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PREPARATION OF HIGHLY REACTIVE ELECTROGENERATED ZINC

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Abstract. Highly reactive electrogenerated zinc metal (EGZn/Naph) was readily prepared by the electrolysis of an *N*,*N*-dimethylformamide (DMF) solution containing naphthalene and a supporting electrolyte in a one-compartment cell fitted with a platinum cathode and a zinc anode. This EGZn/Naph is an aggregation of very fine particles which are much smaller in size than commercial zinc metal or the usual electrogenerated zinc (EGZn). The reactivity of this highly reactive zinc was elucidated by the efficient transformation of bromoalkane into the corresponding organozinc bromide, which cannot be achieved by the use of both usual zinc or EGZn metals. Subsequent cross-coupling reaction of the organozinc bromide with iodobenzene readily took place in the presence of a palladium catalyst to give the corresponding cross-coupled product, ethyl 4-phenylbutanoate in 96% yield.

Keywords: Electrolysis, reactive zinc, naphthalene, bromoalkanes, organozinc compound.

Abstrak. Logam zink berkereaktifan tinggi yang dihasilkan secara elektrolisis (EGZn/Naph) disediakan dengan mudah dalam larutan *N,N*-dimetilformamida (DMF) yang mengandungi naftalena dan elektrolit penyokong di dalam sebuah sel yang telah dipasang siap dengan katod platinum dan anod zink. EGZn/Naph ini adalah agregat zarah sangat halus yang lebih kecil berbanding logam zink komersial ataupun zink yang dihasilkan secara elektrolisis biasa (EGZn). Kereaktifan zink berkereaktifan tinggi ini dibuktikan dengan transformasi bromoalkana kepada organozink bromida yang berkesan, yang tidak boleh dicapai dengan menggunakan zink biasa mahupun logam EGZn. Reaksi ganding silang organozink bromida ini dengan iodobenzena mudah berlaku dalam kehadiran mangkin paladium untuk menghasilkan produk terganding silang, etil 4-fenilbutanoata sebanyak 96%.

Kata kunci: Elektrolisis, reaktif zink, naftalena, bromoalkana, organozink kompoun.

1.0 INTRODUCTION

Organozinc compounds are very useful organometallic compounds for the formation of carbon-carbon bonds [1]. Organozinc halides can usually be prepared by direct insertion of zinc metal into organic halides [2-4], but commercially available zinc metal

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is generally poorly reactive. Therefore, activation of the metal is necessary for the 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.

On the other hand, an electrochemical method is one of the useful methods to induce the efficient carbon-carbon bond formation [5,6]. In an electrochemical reaction, an electron is used as a clean reagent, and the reaction takes place efficiently and selectively under mild conditions to give desired products in high yields. Therefore, the electrochemical reaction may also be useful for environmentally benign organic synthesis, which will be very important in this 21st century [7].

For the development of efficient carbon-carbon bond formations, the electrochemical reductive methods using a reactive-metal anode have often been used [8]. Electrode materials have played important roles in such electrochemical reactions [9,10]. In this method, electrolysis can be carried out without diaphragm that can be easily applied to large-scaled synthesis. Furthermore, oxidation of the reactive species generated by cathodic reduction is restricted due to a preferential dissolution of anode metal, and the formation of side-reaction products is thus suppressed.

Previously, the author reported a new method for the preparation of reactive zinc by an electrolysis of a DMF solution containing 0.1 M tetraethyl ammonium perchlorate (TEAP) with a platinum cathode and a zinc anode (Figure 1). The zinc thus prepared (EGZn) was an aggregation of very fine, crystalline zinc particles with a large specific area [11]. This EGZn was very reactive and was successfully used in isoprenylation [12] and allylation [11,13] of aldehydes, and ketones. The author also reported that the corresponding organozinc compounds could be readily prepared under mild conditions by the reaction of EGZn with functionalized alkyl iodides and the cross-coupling reaction of the organozinc compounds with various aryl iodides, which readily took place in the presence of a palladium catalyst, to give the corresponding products in high yields (Figure 2) [14].

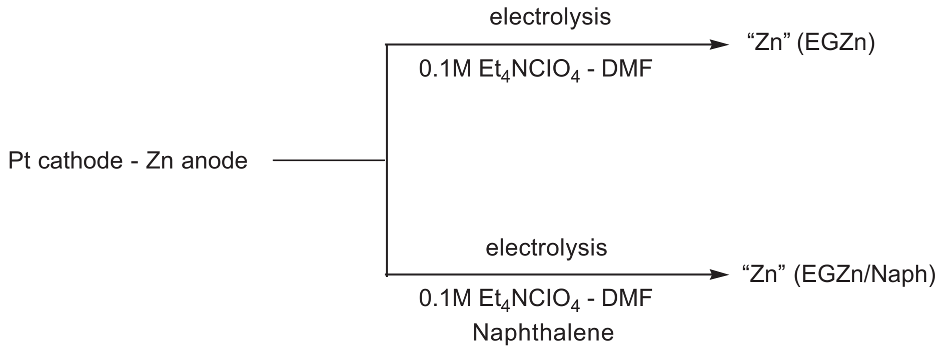


Figure 1 Preparation of reactive zinc metals by using electrochemical method

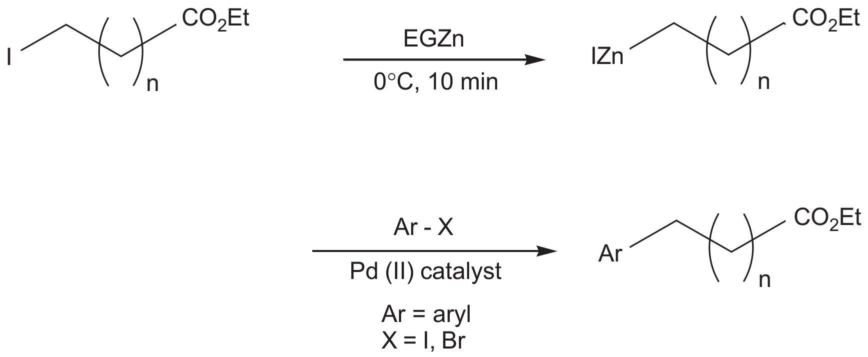


Figure 2 Preparation of organozinc iodides by reactive zinc metal (EGZn) and its subsequent cross-coupling reaction

However, organozinc bromides were rarely obtained or were obtained in low yields from the corresponding organic bromides, even if the reactive EGZn was used. Therefore, a new method for the preparation of a much more highly reactive zinc was desired in order to pursue a more efficient transformation of organic bromides into the corresponding organozinc reagents. As a result, we have developed a new electrochemical method for the preparation of a more highly reactive zinc (EGZn/Naph) by using naphthalene as a mediator. In this paper, the authors describe the preparation and reactivity of this highly reactive zinc.

2.0 MATERIAL AND METHODOLOGY

2.1 General Methods

Gas chromatographic analysis was carried out with a Hitachi G-5000 using a capillary column (OV-17, 20m). 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 (270 MHz) and JNM-LA400FT NMR (400 MHz). ^{1}H chemical shift is reported in ppm (δ) using tetramethylsilane as an internal standard. High and low resolution mass spectra were determined with a JEOL JMS-AX500 or JEOL JMS-SX102A spectrometer. Products were isolated by column chromatography (Merck Kieselgel 60 PF_{254}).

2.2 Solvent and Reagents

Commercially available anhydrous *N,N*-dimethylformamide (DMF) packed under a nitrogen atmosphere (Kanto Chemical) was used without further purification. Tetraethylammonium perchlorate was prepared according to the previous reported method [14]. The zinc metal plate (Nilaco) is commercially available in more than 99.9% purity, and was washed with 2N HCl, methanol, acetone and dried before electrolysis. Commercially available naphthalene (Junsei Chemical, 99%) was used after recrystallization from methanol. Ethyl 4-bromobutanoate and iodobenzene are commercially available and they were purified by distillation, prior to use.

2.3 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 zinc EGZn/Naph (6 mmol) was prepared by the electrolysis of a DMF solution (10 ml) containing 0.1M 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^oC at a constant current of 60 mA/cm^2 (electricity 2.0 F/mol) under nitrogen atmosphere. A solution containing EGZn/Naph was directly used for the preparation of organozinc compounds after the zinc anode was removed from the electrolysis cell.

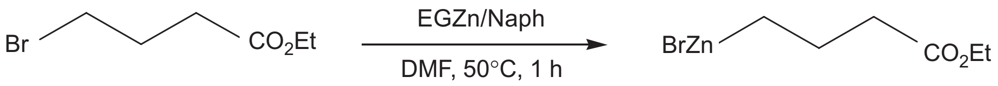
2.4 Procedure for Cross-coupling Reaction Using EGZn/Naph

DMF solution containing EGZn/Naph was added ethyl 4-bromobutanoate (**1**) (5 mmol) and the mixture was stirred at 50^oC under nitrogen atmosphere for 1 hour. DMF solution (5 ml) of iodobenzene (**3**) (4 mmol) and 5 mol % $Pd(P(\textit{o}\text{-}Tol)_3)_2Cl_2$ (0.11 mmol) was added, and the reaction mixture was stirred at 70^oC for 3 hour. 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 $Na_2S_2O_3$ (100 ml × 1) and NaCl (100 ml × 1), solution 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 4-phenylbutanoate (**4**) bp 97°C/4 mmHg. IR (neat) 1734, 1498, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.23 (5H, m), 4.12 (2H, q, $J = 7.26$ Hz), 2.65 (2H, t, $J = 7.59$ Hz), 2.32 (2H, t, $J = 7.59$ Hz), 1.96 (2H, quin, $J = 7.59$ Hz), 1.25 (3H, t, $J = 7.26$ Hz). EIMS m/z (relative intensity) 192 (60), 147 (76), 117 (18), 104 (100), 91 (85), 88 (79), 70 (25). HRMS Calcd for $C_{12}H_{16}O_2$ m/z 192.1124. Found m/z 192.1137. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.75; H, 8.45.

3.0 RESULTS AND DISCUSSION

3.1 Electrochemical Preparation of Highly Reactive Electrogenerated Zinc (EGZn/Naph)

The transformation of ethyl 4-bromobutanoate into the corresponding organozinc compound proceeded only in a 37% yield when EGZn was used, and the use of commercially available zinc powder (Rare metallic) in DMF containing naphthalene gave no organozinc compound at all. Therefore, a new electrochemical method must be developed in order to prepare a more highly reactive zinc. As a result of several attempts, electrolysis of a DMF solution of 0.1M TEAP in the presence of naphthalene as mediator gave EGZn/Naph higher reactivity, which could transform ethyl 4-bromobutanoate into the corresponding organozinc compound in almost quantitative yield (> 95%) (Figure 3). When EGZn was used in the presence of naphthalene after the electrolysis, organozinc compound was also obtained in 37% yield. These results showed that the use of EGZn with the addition of naphthalene was not effective in terms of reactivity and the presence of naphthalene molecules in the electrochemical reduction step was needed for the preparation of more highly reactive zinc.



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2 (> 95%)

Figure 3 Transformation of ethyl 4-bromobutanoate to the corresponding organozinc compound by EGZn/Naph

The formation of organozinc compound was monitored by gas chromatograph and determined by the disappearance of ethyl 4-bromobutanoate and by the formation of protonated alkane after hydrolysis with dilute HCl solution.

Various parameters such as temperature, current density, amount of naphthalene, and type of solvents had been studied in order to find the optimum conditions for the reaction of ethyl 4-bromobutanoate with EGZn/Naph. As a result, EGZn/Naph (6 mmol) was readily prepared by the electrolysis of a DMF (10 ml) solution containing naphthalene (2 equivalents) and 0.1M Et_4NClO_4 in a one compartment cell fitted with a platinum cathode (2×2 cm^2) and a zinc plate anode (2×2 cm^2). Electrolysis at –10°C at a constant current of 60 mA/cm^2 in a nitrogen atmosphere was found to produce highly reactive zinc.

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 colour which appeared on the surface of the cathode [15]. 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 (Figure 1).

The EGZn/Naph was an aggregation of very fine zinc particles which were much smaller than those of EGZn [8] and was dispersed in the DMF solution. Although the nature and structure of EGZn/Naph were 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 transformation reaction of ethyl 4-bromobutanoate (**1**) into the corresponding organozinc bromide (**2**) followed by its cross-coupling with iodobenzene (**3**), to give ethyl 4-phenylbutanoate (**4**) in 96% yield (Figure 4).

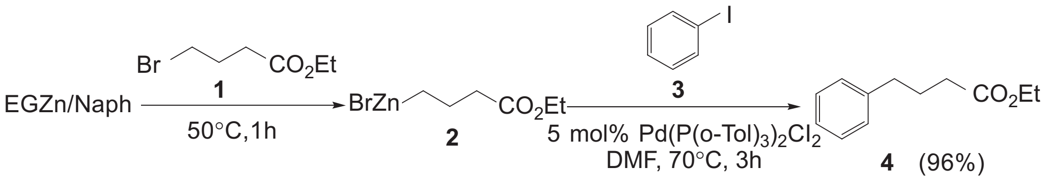

Figure 4 Transformation of ethyl 4-bromobutanoate (**1**) to the corresponding organozinc compound (**2**) and its subsequent cross-coupling reaction with iodobenzene (**3**)

3.2 Reaction Pathways

According to Lund [5] and our previous studies [14], probable reaction pathways of the preparation of EGZn/Naph are shown in Figure 5. 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 the appearance of dark green colour on the surface of the cathode. Reduction of zinc ion with naphthalene radical anion would give zero-valent reactive zinc (EGZn/Naph).

The probable reaction pathway of the present cross-coupling is shown in Figure 6 [14]. Oxidative addition of Pd(0) to iodobenzene would give Ph-Pd-I (**5**), which undergoes metal exchange reaction with organozinc bromide (**2**) to give an intermediate (**6**). Reductive elimination of (**6**) would give the cross-coupling product, ethyl 4-phenylbutanoate (**4**).

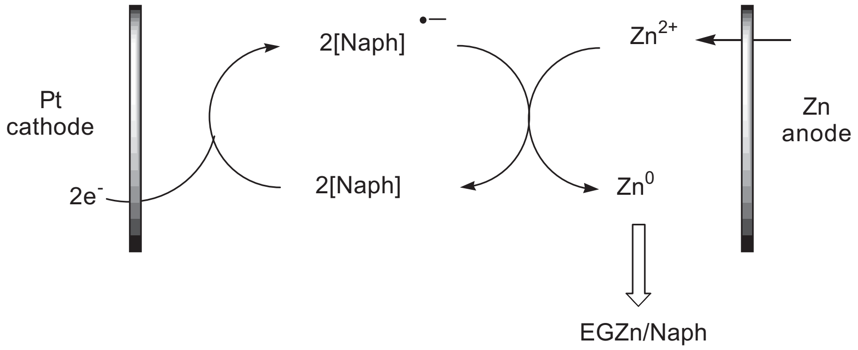

Figure 5 Probable reaction pathways of EGZn/Naph

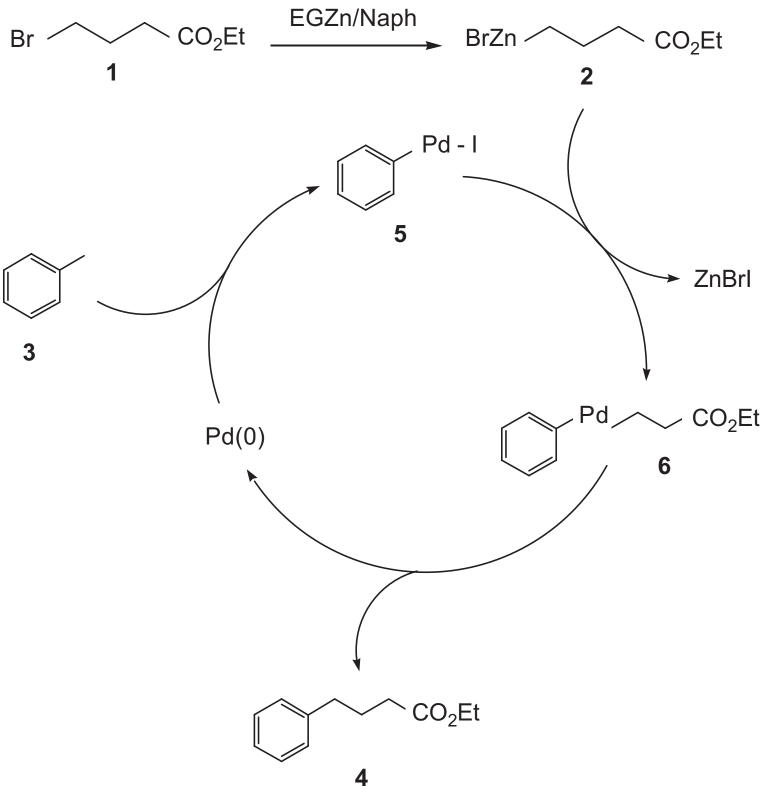

Figure 6 Probable reaction pathways of cross-coupling reaction

4.0 CONCLUSION

A new electrochemical method for the preparation of highly reactive zinc (EGZn/Naph) has been developed by using naphthalene as a mediator in the electrolysis. The corresponding organozinc bromide could readily be prepared under mild conditions by the reaction of ethyl 4-bromobutanoate with EGZn/Naph. Subsequent cross-coupling reaction of the organozinc bromide with iodobenzene readily took place in the presence of palladium catalyst to give the corresponding cross-coupled product, ethyl 4-phenylbutanoate in 96% yield.

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