

Efficient Cross-coupling Reaction of Functionalized Alkyl Bromides with Aryl Halides by Using Electrochemical Method

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Abstract

Highly reactive zinc metal was readily 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 (EGZn/Naph) was used for transformation of bromoalkanes into the corresponding organozinc bromides, which can not be achieved by the use of usual zinc metals. Reaction of the organozinc compounds thus prepared with various aryl iodides in the presence of 5 mol% of palladium catalyst gave the corresponding cross-coupling products in high yields. Arylzinc iodides were also prepared by the use of EGZn/Naph, and they were reacted with other aryl iodides to give the corresponding cross-coupled biaryl in good yields.

Keywords: electrolysis, reactive zinc, alkylbromide, cross-coupling, palladium catalyst

Introduction

We have already reported a new method for preparation of reactive zinc (EGZn) by electrolysis [1-3] and its use in facile isoprenylation [1] and allylation [2,3] as well as cross-coupling of functionalized alkyl iodides with aryl halides [4]. Recently, we further developed a new electrochemical method for preparation of more highly reactive zinc (EGZn/Naph) by using naphthalene as a mediator. EGZn/Naph could readily be prepared by electrolysis of a DMF solution containing 0.1M Et₄NClO₄ and naphthalene using a platinum cathode and a zinc anode. Although the true nature and structure of this EGZn/Naph are not clear at the present stage, it was found that this zinc was very reactive toward an oxidative addition to organic bromide such as ethyl 4-bromobutanoate. Commercial zinc metals, Zn-Cu couple and EGZn were not reactive in such oxidative addition.

Usually, organozinc compounds can be prepared by direct reaction of organic halides with activated zinc [5] or by transmetalation of the corresponding organolithium or Grignard reagents with zinc halides [6]. However, an activation of zinc metal by these methods requires high temperature, long reaction times, the use of hazardous lithium metal, or vigorous stirring during the reaction. Contrary to these methods, the use of the electrogenerated highly reactive zinc (EGZn/Naph) is environmentally benign and economical since the used naphthalene can be isolated after the reaction and reused for further preparation of EGZn/Naph.

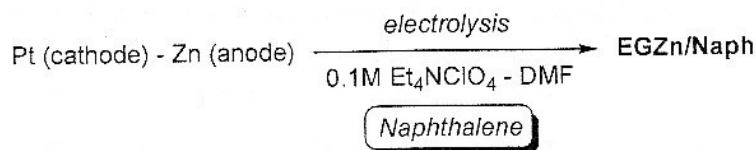
On the other hand, cross-coupling reactions of organozinc compounds with a variety of organic electrophiles using transition metal catalysts provide efficient methods for chemo- and regioselective formation of carbon-carbon bonds [6]. For example, organozinc compounds derived from alkyl, aryl and vinyl halides using Rieke zinc underwent a variety of cross-coupling reactions with acid chlorides, α,β -unsaturated ketones, allylic halides and aryl or vinyl halides [5]. Although these results are of synthetic interest, the use of lithium metal for preparation of Rieke zinc might be one of disadvantages from safety problem.

After several attempts, the authors have found that not only ethyl 4-bromobutanoate but also various alkyl bromides could be readily converted under mild conditions within a short reaction time to the corresponding organozinc compounds by using EGZn/Naph. Therefore, in this paper the authors describe the efficient cross-coupling reactions of organozinc compounds derived from functionalized alkyl bromides with various aryl iodides in a one-pot DMF solution in the presence of palladium catalyst which gave the corresponding cross-coupled products in high yield.

Result and Discussion

Electrochemical preparation of highly reactive zinc (EGZn/Naph)

Electrogenerated highly reactive zinc (EGZn/Naph) was readily prepared by electrolysis of a DMF solution containing 0.1M Et_4NClO_4 in the presence of naphthalene as a mediator in a one-compartment cell fitted with a platinum plate cathode ($2 \times 2 \text{ cm}^2$) and a zinc plate anode ($2 \times 2 \text{ cm}^2$).

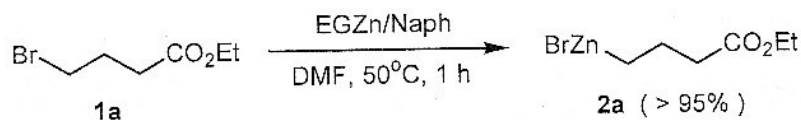


Scheme 1

Electrolysis at -10°C at a constant current of 60 mA/cm^2 in a nitrogen atmosphere was found to give highly reactive zinc metal, EGZn/Naph (Scheme 1).

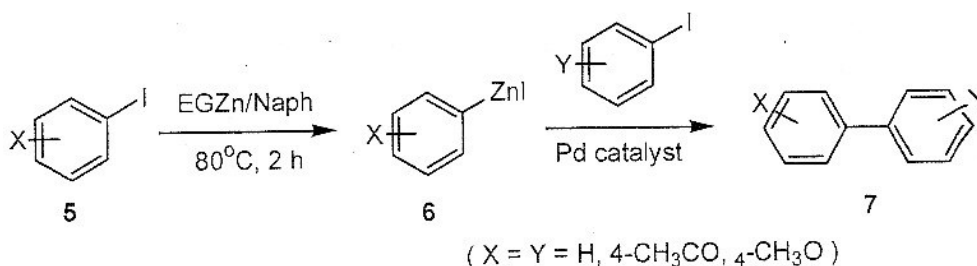
Cross-coupling of functionalized bromoalkanes with aryl iodides using EGZn/Naph

A DMF solution containing EGZn/Naph was readily used in the preparation of organozinc compounds after the zinc anode was removed from the electrochemical cell. The reaction of ethyl 4-bromobutanoate (1) with the EGZn/Naph thus prepared (1.2 equivalents) at 50°C for 1 h gave the corresponding organozinc bromide (2) in an almost quantitative yield.



Scheme 2

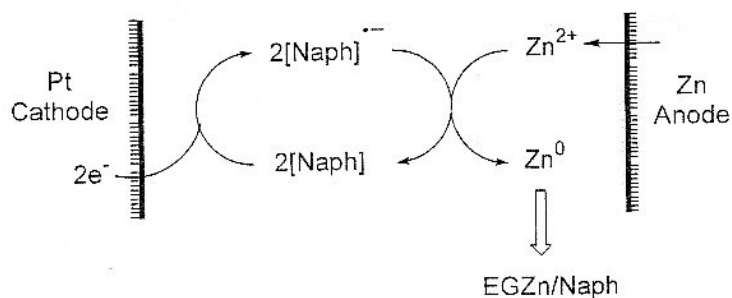
To a DMF solution containing alkylzinc bromide 2a were added aryl iodides (4 mmol) and 5 mol% $\text{Pd(P}(o\text{-Tol})_3)_2\text{Cl}_2$ and the reaction mixture was stirred at 70°C for 3 h. The results of the cross-coupling reaction are summarized in Table 1. Cross-coupling of 2a with iodobenzene, 4-



Scheme 4

Reaction pathways

Probable reaction pathway for the formation of EGZn/Naph is shown in Scheme 5. 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 which 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 EGZn/Naph.

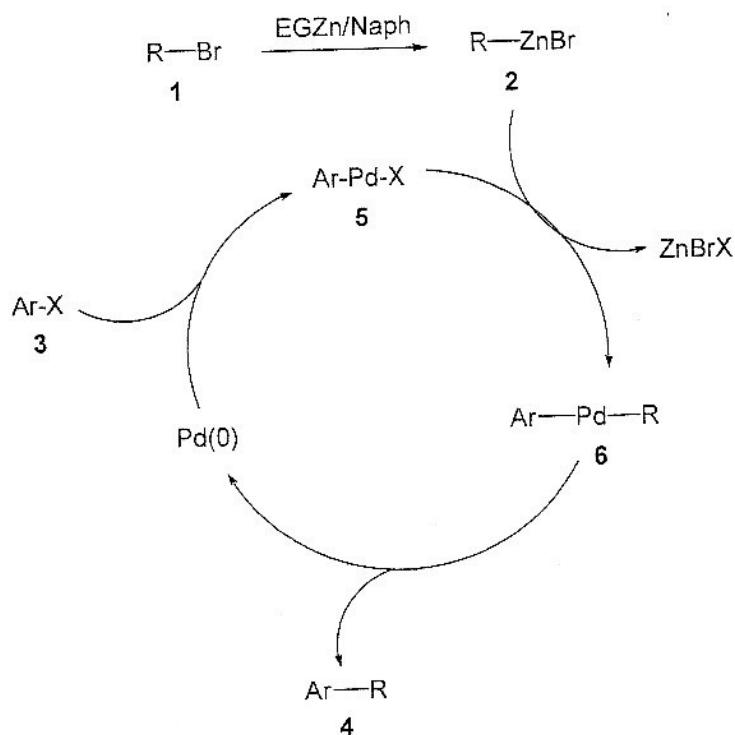


Scheme 5

Probable reaction pathways of the present cross-couplings are shown in Scheme 6. Oxidative addition of Pd(0) to aryl halides would give Ar-Pd-X (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, 4.

Conclusion

We developed a new electrochemical method for the preparation of highly reactive zinc (EGZn/Naph) by using naphthalene as a mediator in the electrolysis. The corresponding organozinc bromide could readily be prepared under mild conditions by the reaction of bromoalkanes with EGZn/Naph. Subsequent cross-coupling reaction of the organozinc bromide thus prepared with various aryl iodides readily took place in the presence of a palladium catalyst to give the corresponding cross-coupled products, 4 in high yields. Arylzinc iodides were also prepared by the use of EGZn/Naph, and they were reacted with other aryl iodides to give the corresponding cross-coupled biaryl 7 in good yields.



Scheme 6

Acknowledgement

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