Applied
Organometallic
Chemistry

Received: 24 August 2008 Revised: 27 September 2008 Accepted: 27 September 2008 Published online in Wiley Interscience: 10 November 2008

(www.interscience.com) DOI 10.1002/aoc.1470

Hydrodebromination of bromoarenes using Grignard reagents catalyzed by metal ions

Miao Shen[a] and Wen-Hua Sun[a,b*]

The metal salts, $FeCl_2 4H_2O$, $FeCl_3$, $NiCl_2$, $CoCl_2$, CuBr and some iron complexes were found to be efficient catalysts for hydrodebromination of bromoarenes under mild reaction conditions with two equivalents of Grignard reagents. Among them, the iron systems showed the best behavior regarding economic and environmental considerations. All the alkyl Grignard reagents (except CH_3MgCl) and *p*-tolylMgBr were promising reductive reagents with the formation of their homo-coupling products. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: hydrodebromination; metal salts/complexes; Grignard reagent; bromoarenes

Introduction

Organic halides remain important and versatile in their synthetic applications both academically and industrially. Despite the fact that natural organohalogens often possess astonishing biological activities,[1] synthesized organohalogens are commonly classified as high pollutants due to their toxic effects on the environment.[2] In particular, halogenated aromatic compounds have been shown to be a source of dioxins. Therefore, efficient methods and techniques in dehalogenating and reducing certain organic moieties contained in these compounds or solvents are very desirable. Different techniques have been developed in order to solve this environmental problem, i.e. incineration, pyrolysis and chemical[3] and biochemical degradation.[4] However, some of them lead to other halogenated pollutants. As regards low content of organohalogens in solution, chemical methods[5] have demonstrated to be the most effective and have consequently been more studied. Among them, the reductive hydrodehalogenation of organic halides[6] represents an attractive alternative to the more noxious oxidative methods, and catalytic hydrodehalogenation is efficiently accomplished by metals or their low-valency compounds.[6a] On the other hand, Grignard reagents have been reported for effective hydrodehalogenation of aromatic halides with catalytic amounts of metallocene[7] or metal salts[8] beyond their application in organic synthesis.[9] As an extension, it would be interesting to use other common metal salts or complexes as catalysts along with Grignard reagents. Therefore, a general scanning of transition metals was conducted where Fe, Co, Ni and Cu salts were found to be effective in hydrodebromination, especially active catalysts of iron and its complexes. This phenomenon provides iron compounds as promising catalysts in hydrodebromination of bromoarenes because of the inherent advantages of iron as a safe and abundant metal. Herein the preliminary results of hydrodebromination of bromoarenes by Grignard reagents in the presence of catalytic amounts of metal salts or complexes are reported.

Experimental

Materials

All moisture-sensitive reactions were carried out under a nitrogen atmosphere. Anhydrous tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone. Other solvents were treated prior to use by standard methods. All organohalogens were commercially obtained and used without further purification. EtMgBr ($1.0\ \text{mol}\ l^{-1}$) solution in THF was purchased from Aldrich, and other Grignard reagents were prepared according to literature procedures.

Instrumentation and analysis

Nuclear magnetic resonance (NMR) spectra were recorded on a Jeol AL-300 spectrophotometer using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as internal reference. GC analyses were preformed on a gas chromatograph Shimadzu GC-14B equipped with a flame ionization detector using a capillary column (CBP1-M25-025). GC-MS spectra were obtained with a Hewlett Packard 5973 GC-MS detector system.

General Procedure of hydrodehalogenation

To a solution of the aromatic halide (1.0 mmol) and metal salts or complexes (0.01 mmol, 1.0% equivalent to the substrate) in THF

---

* Correspondence to: Wen-Hua Sun, Key Laboratory of Engineering Plastics and Beijing National Laboratory for Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, People's Republic of China. E-mail: whsun@iccas.ac.cn

a Key Laboratory of Engineering Plastics and Beijing National Laboratory for Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, People's Republic of China

b State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, People's Republic of China

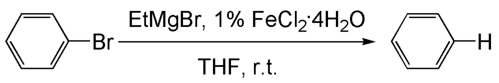
Copyright © 2008 John Wiley & Sons, Ltd.

(2 ml) was added 2.0 ml EtMgBr THF solution (1.0 M solution, 2.0 mmol, 2.0 equivalents respect to the substrate) at room temperature under a nitrogen atmosphere, except for $FeCl_2 \cdot 4H_2O$ as catalyst with 2.1 ml EtMgBr THF solution (1.0 M solution, 2.1 mmol, 2.1 equivalents with respect to the substrate). The dark blue mixture changed to deep brown. The reaction was quenched by addition of water (3 ml). The mixture was extracted with Et_2O (5 ml) and examined by GC/FID. The conversion and product yields were monitored by GC using *n*-dodecane as an internal standard, along with response signals by comparing commercially available samples (*n*-nonane, *n*-dodecane, ethylbenzene, anisole, naphthalene, benzene, toluene, and biphenyl) and purified products confirmed by NMR spectra. Isolation of solid products was done by column chromatography (silica gel; petroleum ether/ethyl acetate).

Results and Discussion

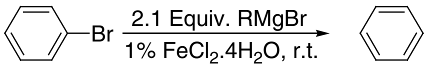
Following the procedure by Takahashi,[7,8] the bromobenzene reacted with various amounts of EtMgBr (0.5, 1.0, 1.5, 2.0 equivalents referred to bromobenzene) in the presence of 0.01 equivalents of $FeCl_2 \cdot 4H_2O$, and the benzene was detected in 24, 47, 73 and 96% yields, respectively (Scheme 1). When the reaction was carried out without $FeCl_2 \cdot 4H_2O$, however, the benzene was not detected.

Owing to the presence of four molecules of water incorporated with iron dichloride, some Grignard reagent was consumed by these water molecules. Thus 0.1 equivalent of EtMgBr in excess was necessary for the reaction with 2.0 equivalents of EtMgBr to bromobenzene, therefore 2.1 equivalents of EtMgBr to bromobenzene within the catalytic system of $FeCl_2 \cdot 4H_2O$ achieved the 100% conversion of bromobenzene and benzene formation was detected in 99% yield. In an extensive study, other Grignard reagents also showed good performance towards debromination of bromobenzene (Table 1). The alkyl Grignard reagents were equally efficient in the hydrodebromination, as was *p*-tolylMgBr. The homocoupling product of Grignard reagents was formed almost quantitatively as a byproduct. Quenched with 3 M DCl in D_2O, there was no deuterated product detected, so the hydrogens for the reduction mostly came from the solvent. This result was consistent with the observation by the Kharasch group.[11] There was no significant activity difference between THF and Et_2O solvents, but it was a little lower in toluene. This observation could be explained in terms of the relative lower solubility of Grignard reagents in toluene. In addition, the aryl Grignard reagents such as PhMgBr, PhMgCl and *p*-MeOPhMgBr did not efficiently hydrodehalogenate bromobenzene, and the reaction was not clear.



Scheme 1. Hydrodebromination of bromobenzene.

Table 1. Hydrodebromination of bromobenzene with various Grignard reagents



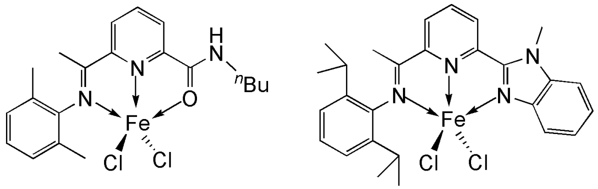
Entry	RMgX	Solvent	Yield (%)[a]
1	EtMgBr	THF	>99
2	EtMgBr	Et_2O	96
3	*i*-PrMgBr	THF	>99
4	*n*-BuMgBr	THF	>99
5	*n*-BuMgCl	THF	97
6	*n*-C_8H_{17}MgBr	THF	>99
7	*n*-C_8H_{17}MgBr	Et_2O	>99
8	*n*-C_8H_{17}MgBr	Toluene	76
9	*n*-$C_{10}H_{21}$MgBr	THF	>99
10	*n*-$C_{10}H_{21}$MgBr	Et_2O	>99
11	*p*-tolyMgBr	THF	98
12	*p*-tolyMgBr	Et_2O	96

Conditions: 1.0 mmol bromobenzene; 0.01 mmol $FeCl_2 \cdot 4H_2O$; 2.1 mmol RMgX; 4 mL solvent; room temperature. [a]Determined by GC.

Encouraged with the above results observed by $FeCl_2 \cdot 4H_2O$, other iron derivatives such as iron (III) chloride and iron complexes **C1** and **C2** (see Scheme 2) were employed as catalysts in the reaction. All iron salts or complexes were found to be effective catalysts, quantitatively transforming bromobenzene into benzene in 10 min (Table 2, entries 1, 2, 3 and 4).

Other metal salts could also enhance the hydrodebromination of bromobenzene; however, a much longer reaction time was required. For example, the transformation was completed in 3 h for $NiCl_2$ (Table 2, entry 5) and 6 h for $CoCl_2$ (Table 2, entry 6), respectively. It required a large amount (10%) of copper (I) bromide and 6 h to complete such transformation (Table 2, entry 7).

With the above results, either iron salts or complexes demonstrated the highest activity for hydrodebromination of bromobenzene. Considering the practical use, the cheap iron dichloride ($FeCl_2 \cdot 4H_2O$) was selected for further exploration of the reduction of various aryl halides with the addition of 2.1 equivalents of EtMgBr



C1 **C2**

Scheme 2. Structures of **C1** and **C2**.

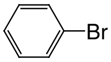
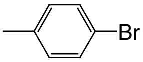
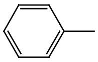
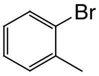
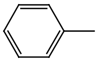
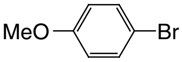
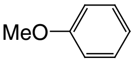
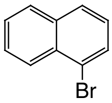
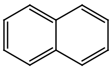
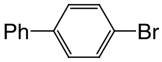
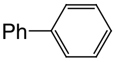
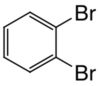
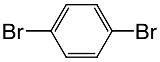
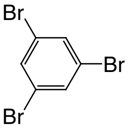
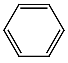
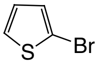
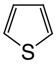
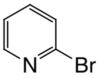
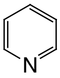
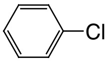
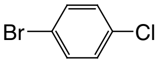
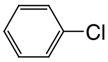
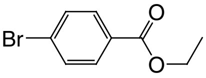
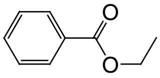
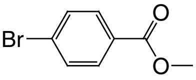
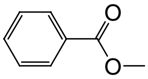
Table 2. Hydrodebromination of bromobenzene using different catalysts

Entry	Catalyst	Time (min)	Yield (%)[a]
1	$FeCl_2 \cdot 4H_2O$	10	98
2	$FeCl_3$	10	98
3	C1	10	>99
4	C2	10	>99
5	$NiCl_2$	180	93
6	$CoCl_2$	360	98
7[b]	CuBr	360	96

Conditions: bromobenzene (1.0 mmol); catalyst (0.01 mmol, 1.0%); RMgBr (2.1 mmol); THF (4 ml); room temperature.
[a] Determined by GC;
[b] catalyst (0.1 mmol, 10%).

Copyright © 2008 John Wiley & Sons, Ltd.

Table 3. Hydrodehalogenation of aryl halides

Entry	Substrate	Product	Time (min)	Yield (%)[a]
1			10	99
2			10	99
3			10	99
4			30	98 (90)
5			30	94
6			30	99
7			30	99
8			30	99
9			30	99
10			30	96
11			30	92
12			120	8
13			120	94
14[b]			120	87 (69)
15[b]			120	89 (73)

Conditions: aryl halide (1.0 mmol); $FeCl_2 4H_2O$ (0.01 mmol, 1.0%); EtMgBr (2.1 equivalents with respect to the substrate); THF (4 ml); room temperature. [a] Determined by GC, isolated yield shown in parentheses. [b] Reaction carried out at −20 °C.

to each bromide-function in the substrate (Table 3). In general, the reducing system was shown to be effective in the reduction of all various aryl bromides under mild reaction conditions. The aryl bromides were easily transformed into the corresponding arene products. Compared with other hydrodebromination systems,[7] the current system consumed less Grignard reagent under mild reaction conditions, and gave the homo-coupling products from alkyl Grignard reagents. In an extensive study, the chlorobenzene was also investigated with only 8% chlorobenzene transformed to benzene at room temperature and not obviously improved at a higher temperature (50 °C). This property was exploited for the hydrodebromination of bromo-chloroarene to form chloroarene (Table 3, entry 13). Moreover, it is noteworthy that the reducing system could effectively hydrodebrominate aryl bromides with an ester functionality in a short time at low temperature (Table 3, entries 14 and 15), which could be useful for organic synthesis.

Conclusion

The metal salts, $FeCl_2 4H_2O$, $FeCl_3$, $NiCl_2$, $CoCl_2$, CuBr and some iron complexes with benzimidazole ligand are efficient catalysts for hydrodebromination of bromoarenes under mild reaction conditions with two equivalents of Grignard reagents. The economic and safe iron systems were demonstrated to be the most efficient ones. All the alkyl Grignard reagents, except CH_3MgCl, were shown to be promising reductive reagents with the additional formation of the corresponding homo-coupling products. From the environmental point of view, this new finding could be useful in the final processing of organic compounds with total removal of bromine from aromatic compounds, and might be useful for processing chloro-aromatic compounds.

Acknowledgment

This work was supported by NSFC no. 20 674 089. We are grateful to Dr Sherrif Adewuyi for the English corrections.

References

[1] G. W Gribble, *J. Chem. Educ.* **2004**, *81*, 1441.

[2] W. W Mohn, J. M. Tiedje, *Microbiol. Rev.* **1992**, *56*, 482; b) R. E. Hinchee, A. Leeson, L. Semprini, *Bioremediation of Chlorinated Solvents*, vol 4, Batelle Press: Columbus, OH, **1997**; c) S. D. Copley, *Chem. Biol.* **1997**, *4*, 169; d) C. E Castro, *Rev. Environ. Contam. Toxicol.* **1998**, *155*, 1; e) S. Fetzner, *Appl. Microbiol. Biotechnol.* **1998**, *50*, 633; f) S. D. Copley, in *Comprehensive Natural Products Chemistry* (Eds.: D. H. R. Barton, K. Nakanishi, O. Meth-Cohn, C. D. Poulter), Elsevier, Amsterdam: **1999**, pp. 401; g) J. Wiegel, Q. Wu, *FEMS Microbiol. Ecol.* **2000**, *32*, 1; h) C. Wichnak, R. Muller, in *Biotechnology* (Ed.: J. Klein), 2nd edn, vol. 11b, Wiley/VCH, Weinheim: **2000**, pp. 241; i) D. B. Janssen, J. E. Oppentocht, G. J. Poelarends, *Curr. Opin. Biotechnol.* **2001**, *12*, 254.

[3] C. Seignez, A. Vuillenium, N. Adler, P. Peringer, *J. Hazard. Mater.* **2001**, *84*, 265.

[4] J. Frimmel, M. Zdrazil, *J Chem. Technol. Biotechnol.* **1995**, *63*, 17; b) J. He, K. M. Ritalahti, K.-L. Yang, S. S. Koenigsberg, F. E. Löffler, *Nature* **2003**, *424*, 62.

[5] I. Fleming, in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), vol. 8, Pergamon Press: Oxford, **1991**, (Chapters 4.1, 4.5, 4.7 and 4.8); b) A. G. Sutherland, in *Comprehensive Organic Functional Group Transformations* (Eds.: A. R. Katritzky, O. Meth-Cohn, C. W. Rees, S. M. Roberts), vol. 1 Pergamon Press: Oxford, **1995**, pp 1–11; c) M. Hudlický, *Reductions in Organic Chemistry* 2nd end, American Chemical Society: Washington, DC, **1996**, (Chapter 7).

[6] F. Alonso, I. Beletskaya, M. Yus, *Chem. Rev.* **2002**, *102*, 4009; b) Z. Kónya, Á. Kukovecz, *Appl. Catal. A: Gen.* **2004** *271*, 1.

[7] R. Hara, W.-H. Sun, Y. Nishihara, T. Takahashi, *Chem. Lett.* **1997**, *26*, 1251; b) R. Hara, K. Sato, W.-H. Sun, T. Takahashi, *Chem. Commun.* **1999**, 845.

[8] H. Guo, K.-I. Kanno, T. Takahashi, *Chem. Lett.* **2004**, *33*, 1356.

Copyright © 2008 John Wiley & Sons, Ltd.

[9] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Edn* **2004**, *43*, 3333; b) L. Boymond, M. RottlJnder, G. Cahiez, P. Knochel, *Angew. Chem. Int. Edn* **1998**, *37*, 1701; c) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Edn* **2003**, *42*, 4302.

[10] W.-H. Sun, P. Hao, S. Zhang, Q. Shi, W. Zuo, X. Tang, *Organometallics* **2007**, *26*, 2720.

[11] M. S. Kharasch, F. L. Lambert, W. H. Urry, *J. Org, Chem.* **1945**, *10*, 298; b) M. S. Kharasch, W. H. Urry, *J. Org, Chem.* **1948**, *13*, 101.

Copyright © 2008 John Wiley & Sons, Ltd.