

## Zirconocene Catalyzed Dehalogenation of Aromatic Halides by Alkylmagnesium Reagents

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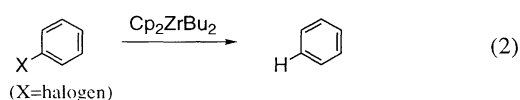
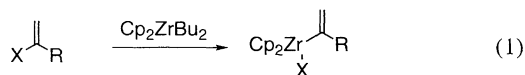
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When aromatic halides were treated with alkylmagnesium reagents (which have  $\beta$ -hydrogens) and a catalytic amount of zirconocene dichloride, dehalogenation proceeded smoothly in high yields. The stoichiometric dehalogenation using dialkylzirconocenes also proceeded with high selectivities.

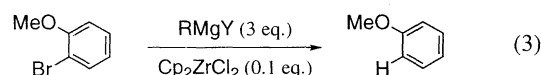
Dehalogenation of aromatic halides can be generally accomplished by transition metal catalyzed hydrogenation or reduction with metal hydrides.<sup>1</sup> However, highly selective dehalogenation of aromatic halides still remains to be studied. In this paper we would like to report selective dehalogenation reaction of aromatic halides using dialkylzirconocenes or alkylmagnesium reagents with a catalytic amount of zirconocene dichloride.

We have recently reported an oxidative addition reaction of alkenyl halides to 'Cp<sub>2</sub>Zr',<sup>2</sup> which was generated *in situ* from Cp<sub>2</sub>ZrBu<sub>2</sub> (Negishi reagent),<sup>3</sup> to give alkenylzirconium species which were very useful for further carbon-carbon bond formation reactions (eq. 1). However, when aryl halides were treated under the same conditions, dehalogenation reaction proceeded instead in very high yields (eq. 2). Deuterolysis did not give any trace of monodeuterated benzene. <sup>13</sup>C-NMR spectrum of the reaction mixture clearly showed the formation of free benzene.



We found this reaction to be general and applicable to various halogenated aromatic compounds (Table 1). As in Entry 2, 2-bromoanisole was debrominated by Cp<sub>2</sub>ZrBu<sub>2</sub> to give anisole in 90% yield. This is quite different from the reaction of aromatic halides such as bromoanisole with *n*-BuLi which gives

anisyllithium after the halogen-metal exchange. Grignard reagents are usually inert toward aromatic halides under conditions used here. Interestingly, when bromoanisole was treated with 3 equiv. of *n*-BuMgCl and a catalytic amount (10% mol) of Cp<sub>2</sub>ZrCl<sub>2</sub>, the dehalogenation of bromoanisole proceeded (eq. 3). Therefore, the catalytic reaction conditions were investigated hereafter.



Several alkylmagnesium reagents were examined under the catalytic reaction conditions for reduction of 2-bromoanisole (Table 2). Among Grignard reagents listed below, *n*-BuMgCl was found to be the most satisfactory. The reaction completed at room temperature for 6 h to give anisole nearly quantitatively. *i*-PrMgBr was less reactive and required higher temperature and longer time to complete the reaction. Methylmagnesium bromide was ineffective in this reaction. This indicates that the reduction requires a  $\beta$ -hydrogen on alkylmagnesium reagents in order to transfer the hydrogen to aromatic ring.

**Table 2.** Various Alkylmagnesium Reagents for Reduction of 2-Bromoanisole

Entry	RMgY	Temp.	Time/h	Yield/%
1	MeMgBr	r.t.	20	—
2	EtMgBr	r.t.	20	30
3	<i>i</i> -PrMgBr	r.t.	20	70
4	<i>i</i> -PrMgBr	50°C	9	95
5	<i>n</i> -BuMgCl	r.t.	6	98
6	<i>n</i> -C <sub>8</sub> H <sub>17</sub> MgBr	r.t.	12	93
7	<i>n</i> -C <sub>10</sub> H <sub>21</sub> MgBr	r.t.	12	91

Table 3 shows the results of the dehalogenation reaction of various aromatic halides using *n*-BuMgCl/*cat.* Cp<sub>2</sub>ZrCl<sub>2</sub>. All reactions were carried out according to the typical procedure as follows. To a mixture of an aryl halide (1.0 mmol), Cp<sub>2</sub>ZrCl<sub>2</sub> (0.1 mmol) and dry THF (5 ml) was slowly added *n*-BuMgCl (3.0 mmol) at -78 °C. The reaction mixture was stirred at room temperature for several hours as listed in the table and monitored by GC.



















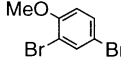
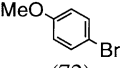
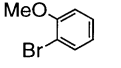
Several dihalobenzenes were employed for the reduction and the reactivity of halogens was found to follow the general order of I>Br>Cl as observed in numerous reduction reactions.<sup>1</sup> Because of their different reactivities, the selectivity of dehalogenation could be controlled by the reaction conditions. For example, 2-chlorobromobenzene and 4-chlorobromobenzene were debrominated for 6 h, and 4-chloriodobenzene was deiodinated within 1 h, giving in both cases chlorobenzene in excellent yields. In all cases, over-reduction of the less reactive halogen atom was negligible. *p*-Halophenols were also reduced to phenol from *p*-bromophenol for 6 h and from *p*-iodophenol in 3 h.

**Table 1.** Stoichiometric Reduction by Cp<sub>2</sub>ZrBu<sub>2</sub><sup>a</sup>

Entry	Substrate	Product	Time/h	Yield/%
1			12	94
2			1	90
3			6	96
4			1	98
5 <sup>b</sup>			3	98

<sup>a</sup> Unless otherwise noted, substrates were treated with 1 eq. of Cp<sub>2</sub>ZrBu<sub>2</sub> at room temp. <sup>b</sup> Reaction was carried at 0°C.

**Table 3.** Dehalogenation using *n*-BuMgCl/cat. Cp<sub>2</sub>ZrCl<sub>2</sub>

Entry	Substrate	Time/h	Product	Yield/%
1		6		94
2	 (X=Br)	6		97
3		1		
4		1		98
5		3		95
6		12		98
7	 (X=Br)	6		94
8		3		
9		6		93
10		20		98
11		1		94
12		3	 + 	

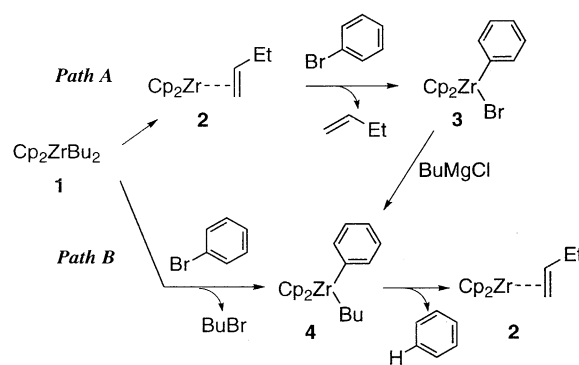
<sup>a</sup> After hydrolysis

Often encountered problem is the selectivity between bromide and iodide. It has been known to be difficult to reduce bromiodobenzene selectively to bromobenzene. There is only one example using an *electrochemical* reduction method,<sup>4</sup> but no *simple* chemical method has been reported so far that gives more than 90% of bromobenzene selectively. Meunier has reported a selective method using NaBH<sub>4</sub>/cat.Cp<sub>2</sub>TiCl<sub>2</sub> in DMF at 70 °C for 24 h which gave 85% yield of bromobenzene along with over-reduced product, benzene (12%).<sup>5,6</sup> Dehalogenation of *p*-bromiodobenzene using the *n*-BuMgCl/cat.Cp<sub>2</sub>ZrCl<sub>2</sub> system was found to be superior and selectively proceeded at room temperature in 1 h to give bromobenzene in 98% yield.

Selective reduction of 2,3-dibromothiophene was achieved with high selectivity to give 3-bromothiophene in 94% yield. However, the reaction of 2,4-dibromoanisole under these conditions did not show high selectivity, and 4-bromo- and 2-bromoanisole were obtained in 72% and 22% yields after 3 h, respectively.

The mechanism is not clear yet. However, we would like to consider two paths in the reaction of Cp<sub>2</sub>ZrBu<sub>2</sub> with bromobenzene. One involves the oxidative addition reaction of aromatic halides to Cp<sub>2</sub>Zr<sup>II</sup> species (*Path A*). Recently was reported a stoichiometric hydrogenolysis of aromatic perfluorocarbons using stoichiometric amount of Cp<sub>2</sub>ZrCl<sub>2</sub>, Mg and HgCl<sub>2</sub>,<sup>7</sup> in

which authors explained that the oxidative addition might be involved. However, if bromobenzene adds to Cp<sub>2</sub>Zr-(CH<sub>2</sub>=CHEt) (**2**), the complex **3** should be formed, but not free benzene. In fact, the reactions of the typical zirconium (II) complex, *i.e.* Cp<sub>2</sub>Zr(CH<sub>2</sub>=CHEt)(PMe<sub>3</sub>),<sup>8</sup> with bromobenzene or iodobenzene did not give oxidative addition products, but 94% of bromobenzene and 96% of iodobenzene remained unreacted even after 24 h at room temperature. Therefore, oxidative addition mechanism is not likely for the stoichiometric reaction. However, *Path A* can not be ruled out in the catalytic reaction, since the reaction of **3** with BuMgBr can afford **4** which gives free benzene.

**Scheme 1.**Possible Pathways for the Stoichiometric Dehalogenation of Bromobenzene by Cp<sub>2</sub>ZrBu<sub>2</sub>.

Another possible mechanism is *Path B* which involves metal-halogen exchange reaction. Bromobenzene reacts with dialkylzirconocene (**1**) to give phenylbutylzirconocene (**4**) with release of bromobutane. The  $\beta$ -hydrogen abstraction from the butyl group of **4** gives free benzene and Cp<sub>2</sub>Zr<sup>II</sup> complex (**2**).

Nonetheless, either one of the two mechanisms may not be the sole mechanism in this reduction reaction. The actual reaction might be further complicated with multiple paths. In order to clarify the mechanism, we must await further investigations.

**References and Notes**

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