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Communications

Organic Electrochemical Synthesis Utilizing Mg Electrodes (1) – Facile Reductive Coupling Reactions of Aromatic Halides –

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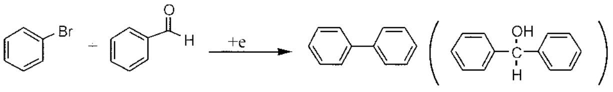
As a part of our efforts to develop efficient reactions for organic synthesis,[1] we turned our attention to investigate organic electrochemistry[2] (OEC). Early investigation of organic electrochemical reaction was originated by Faraday and Kolbe[3] in mid 19th century. It has been good examples of application of laboratory procedures to industrial processes. Major advantage of utilizing OEC is a substitution of hazardous chemical reagents by electricity which is economical, flexible for large scale reactions and compatible with environment. Many industrial processes[4] using OEC are now known which can be carried out milder, cleaner, and/or in higher yield than with conventional methods. For example, the Kolbe synthesis for long chain diacids from shorter chain diacids is still practiced in industry. Monsato[4] produces adiponitrile for the nylon intermediate from acrylonitrile 400 million lb a year.

In theory, electrochemistry dealing with oxidation and reduction was readily applicable for noble organic reactions involving anion,[5] cation[6] and radical intermediates.[7] However, it was not easy to enter this interesting research field of OEC since there were too many variations in its scope and reaction conditions (*e.g* electrodes, voltage, current, amount of electricity, electrocatalysts, cell parts, electrolytes, solvent etc). Recent advances[8] in organic and electrochemistry have provided better understanding about materials and reaction mechanisms for electrochemical reactions to promote investigation of chemical transformation for novel synthesis routes. Also of increasing emphasis on green chemistry,[9] in the light of environmental considerations, organo electric reactions are expected to be important organic synthetic tools in future.

Mg electrode was chosen for our preliminary attempts in OEC since it has been extensively applied in organometallic chemistry and relatively stable for handling. We used Mg electrodes for both anode and cathode and utilized alternating electrodes method[10] to minimize the consumption of metal in reaction medium. At first, bromobenzene and benzaldehyde were submitted under our reaction condition, $LiClO_4$, 50 V, 350 mA, THF, in order to induce Grignard type reaction (eq. 1). The electro- reduction was carried out with a Mg rod cathode and anode in an undivided cell. The cathode and anode were altered at an interval of 30 seconds.



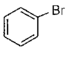
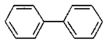
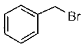
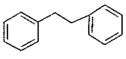
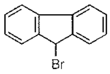
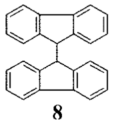
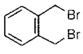
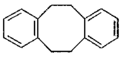
(1)

1 **2** **3** **4**

The reaction mixture was carefully monitored by TLC and then worked up to give rise to the reductive coupling product **3** in 33.0% with no trace of the desired addition product **4** and recovery of benzaldehyde **2** (>95%). In order to confirm the un- expected coupling reaction, bromobenzene without benzaldehyde was exposed under the same condition to provide **3** in 62.3%. The amount of Mg consumed during the reaction was less than 5.0% for each attempt. Without electricity, Mg electrode was completely dissolved by forming Grignard reagent in the reaction medium.

It strongly suggested that our facile reductive coupling reaction could replace Ullmann reaction[11] which was known for harsh reaction condition and low yield. Several reductive coupling reaction[12] utilizing transition metals in a low oxidation state have been reported. However, low-valent reagents originating from transition metal have the limitation of not being efficient and environmentally compatible.

Table 1. Reductive Coupling Reaction of Aromatic Halides

Entry	Halide	Product	Electrode	Electrolyte	Additive	Electricity F/mol	Yield (%)*
I	 1	 4	Mg	$LiClO_4$		4.77	62.3%
			Mg	$AgClO_4$		4.77	N.R.
			Ag	$LiClO_4$		14.3	60.5%
			C	$LiClO_4$		14.3	N.R.
II	 5	 6	Mg	$LiClO_4$		4.77	62.0%
					NaI	3.18	86.8%
III	 7	 8	Mg	$LiClO_4$		5.49	97.0%
IV	 9	 10	Mg	$LiClO_4$		11.8	19.0%

*All reactions were performed at room temperature.

Several aromatic halides were submitted under the same reaction condition to find out the optimized conditions for our transformation (Table 1). The reaction with $AgClO_4$ instead of $LiClO_4$ with Mg electrodes gave rise to no coupling product even in extended reaction time. Replacement of Mg to Ag electrode with $LiClO_4$ provided the product **3** in comparable yield but in prolonged reaction time (× 3). Carbon electrode did not show any reactivity at all (Entry I). Addition of catalytic amount of NaI[13] in reaction mixture facilitated the reaction, and improved the yield more than 30% (Entry II). Compound **7** which contained bis-benzylic carbon gave rise to the product 8 in quantitative yield[14] (Entry III). Several dibromo aromatic compounds were submitted under our condition, but did not give any product. Only α,α'-dibromo-*o*-xylene **9** afforded the compound **10** in low yield[15] from the compelx reaction mixture (Entry IV). Based on these results from simple monobromo aromatic compounds, the optimized reaction conditions for further investigation were established.[16,17]

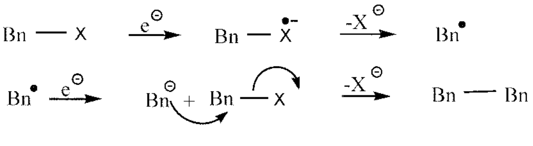
The mechanism of electrochemical cleavage of the carbon-halogen bond is well established. In the first step, one electron is transferred and the carbon-halogen bond is broken to produce an aryl radical which is subsequently dimerized[18] (Scheme 1).

$$\mathrm{Ar-X} \xrightarrow{e^{\ominus}} \mathrm{Ar-\overset{\bullet -}{X}} \xrightarrow{-X^{\ominus}} \mathrm{Ar^{\bullet}}$$

$$\mathrm{Ar^{\bullet}} + \mathrm{Ar^{\bullet}} \longrightarrow \mathrm{Ar-Ar}$$

Scheme 1

However, in the case of benzyl bromide, the possibility to form a dimer by S_N2 attack by a benzyl carbanion on the starting halide should not be excluded[19] (Scheme 2).



Scheme 2

In summary, we report the preliminary result of facile reductive coupling reaction utilizing OEC which can replace Ullmann type reaction. Now we are able to synthesize the coupling products of aromatic halides in preparative scale in good to excellent yield under mild condition. Further study for its general application for other aromatic halides and elucidation of reaction mechanism is currently under investigation in our laboratory and will be reported in detail.

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References and Notes

1. Lee, K.; Yun, H.; Kim, H. *Bull. Korean Chem. Soc*. **2001**, *22*, 133.
2. (a) Fry, A. J. *Aldrichimica Acta* **1993**, *26*, 3. (b) Shono, T. *Electroorganic Synthesis*; Academic Press: New York, 1991.
3. Kolbe, H. *Liebigs Ann*. **1984**, *69*, 257.
4. Jansson, R. *C&EN*. **1984**, 43.
5. Marta, F.; Armando, G.; Achille, I. *Tetrahedron Lett.* **2002**, *43*, 5863.
6. Kimihiro, S.; Osamu, O.; Toshihide, M. *Tetrahedron Lett.* **2000**, *41*, 5873.
7. (a) Manabu, K.; Hiroshi, Y.; Zake, G. *Tetrahedron Lett.* **2000**, *41*, 8131. (b) Ford, W. T.; Nishioka, T. *J. Org. Chem*. **1999**, *64*, 6257.
8. Lund, H.; Hammerich, O. *Organic Electrochemistry*; Marcel Dekker, Inc.: New York, 2000.
9. Matthews, M. *Pure Appl. Chem.* **2001**, *73*, 1305.
10. Kashimura, S.; Shono, T. *J. Org. Chem*. **1999**, *64*, 6615.
11. Trost, B. M. In *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, U. K., 1991; Vol. 3, p 499.
12. (a) Cannes, C.; Condon, S.; Durandetti, M. *J. Org. Chem*. **2000**, *65*, 4575. (b) Munavalli, S.; Rossman, D. *Journal of Fluorine Chemistry* **1995**, *73*, 1.
13. Ugeuen, D.; Fisher, J. *Tetrahedron Lett.* **1998**, *39*, 8089.
14. Rieke, R.; Matsumoto, H. *J. Org. Chem*. **1984**, *49*, 2093.
15. Han, B.; Boudjouk, P. *J. Org. Chem*. **1982**, *47*, 752.
16. Typical procedure is the following: $LiClO_4$ (3.90 g, 36.7 mmol 6.27 eq.) and 40 mL of dry THF were added to three neck jacket reactor equipped with Mg electrodes (3 × 4 cm) for both cathode and anode fitted with condenser in argon atmosphere. The reaction mixture was continuously stirred till all $LiClO_4$ was dissolved and followed by addition of NaI (900 mg, 0.585 mmol, 0.10 eq.). Benzyl bromide **5** (1.00 g, 0.69 mL, 5.85 mmol, 1.00 eq.) in 20 mL THF solution was added by syringe pump for 1 hour. The constant current was supplied with Takasako GPO 50-2 regulated DC power supply. During the electro-reduction, the polarity of the electrode was altered with an interval of 30 second using a alternator. The progress of the reaction was monitored by TLC. After 3.18F/mole of electricity based on **5** (constant current conditions of 500 mA) was passed through the reactor, the reaction mixture was poured into ice cold 1 N HCl 30 mL. The aqueous solution was extracted with ether (30 mL × 3). The combined organic layers were washed with 30 mL of brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column, as ethylacetate : hexane (1 : 1) as eluent gave rise to the bibenzyl **6** (0.460 g, 86.8%). After reaction finished, Mg was recovered more than 95.0% by subsequent cleaning with H_2O and 1 N HCl.
17. All compounds were isolated and fully characterized by comparison with authentic sample or by spectroscopic methods.
18. Fry, A. J.; Porter, M.; Fry, P. F. *J. Org. Chem*. **1996**, *61*, 3191.
19. Fry, A. J. *Synthetic Organic Electrochemistry*, 2nd ed.; Wiley: New York, 1989.