give ethyl 2-arylpropenoate **4**.

Cross-coupling using aryl bromides: To the DMF solution containing EGZn/Naph was added ethyl 2-bromoacrylate (**1**) (3 mmol) and the mixture was stirred at −20°C under nitrogen atmosphere for 1 h. The reaction mixture was added to a THF solution (50 ml) of aryl bromide (2 mmol) and $Pd(P(o\text{-}Tol)_3)_2Cl_2$ (0.11 mmol). Similar work-up and purification as those of the cross-coupling using aryl iodides gave ethyl 2-arylpropenoate **4**.

4.4.1. Ethyl 2-phenylpropenoate (4a). 98%; IR (neat) 1724, 1602, 1497, 1199, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44–7.33 (5H, m), 6.35 (1H, d, J=1.3 Hz), 5.89 (1H, d, J=1.3 Hz), 4.29 (2H, q, J=7.3 Hz), 1.33 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.07, 141.08, 136.28, 127.78, 127.60, 127.55, 125.80, 60.47, 13.66; EIMS *m/z* (relative intensity) 176 (63), 131 (87), 103 (100), 77 (37); HRMS Calcd for $C_{11}H_{12}O_2$ *m/z* 176.0837. Found *m/z* 176.0848; Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.79; H, 6.96.

4.4.2. Ethyl 2-(4-methoxyphenyl)propenoate (4b). ^1H NMR ($CDCl_3$) δ 7.37 (2H, dd, J=2.0, 6.6 Hz), 6.89 (2H, dd, J=2.0, 6.6 Hz), 6.25 (1H, d, J=1.3 Hz), 5.83 (1H, d, J=1.3 Hz), 4.29 (2H, q, J=7.3 Hz), 3.82 (3H, s), 1.33 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.08, 159.55, 140.88, 129.45, 129.20, 124.92, 113.48, 61.03, 55.26, 14.20; IR (neat) 1723, 1611, 1195, 1177, 1033, 836 cm^{-1}; EIMS *m/z* (relative intensity) 206 (47), 162 (15), 133 (100), 118 (12), 90 (14), 77 (11), 63 (10); HRMS Calcd for $C_{12}H_{14}O_3$ *m/z* 206.0943. Found *m/z* 206.0958; Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.72; H, 6.88.

4.4.3. Ethyl 2-(4-tolyl)propenoate (4c). ^1H NMR ($CDCl_3$) δ 7.32 (2H, dd, J=2.0, 6.6 Hz), 7.16 (2H, dd, J=2.0, 6.6 Hz), 6.29 (1H, d, J=1.0 Hz), 5.85 (1H, d, J=1.0 Hz), 4.29 (2H, q, J=7.3 Hz), 2.36 (3H, s), 1.33 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.88, 141.33, 137.86, 133.80, 128.70, 128.05, 125.59, 60.94, 21.08, 14.11; IR (neat) 1722, 1613, 1198, 1182, 1023, 825 cm^{-1}; EIMS *m/z* (relative intensity) 190 (64), 146 (30), 117 (100), 115 (36), 91 (27); HRMS Calcd for $C_{12}H_{14}O_2$ *m/z* 190.0994. Found *m/z* 190.0981; Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.90; H, 7.28.

4.4.4. Ethyl 2-(3-tolyl)propenoate (4d). ^1H NMR ($CDCl_3$) δ 7.24 (3H, m), 7.16 (1H, s), 6.32 (1H, d, J=1.3 Hz), 5.87 (1H, d, J=1.3 Hz), 4.29 (2H, q, J=7.3 Hz), 2.37 (3H, s), 1.33 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.95, 141.69, 137.68, 136.73, 128.96, 128.89, 127.99, 126.22, 125.37, 61.08, 21.44, 14.23; IR (neat) 1721, 1606, 1226, 1174, 1026, 792, 715 cm^{-1}; EIMS *m/z* (relative intensity) 190 (69), 146 (31), 117 (100), 115 (42), 91 (24); HRMS Calcd for $C_{12}H_{14}O_2$ *m/z* 190.0994. Found *m/z* 190.0979; Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.63; H, 7.62.

4.4.5. Ethyl 2-(2-tolyl)propenoate (4e). ^1H NMR ($CDCl_3$) δ 7.18 (4H, m), 6.50 (1H, d, J=1.7 Hz), 5.70 (1H, d, J=1.7 Hz), 4.24 (2H, q, J=7.3 Hz), 2.21 (3H, s), 1.27 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.66, 142.12, 137.34, 136.10, 129.83, 129.50, 128.28, 128.08, 125.62, 61.06, 19.84, 14.20; IR (neat) 1721, 1624, 1208, 1187, 1026, 746 cm^{-1}; EIMS *m/z* (relative intensity) 190 (34), 161 (29), 133 (40), 117 (83), 115 (100), 91 (29); HRMS Calcd for $C_{12}H_{14}O_2$ *m/z* 190.0994. Found *m/z* 190.0993; Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.93; H, 7.30.

4.4.6. Ethyl 2-(4-cyanophenyl)propenoate (4f). ^1H NMR ($CDCl_3$) δ 7.65 (2H, dd, J=2.0, 6.6 Hz), 7.54 (2H, dd, J=2.0, 6.6 Hz), 6.50 (1H, s), 5.98 (1H, s), 4.30 (2H, q, J=7.3 Hz), 1.34 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 165.62, 141.26, 140.05, 131.84, 129.08, 128.86, 118.63, 111.79, 61.46, 14.13; IR (neat) 2228, 1723, 1608, 1198, 1179, 848 cm^{-1}; EIMS *m/z* (relative intensity) 201 (27), 173 (20), 157 (23), 128 (100), 101 (24), 77 (15), 51 (13); HRMS Calcd for $C_{12}H_{11}O_2N$ *m/z* 201.0790. Found *m/z* 201.0773; Anal. Calcd for $C_{12}H_{11}O_2N$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.66; H, 5.72; N, 6.33.

4.4.7. Ethyl 2-(4-methoxycarbonylphenyl)propenoate (4g). ^1H NMR ($CDCl_3$) δ 8.02 (2H, dd, J=2.0, 6.9 Hz), 7.49 (2H, dd, J=2.0, 6.9 Hz), 6.43 (1H, d, J=1.0 Hz), 5.95 (1H, d, J=1.0 Hz), 4.29 (2H, q, J=7.3 Hz), 3.90 (3H, s), 1.32 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.49, 165.91, 141.02, 140.54, 129.45, 129.13, 128.16, 127.75, 61.06, 51.88, 13.95; IR (neat) 1720, 1610, 1194, 869 cm^{-1}; EIMS *m/z* (relative intensity) 234 (68), 203 (67), 190 (44), 161 (100), 102 (46), 76 (17), 59 (16); HRMS Calcd for $C_{13}H_{14}O_4$ *m/z* 234.0892. Found *m/z* 234.0890; Anal.

Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.55; H, 6.19.

4.4.8. Ethyl 2-(2-methoxycarbonylphenyl)propenoate (4h). ^{1}H NMR ($CDCl_3$) δ 7.99 (1H, dd, J=1.3, 7.6 Hz), 7.56–7.39 (2H, dt, J=1.3, 7.6 Hz), 7.30 (1H, dd, J=1.3, 7.6 Hz), 6.42 (1H, d, J=1.3 Hz), 5.73 (1H, d, J=1.3 Hz), 4.20 (2H, q, J=7.3 Hz), 3.82 (3H, s), 1.24 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.24, 166.15, 143.02, 138.89, 132.27, 130.96, 130.08, 129.45, 128.12, 125.43, 60.83, 51.88, 14.02; IR (neat) 1722, 1624, 1195, 773 cm^{-1}; EIMS *m/z* (relative intensity) 234 (47), 175 (25), 161 (100), 129 (83), 101 (29), 76 (23), 51 (15); HRMS Calcd for $C_{13}H_{14}O_4$ *m/z* 234.0892. Found *m/z* 234.0890; Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.40; H, 5.97.

4.4.9. Ethyl 2-(4-bromophenyl)propenoate (4i). ^{1}H NMR ($CDCl_3$) δ 7.41 (2H, dd, J=2.0, 6.6 Hz), 7.30 (2H, dd, J=2.0, 6.6 Hz), 6.38 (1H, d, J=1.0 Hz), 5.89 (1H, d, J=1.0 Hz), 4.29 (2H, q, J=7.3 Hz), 1.33 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.20, 140.40, 135.58, 131.14, 129.92, 126.99, 122.28, 61.19, 14.13; IR (neat) 1721, 1617, 1200, 834 cm^{-1}; EIMS *m/z* (relative intensity) 256 (21), 254 (20), 183 (100), 155 (24), 102 (67), 76 (40), 50 (26); HRMS Calcd for $C_{11}H_{11}O_2Br$ *m/z* 253.9942. Found *m/z* 253.9927; Anal. Calcd for $C_{11}H_{11}O_2Br$: C, 51.79; H, 4.35; Br, 31.32. Found: C, 51.82; H, 4.39; Br, 31.07.

4.4.10. Ethyl 2-(4-acetylphenyl)propenoate (4j). ^{1}H NMR ($CDCl_3$) δ 7.95 (2H, dd, J=2.0, 6.6 Hz), 7.52 (2H, dd, J=2.0, 6.6 Hz), 6.45 (1H, d, J=1.0 Hz), 5.97 (1H, d, J=1.0 Hz), 4.30 (2H, q, J=7.3 Hz), 2.62 (3H, s), 1.34 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 197.57, 166.04, 141.31, 140.61, 136.44, 128.48, 128.03, 127.98, 61.24, 26.56, 14.09; IR (neat) 1719, 1689, 1607, 1201, 847 cm^{-1}; EIMS *m/z* (relative intensity) 218 (29), 203 (100), 175 (24), 145 (12), 102 (10); HRMS Calcd for $C_{13}H_{14}O_3$ *m/z* 218.0943. Found *m/z* 218.0923; Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.38; H, 6.54.

4.4.11. Ethyl 2-(4-nitrophenyl)propenoate (4k). ^{1}H NMR ($CDCl_3$) δ 8.22 (2H, dd, J=2.0, 6.9 Hz), 7.60 (2H, dd, J=2.0, 6.9 Hz), 6.54 (1H, s), 6.03 (1H, s), 4.32 (2H, q, J=7.3 Hz), 1.35 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 165.53, 147.49, 143.18, 139.78, 129.40, 129.33, 123.29, 61.55, 14.13; IR (neat) 1721, 1599, 1520, 1198, 858, 707 cm^{-1}; EIMS *m/z* (relative intensity) 221 (86), 193 (78), 177 (68), 148 (100), 102 (54), 76 (27); HRMS Calcd for $C_{11}H_{11}NO_4$ *m/z* 221.0688. Found *m/z* 221.0676; Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.87; H, 4.98; N, 6.11.

4.4.12. Ethyl 2-(2-naphthyl)propenoate (4m). ^{1}H NMR ($CDCl_3$) δ 7.91 (1H, d, J=1.3 Hz), 7.84 (3H, m), 7.51 (3H, m), 6.43 (1H, d, J=1.3 Hz), 6.01 (1H, d, J=1.3 Hz), 4.33 (2H, q, J=7.3 Hz), 1.35 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.31, 141.98, 134.65, 133.51, 133.41, 128.70, 128.21, 127.98, 127.89, 127.19, 126.72, 126.61, 126.58, 61.60, 14.67; IR (neat) 1721, 1613, 820, 751 cm^{-1}; EIMS *m/z* (relative intensity) 226 (85), 153 (100), 127 (12); HRMS Calcd for $C_{15}H_{14}O_2$ *m/z* 226.0994. Found *m/z* 226.0988; Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.79; H, 6.37.

4.4.13. Ethyl 2-(6-methoxynaphthalen-2-yl)propenoate (7a). ^{1}H NMR ($CDCl_3$) δ 7.84 (1H, d, J=1.7 Hz), 7.74 (2H, t, J=8.3 Hz), 7.71 (1H, d, J=8.3 Hz), 7.50 (1H, dd, J=1.7, 8.3 Hz), 7.15 (1H, dd, J=2.0, 8.3 Hz), 7.13 (1H, s), 6.38 (1H, d, J=1.0 Hz), 5.98 (1H, d, J=1.0 Hz), 4.32 (2H, q, J=7.3 Hz), 3.91 (3H, s), 1.35 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.72, 157.81, 141.22, 134.00, 131.70, 129.52, 128.27, 126.99, 126.34, 126.16, 125.61, 118.78, 105.27, 60.83, 54.92, 13.95; IR (neat) 1711, 1605, 1459, 1262, 1196, 1030, 859, 829, 813 cm^{-1}; EIMS *m/z* (relative intensity) 256 (100), 228 (14), 183 (71), 168 (15), 139 (19); HRMS Calcd for $C_{16}H_{16}O_3$ *m/z* 256.1099. Found *m/z* 256.1097; Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.24; H, 6.39.

4.4.14. Ethyl 2-(fluoren-2-yl)propenoate (7b). ^{1}H NMR ($CDCl_3$) δ 7.80–7.62 (2H, m), 7.62 (1H, d, J=0.7 Hz), 7.53 (1H, d, J=0.7 Hz), 7.46–7.31 (3H, m), 6.35 (1H, d, J=1.3 Hz), 5.95 (1H, d, J=1.3 Hz), 4.32 (2H, q, J=7.3 Hz), 3.92 (2H, s), 1.35 (3H, t, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.08, 143.52, 143.31, 143.02, 141.74, 141.22, 135.20, 127.04, 126.85, 126.76, 125.89, 125.01, 124.91, 120.02, 119.43, 61.12, 36.88, 14.22; IR (neat) 1720, 1610, 1457, 1209, 738 cm^{-1}; EIMS *m/z* (relative intensity) 264 (85), 235 (22), 190 (100), 165 (16), 96 (7), 83 (6); HRMS Calcd for $C_{18}H_{16}O_2$ *m/z* 264.1150. Found *m/z* 264.1162; Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.84; H, 5.92.

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