New Efficient Preparation of Arylzinc Compounds from Aryl Halides Using Cobalt Catalysis and Sacrificial Anode Process

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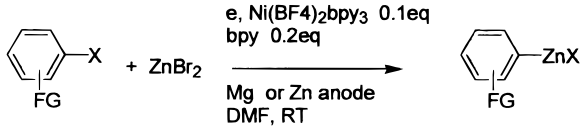
Electroreduction of aryl-chlorides or -bromides in an electrochemical cell fitted with a sacrificial zinc anode and in the presence of cobalt halide associated with pyridine as ligand in DMF or acetonitrile as solvent affords the corresponding organozinc species in good yields.

Introduction

Organozinc compounds have gained a very significant place in the development of new methods in organic synthesis.[1] Their high functional-group tolerance and their good reactivity in the presence of appropriate catalysts have found numerous applications to introduce carbon substituents on various substrates, notably on aromatic nuclei. Whereas alkylzinc iodides are conveniently prepared by direct reaction of alkyl iodides with either zinc dust[2] or electrogenerated reactive zinc,[3] the same methods fail with aryl iodides unless ultrasonic activation[4] or polar solvent[5] are used. The preparation of organozinc species from aryl-bromides and -chlorides is therefore usually achieved via the preliminary formation of aryl-lithium or -magnesium compounds followed by transmetalation with zinc halides. This approach makes a large class of useful compounds hardly accessible, i.e., those bearing a reactive functional group such as aldehyde, ketone, ester, or nitrile on the aromatic nuclei, inasmuch as use of very low temperature is required.[6] Alternatively, the Rieke method,[7] which uses activated zinc obtained by reduction of zinc halide with alkali metal naphthalenide, is convenient with various aromatic bromides or chlorides, even those bearing an electron-withdrawing group.

Some years ago, we reported a simple electrochemical method to form arylzinc compounds from aryl-bromides and -chlorides in DMF as solvent.[8] This process involves nickel-complex catalysts associated with the electroreduction of the aromatic halide in an undivided cell fitted with a sacrificial zinc or magnesium anode (eq 1). All types of aryl halides can be converted, even those unreactive in the Rieke process, such as 3-thienyl bromide.[9]



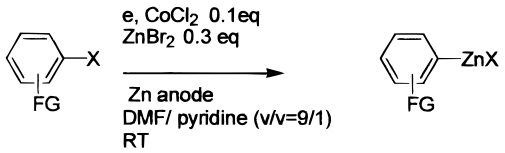
(1)

Nevertheless, this method presents some limitations because of the following:

- one has to use a large amount of the ligand 2,2′-bipyridyl (5 equiv/Ni) to stabilize the low valent nickel catalyst and restrict the formation of biaryl;
- DMF is the only solvent convenient for these electrosyntheses;
- discard of nickel is now recommended for environmental reasons.

Therefore, we have tried to find new transition-metal complexes as catalysts and a wider range of solvent to realize the electrochemical synthesis of zinc reagents using the dissolving anode process.

We first tried to replace bipyridine. We have notably found recently that, in some nickel-catalyzed coupling reactions, pyridine used as cosolvent in DMF can advantageously replace bipyridine.[10] However, these nickel−pyridine complexes are not convenient for the preparation of organozinc compounds. We also found recently[11] that low-valent cobalt complexes, electrogenerated from CoX_2 in DMF−pyridine, can unprecedentedly also activate aryl halides. We now report that, in the presence of zinc bromide, these cobalt−pyridine complexes in DMF are also suitable for the efficient conversion of various aryl halides to the corresponding arylzinc intermediates (eq 2). The starting reagents are aryl-bromides or -chlorides and also other types of organic halides.



(2)

We first used DMF as solvent, and then we looked for other solvents and found that a mixture of acetonitrile and pyridine is also convenient for conducting this reaction.

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Table 1. Preparation of Aryl-Zinc Compounds Substituted by Electron-Donating Groups

	FG-C_6H_4-X		%	%	%	%ArX
entry	FG	X	ArZnX	ArH	Ar-Ar	recovrd
1	H	Cl	6	10	0	84
2	H	Br	70	30	0	0
3	*p*-CH_3O	Br	82	18	0	0
4	*o*-CH_3O	Br	75	25	0	0
5	*m*-CH_3O	Br	62	38	0	0
6	*p*-CH_3O	Cl	6	20	0	74
7	*p*-CH_3	Br	75	25	0	0
8	*p*-$(CH_3)_2N$	Br	90	10	0	0
9	*p*-NH_2	Br	85	15	0	0
10	*p*-OH	Br	0	0	0	100

The overall process can be summarized as follows:

$$\text{At the anode} \quad Zn \rightarrow Zn^{2+} + 2e^-$$

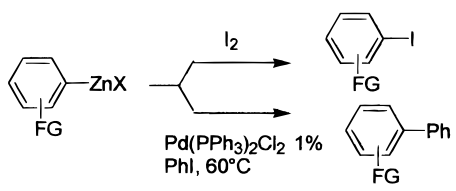
$$\text{At the cathode} \quad ArX + 2e^- + Zn^{2+} \xrightarrow{CoX_2\ \text{cat.}} ArZnX$$

The cathodic process is certainly more complex, as it should involve the transitory electrogenerated Co(I)−pyridine species which is likely associated with Zn(II). This remains to be studied, and results will be reported in due time.

Results and Discussion

All reactions are conducted in a one-compartment cell already described,[12] using a consumable zinc anode and a nickel or stainless steel cathode. Commercial solvents are used without purification. The presence of a supporting electrolyte is not necessary, the ionic conductivity of the medium being ensured by a small amount of zinc bromide added in the medium. Electrolyses are run at constant current intensity of 0.2 A (0.01 A/cm^2), at room temperature, and under inert atmosphere of argon. They are stopped after consumption of 2.1 faraday/mol of ArX. The cathodic potential during the electrolysis is constant between −1.1 and −1.3 V/SCE, which is the potential of formation of the Co(I) complex from CoX_2−pyridine. In a typical experiment, 50 mL of a mixture of solvent (45 mL of DMF or acetonitrile and 5 mL of pyridine) containing 10 mmol of ArX (0.2 M), 1 mmol of CoX_2 (X = Br or Cl) (0.02 M), and 3 mmol (0.06 M) of $ZnBr_2$ were introduced in the cell. The obtained arylzinc halides are converted into the corresponding aryl iodide by addition of iodine, and the amount of aryl iodide is measured by GC using an internal reference. Additionally, several arylzinc intermediates have been coupled with phenyliodide in the presence of $PdCl_2(PPh_3)_2$ as catalyst, and the resulting products have been isolated (Scheme 1).

Scheme 1



Results obtained in DMF from phenyl halides substituted by electron-donating substituents are reported in Table 1. These results show that this new method gives high yields of ArZnX from aryl bromides (Table 1, entries 2−5 and 7−9). On the contrary, low yields are obtained from the corresponding aryl chlorides, which are not consumed even when an excess of faradic charge is engaged (Table 1, entries 1 and 6). This indicates a too slow reaction with Co(I) aryl chloride. Bromophenol (Table 1, entry 10) is acidic enough to divert the formation of the corresponding arylzinc halide and is recovered unchanged after the workup. On the contrary, bromoaniline (Table 1, entry 9) can be converted without protecting the amino group.

Table 2. Preparation of Arylzinc Compounds Substituted by Electron-Withdrawing Groups

	FG-C_6H_4-X			
entry	FG	X	% ArZnX	% ArX recovrd
11	*p*-CH_3SO_2	Cl	90	0
12	*p*-C_2H_5OCO	Br	85	0
13	*o*-C_2H_5OCO	Br	58	19
14	*p*-CF_3	Br	70	0
15	*p*-Br	Br	70 (BrZn-C_6H_4ZnBr)	0
16	*p*-Cl	Br	60 (Cl-C_6H_4ZnBr)	0
17	*p*-F	Br	79	0
18	*p*-CH_3CO	Br	25	0
19	*p*-CN	Cl	<1	0
20	*p*-CN	Br	<1	0
21	*o*-CN	Br	<1	0

Two arylzinc reagents mentioned in Table 1, (*p*-CH_3-C_6H_4ZnBr and *p*-H_2N-C_6H_4ZnBr, entries 7 and 8, respectively) have been coupled with phenyl iodide in the presence of $PdCl_2(PPh_3)_2$. The resulting products (*p*-CH_3-C_6H_4-C_6H_5 and *p*-H_2N-C_6H_4-C_6H_5) have been isolated in 70% and 85% yield, respectively.

When the benzene ring is substituted by an electron-withdrawing group (Table 2, entries 11−17), the yields of the corresponding arylzinc halide obtained in the standard reaction conditions are good to high even from chloro compounds, except when FG is $COCH_3$ or CN. Figure 1 gives for $MeSO_2$-C_6H_4-Cl the consumption of the aryl chloride and the appearance of the corresponding aryl iodide vs the progress of the reaction.

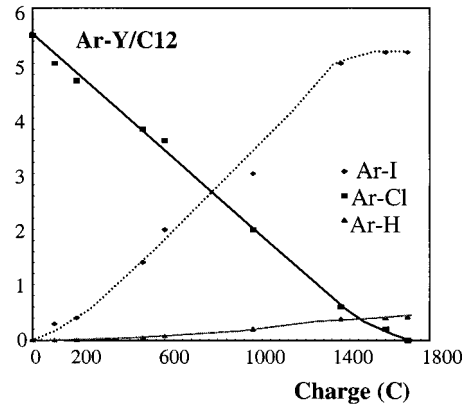


Figure 1.

We observe that the formation of the aryl zinc (*p*-CH_3-SO_2-C_6H_4ZnBr) species is nearly quantitative involving 2 faraday/mol. The arylzinc halide thus obtained (entry 11) has also been coupled with phenyl iodide in the presence of $PdCl_2(PPh_3)_2$ to give the biaryl in 80% yield.

For 1,4-dibromobenzene (Table 2, entry 15), we obtained the dizinc compound in good yield after consumption of 4 faraday/mol.

With $COCH_3$ or CN as substituents (Table 2, entries 18−21) poor results are obtained in the standard reaction conditions. The starting compounds, either chloride or bromide, are mostly converted into ArH. This can be explained by the low cathode potential (−2V/SCE) cor-

responding to the reduction potential of the halide. This indicates a loss of the catalyst. Indeed, the formation of the arylzinc intermediates occurs at ca −1.3V/SCE corresponding to the formation of the catalytic Co(I) species from $CoCl_2$.

Results in Table 3 show that the method can also be applied to the formation of heteroarylzinc compounds, though yields have not been optimized.

Table 3. Preparation of Arylzinc Halides from Heteroaryl Halides

entry	ArX	% ArZnX
22	2Cl−pyridine	50
23	2Br−thiophene	67
24	3B−-thiophene	25

It is quite surprising that ketone and nitrile substituents prevent the formation of the related arylzinc compounds. In trying to increase the yields we found that with these two aryl halides the yields can be increased with the use of a higher amount of the catalyst and/or a higher amount of the initial zinc bromide, as shown in Table 4.

Also, from 3-thienyl bromide, the arylzinc species is obtained in 58% yield (Table 4, entry 34) when 2 equiv of $ZnBr_2$ and 1 equiv of $CoCl_2$ were used instead of the standard reaction conditions (Table 3, entry 24). These results are, however, lower than those obtained previously using $NiBr_2$Bpy as catalyst and a magnesium sacrificial anode.[9]

Table 4. Effect of the Amounts of $CoCl_2$ and $ZnBr_2$ on the Formation of Some Arylzinc Halides

entry	FG-ArX	$ZnBr_2$ (equiv)	$CoCl_2$ (equiv)	% ArZnX
25	*p*-CH_3CO-C_6H_4-Br	2	1	75
26	*p*-CH_3CO-C_6H_4-Br	0.3	0.2	50
27	*p*-CH_3CO-C_6H_4-Br	0.3	0.4	75
28	*p*-CH_3CO-C_6H_4-Cl	2	1	77
29	*p*-NC-C_6H_4-Br	2	1	70
30	*p*-NC-C_6H_4-Br	2	0.4	70
31	*p*-NC-C_6H_4-Cl	2	0.4	50
32	*p*-NC-C_6H_4-Cl	2	1	65
33	*o*-NC-C_6H_4-Br	2	0.4	60
34	3Br−thiophene	2	1	58

We have tried to replace DMF by acetonitrile as solvent using the experimental standard conditions. Table 5 give the results obtained in a mixture of acetonitrile/pyridine (v/v = 9/1)

Table 5. Preparation of Aryl-Zinc Compounds in Acetonitrile/Pyridine

entry	FG-C_6H_4-X	% ArZnX
35	*m*-CF_3-C_6H_4-Br	80
36	*p*-CH_3CO-C_6H_4-Br	57
37	*p*-CH_3SO_2-C_6H_4-Cl	90
38	*p*-HO-C_6H_4-Br	0
39	*p*-EtOOC-C_6H_4-Br	80

It comes out that this solvent mixture is also quite convenient for running the preparation of arylzinc halides. The yield is notably higher than in DMF in the case of *p*-bromoacetophenone (Table 5, entry 36). However, with *p*-bromophenol (Table 5, entry 38), no organozinc species was formed in CH_3CN either, as is the case in DMF (Table 1, entry 10).

This method has also been applied to the formation of organozinc halides from alkyl and alkenyl halides. So far, only low yields have been obtained using the standard reaction conditions in DMF. For example, we have obtained 30%, 42%, and 45% of the corresponding organozinc intermediate from 1-bromodecane, $Br(CH_2)_3$-COOEt, and *β*-bromostyrene, respectively. We now investigate the use of modified reaction conditions to improve these yields and to extend the scope of this method.

Conclusion

This new electrochemical method[13] based on the use of simple cobalt complexes to active aryl halides gives, in many cases, better results than the method we have already described with nickel−bipyridine complexes. The active complex is prepared in situ from $CoCl_2$ and pyridine. The required zinc salt is provided by oxidation of the zinc anode. CH_3CN can be used in place of DMF as solvent. Thus, very simple experimental conditions enable the formation of arylzinc halides in very good yields, and the method applies notably to aryl halides bearing an electron-withdrawing group.

Experimental Section

GC analysis was carried out using a 25-m DB-1 capillary column. Mass spectra were recorded with an ITD spectrometer coupled to a gas chromatograph (DB1, 30 m). Column chromatography was performed on silica gel 60, 70−230 mesh. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 200 MHz with TMS as an internal standard.

The electrochemical cell has been described previously.[12] Unless indicated, all solvents and reagents were purchased and used without further purification. DMF, acetonitrile, and pyridine were stored under argon. Cobalt chloride and zinc bromide were used as obtained commercially.

General Procedure for the Preparation of Aryl Zinc Halide. The electrolysis was fitted with a nickel-sponge or stainless steel cathode (20 cm^2) and a zinc rod (1 cm diameter) anode. To a mixture of DMF or acetonitrile (45 mL) and pyridine (5 mL) containing 3 mmol of $ZnBr_2$ and 1 mmol of $CoCl_2$ was added the aromatic halide (10 mmol). Reactions were performed at room temperature, under argon. The electrolysis (i = 200 mA) was monitored by GC by addition of iodine and was run until the aromatic halide was totally consumed (2−3 h). The aryl iodide is measured by GC using an internal reference and compared with the commercial product.

General Procedure for Coupling with Phenyl Iodide. When the electrolysis was stopped after consumption of the aryl bromide, the solution was heated at 60 °C. Phenyl iodide (10 mmol, i.e., in 1:1 ratio vs initial aryl bromide) and $PdCl_2(PPh_3)_2$ (0.1 mmol) were added. The reaction was monitored by GC and was run until the aromatic zinc halide was totally consumed (2 h). The reactions were then quenched with 1 N HCl and extracted with diethyl ether (3 × 40 mL). The combined extracts were washed with water (5 × 40 mL) to ensure complete removal of DMF. The extracts were dried over $MgSO_4$, and solvent was removed under reduce pressure. The product was isolated by silica gel column chromatography eluted with 95:5 or 90:10 pentane/diethyl ether.

The following compounds were identified by comparison of their physical and spectral data with those given in the cited references: 4-methylbiphenyl;[14a] 4-(dimethylamino)biphenyl;[14b] and 4-(methylsulfonyl)biphenyl.[15]

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