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Efficient homocoupling reactions of halide compounds catalyzed by manganese (II) chloride

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A new efficient homocoupling reaction was reported in one pot by a combination of metallic magnesium and a catalytic amount of manganese (II) chloride. Various aromatic and alkyl halides underwent homocoupling smoothly, affording the corresponding symmetrical homocoupling compounds in moderate to good yields. The readily available $MnCl_2$, the mild reaction conditions and the operational simplicity and practicability allow for an easy and practical procedure for the purpose of carbon–carbon bond formation. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: halides; coupling; manganese; magnesium

Introduction

The homocoupling reaction is one of the most important and powerful methods for carbon–carbon bond formation, especially for generating biaryls and their heteroaromatic analogs, which are used as liquid crystals, ligands and drugs.[1–3] In recent decades, the transition-metal-mediated coupling reaction has been studied extensively. Various metals have been employed in these reactions, such as copper,[4] nickel,[5,6] palladium[7–10] and iron,[11–14] because of their widely applicable scope and excellent compatibility with many functional groups. However, for large-scale preparation most metal complexes are expensive, sensitive to oxygen and water, and toxic (especially for Ni). These disadvantages not only relate to the nature of the metals, but also to the nature of the ligands, which are becoming more and more uneconomical. Thus, new efficient and environmentally friendly catalysts for the homocoupling reaction are needed. Cahiez developed a manganese-catalyzed cross-coupling reaction of activated aryl halides and *o*-chloro arylketones with organomagnesium reagents, affording the corresponding compounds in high yields.[15,16] Rieke developed benzylic manganese reagents undergoing cross-coupling reactions with a variety of electrophiles in high yields.[17,18] Hoffmann determined the stereochemistry of the transmetalation of Grignard reagents to manganese (II).[19] Recently Rueping developed the cross-coupling reaction of heterocyclic chlorides with aryl magnesium halides using manganese (II) catalyst.[20] We report the manganese-catalyzed homocoupling reaction of normal halides in the presence of metallic magnesium.

Results and Discussion

Initially we started the homocoupling reaction of bromobenzene **1a** catalyzed by manganese (II) chloride in the presence of the metallic magnesium in different solvents. As shown in Table 1, the reaction can occur in THF and ethyl ether, which are the usual solvents for preparing Grignard reagents, and the best result was achieved in THF with 78% yield (entries 1 and 2). Unfortunately, in the toluene and dioxane the manganese chloride was not able to catalyze this reaction because of the difficulty of Grignard reagent formation (entries 3 and 4). Tuning the catalyst loading, it was found that 10 mol% $MnCl_2$ was necessary to obtain a reasonable yield since the small amount of catalyst could not catalyze the homocoupling reaction efficiently (entries 5 and 6).

Encouraged by these initial results with $MnCl_2$ catalyst, the homocoupling reaction of a variety of halide compounds was then investigated in the presence of the metallic magnesium catalyzed by 10 mol% manganese (II) chloride in THF at room temperature. The reactions of all of the halide compounds shown in Table 2 took place smoothly to afford the corresponding coupling products in good yields. The electron-withdrawing group at the *para*-position of bromide **1d** slightly decreased the yield of the reaction (entry 3); meanwhile, the electron-donating and bulky group at the *para*-position of bromide **1b, 1c, 1e** is almost ineffective in the reaction (entries 1, 2 and 4). However, a moderate yield was obtained using the bromide with the substitute at the *ortho*-position **1f, 1g** as the substrates because the *ortho*-substitute as the bulky group hindered the homocoupling reaction in this system (entries 5 and 6). 1-Bromonaphthalene **1h** was treated with metallic magnesium and 10 mol% $MnCl_2$ at 93% yield (entry 7). Also, the reaction proceeded well with benzyl bromide **1i** at 88% yield (entry 8). In comparison with the corresponding chloride and iodide, it was shown that the bromide is the most active substrate in this homocoupling reaction with 78% yield (entries 9 and 10).

In contrast with copper, iron and palladium, there have been few discussions on the mechanism of coupling reaction catalyzed by $MnCl_2$. According to reported literatures, a possible mechanism is proposed in Fig. 1. Aryl manganese halide **A** was obtained with transmetallation of the Grignard reagent with manganese chloride. This species reacted with halide compounds

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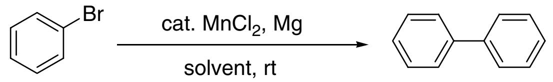
Table 1. Catalytic $MnCl_2$–Mg catalyzed the homocoupling of bromobenzene[a]



1a **2a**

Entry	Solvent	Catalyst amount (mol%)	Yield (%)[b]
1	THF	10	78
2	Ethyl ether	10	44
3	Toluene	10	0
4	dioxane	10	0
5	THF	1	42
6	THF	5	55

[a] Bromobenzene, 1 mmol; $MnCl_2$, 10 mol%; metallic Mg turnings, 2 mmol; anhydrous solvents, 4 ml; vigorous stirring; room temperature; reaction time 24 h. [b] Isolated after chromatography.

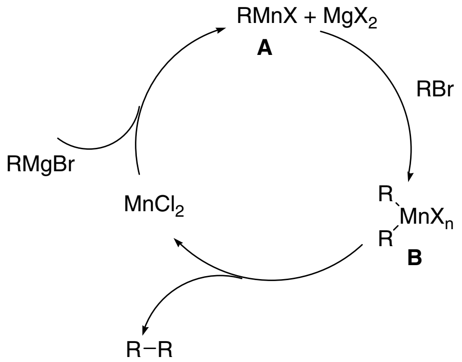


Figure 1. The proposed mechanism of homocoupling reactions of halide compounds catalyzed by manganese (II) chloride.

to form a diaryl-substituted manganese complex intermediate **B**. Reductive elimination of the homocoupling product regenerated catalytically active manganese (II) chloride. Although the detail of the mechanism was not clear in the system, this aspect is currently under further investigation.

Conclusion

In this work, a new efficient homocoupling reaction was reported in one pot by a combination of metallic magnesium and a catalytic amount of manganese (II) chloride. The starting halide compounds can contain a wide variety of substituents. The readily available $MnCl_2$, the mild reaction conditions and the operational simplicity and practicability allow for an easy and practical procedure for the purpose of carbon–carbon bond formation.

Experimental

General procedure

The halide compounds were available without further purification. The halide compound **1e** was prepared according to the literature method.[21] Melting points were recorded on an eletrothermal digital melting point apparatus and uncorrected. ^1H NMR (600 MHz) and ^{13}C NMR(150 MHz) spectra were obtained with a Bruker Avance 600 spectrometer in $CDCl_3$ with TMS as an internal standard. Infrared spectra were recorded with a Bruker Tensor 27 FT-IR spectrophotometer using KBr pellets. GC-MS was performed on a FINNIGAN Trace DSQ chromatograph.

A general procedure for the homocoupling

To a 10 ml flame-dried, two-necked, round-bottom flask with a suspension of 2 mmol (48 mg) of magnesium turnings and 0.1 mmol $MnCl_2$ (12.6 mg) in 4 ml of anhydrous THF was added 1 mmol bromide under an argon atmosphere. The mixture was stirred at room temperature for the time indicated in Table 2 then hydrolyzed with a sodium bicarbonate saturation solution (4 ml). After extraction with aether (3 × 15 ml), the combined organic layers were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by chromatography on silica gel with hexane (products **2c** and **2g** with hexane–AcOEt = 20 : 1).

*Bibenzene (**2a**)*[22]

This compound was prepared from **1a** or **1k** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 68–69 °C. IR (KBr): 3453, 2923, 2853, 1631, 1384, 1089, 812, 721, 668, 658 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.34–7.46$ (m, 6 H), 7.59–7.60 (m, 4 H), ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 126.1$, 126.2, 127.7, 140.2. MS: (EI, 70 eV) *m/z* (%) = 156 (2), 155 (19), 154 (M^+, 100), 153 (60), 152 (46), 151 (16), 115 (5), 76 (11), 51 (4).

*4,4′-Dimethylbiphenyl (**2b**)*[22]

This compound was prepared from **1b** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 122–123 °C. IR (KBr): 3441, 2920, 2854, 1637, 1501, 1384, 1261, 1112, 803, 548, 503 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 2.38$ (s, 6 H), 7.21–7.23 (d, $J = 7.9$ Hz, 4 H), 7.46–7.47 (d, $J = 7.9$ Hz, 4 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 20.0$, 125.8, 128.4, 135.7, 137.3. MS: (EI, 70eV) *m/z* (%) = 183 (20), 182 (M^+, 100), 167 (62), 165 (45), 152 (16), 115 (6), 90 (12), 76 (4).

*4,4′-Dimethoxybiphenyl (**2c**)*[23]

This compound was prepared from **1c** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane–AcOEt = 20 : 1.

M.p.: 178–179 °C. IR (KBr): 3442, 2923, 1609, 1501, 1384, 1276, 1249, 1182, 1041, 824, 809, 553 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 3.83$ (s, 6 H), 6.95 (d, $J = 6.6$ Hz, 4 H), 7.46 (d, $J = 6.6$ Hz, 4 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 54.3$, 113.1, 126.7, 132.5, 157.7. MS (EI, 70 eV): *m/z* (%) = 214 (M^+, 100), 199 (85), 171 (25), 128 (11), 107 (2).

*4,4′-Dichlorobiphenyl (**2d**)*[24]

This compound was prepared from **1d** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 146–147 °C. IR (KBr): 3582, 3546, 3453, 2923, 2853, 1631, 1384, 1089, 812, 668 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.39$ (d,

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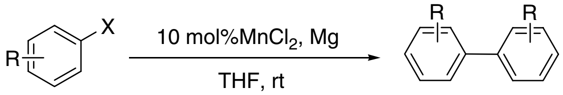
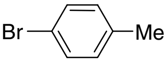
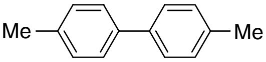
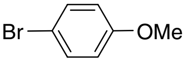
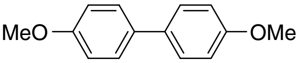
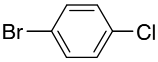
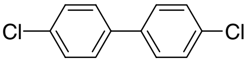
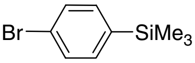
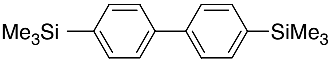
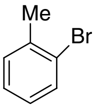
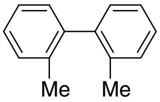
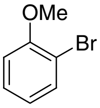
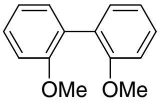
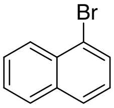
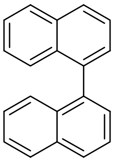
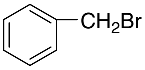
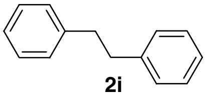
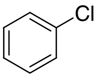
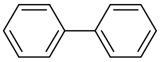
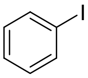
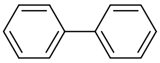
Table 2. Catalytic $MnCl_2$/Mg catalyzed the homocoupling halide compounds[a]



1 2

Entry	Substrate	Product	Yield(%)[b]
1	 **1b**	 **2b**	75
2	 **1c**	 **2c**	73
3	 **1d**	 **2d**	62
4	 **1e**	 **2e**	82
5	 **1f**	 **2f**	55
6	 **1g**	 **2g**	56
7	 **1h**	 **2h**	93
8	 **1i**	 **2i**	88
9	 **1j**	 **2a**	0
10	 **1k**	 **2a**	62

[a] Halide compounds, 1 mmol; $MnCl_2$, 10 mol%; metallic Mg turnings, 2 mmol; anhydrous THF, 4 ml; vigorous stirring; room temperature; reaction time 24 h. [b] Isolated after chromatography.

$J = 8.4$ Hz, 4 H), 7.46 (d, $J = 8.4$ Hz, 4 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 127.2$, 128.0, 132.7, 137.4. MS (EI, 70 eV): *m/z* (%) = 226 (14), 224 (68), 222 (M^+, 100), 186 (8), 153 (2), 152 (72), 151 (22), 150 (14), 126 (4), 111 (8), 75 (9).

*4,4′-Bis(trimethylsilyl)biphenyl (**2e**)*[23]

This compound was prepared from **1e** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 79 °C. IR (KBr): 3442, 2955, 2922, 2851, 1627, 1462, 1382, 1248, 1115, 1092, 839, 805, 753 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.59$ (s, 8 H), 0.29 (s, 18 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = -2.1$, 125.5, 132.8, 138.3, 140.5. MS (EI, 70 eV): *m/z* (%) = 298 (M^+, 25), 283 (100), 224 (5), 195 (5), 165 (4), 134 (23), 120 (4), 73 (6).

*2,2′-Dimethylbiphenyl (**2f**)*[22]

This compound was prepared from **1f** and the catalytic system $MnCl_2$–Mg to give the product as a yellowy liquid after column chromatography with hexane.

M.p.: 18 °C. IR (KBr): 3442, 2919, 2850, 1629, 1462, 1384, 1111, 753, 729, 659 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 2.05$ (s, 6 H), 7.10 (d, $J = 7.2$ Hz, 2 H), 7.20–7.26 (m, 6 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 18.8$, 124.5, 126.1, 128.2, 128.7, 134.8, 140.6. MS (EI, 70 eV): *m/z* (%) = 182 (M^+, 63), 167 (100), 166 (53), 152 (22), 115 (8).

*2,2′-Dimethoxybiphenyl (**2g**)*[23]

This compound was prepared from **1g** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane : AcOEt = 20 : 1.

M.p.: 154–155 °C. IR (KBr): 3442, 2960, 2924, 2851, 1590, 1501, 1482, 1458, 1429, 1284, 1257, 1237, 1164, 1111, 1054, 1022, 1001, 808, 765, 548 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 3.89$ (s, 6 H), 6.83 (t, $J = 7.5$ Hz, 2 H), 6.89 (d, $J = 8.2$ Hz, 2 H), 7.25 (t, $J = 8.3$ Hz, 2 H), 7.52 (d, $J = 7.8$ Hz, 2 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 54.6$, 110.1, 119.3, 126.8, 127.6, 130.4, 156.0. MS (EI, 70 eV): *m/z* (%) = 214 (M^+, 100), 200 (12), 184 (26), 168 (15), 139 (10), 115 (6), 91 (2).

*1,1′-Binaphthalene (**2h**)*[24]

This compound was prepared from **1h** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 142–144 °C. IR (KBr): 3443, 2924, 1639, 1504, 1383, 1014, 803, 780 cm^{-1}. ^{1}H NMR (600 MHz, CDCl3): $\delta = 7.28$–7.94 (m, 14 H). ^{13}C NMR (CDCl3, 150 MHz): $\delta = 124.3$, 124.7, 124.9, 125.5, 126.7, 126.8, 127.1, 131.8, 132.5, 137.4. MS (EI, 70 eV): *m/z* (%) = 255 (19), 254 (M^+, 90), 253 (100), 252 (91), 239 (20), 127 (10), 126 (38), 113 (18), 112 (8).

*1,2-diphenylethane (**2i**)*[25]

This compound was prepared from **1i** and the catalytic system $MnCl_2$–Mg to give the product as a white solid after column chromatography with hexane.

M.p.: 50–52 °C. IR (KBr): 3454, 3028, 2924, 2854, 1641, 1494, 1453, 1386, 1065, 752, 699, 518 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 2.90$ (s, 4 H), 7.15–7.27 (m, 10 H). ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 36.9$, 124.9, 127.3, 127.4, 140.8. MS (EI, 70 eV): *m/z* (%) = 183 (6), 182 (M^+, 46), 165 (4), 104 (4), 92 (10), 91 (100), 65 (9).

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