Tetrahedron Letters 50 (2009) 6795–6797

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Cobalt-catalyzed homo-coupling of aryl and alkenyl bromide using atmospheric oxygen as oxidant

Shan-Yong Chen, Ji Zhang, Ying-Hao Li, Jun Wen, Shao-Quan Bian, Xiao-Qi Yu *

Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, PR China

ARTICLE INFO

Article history:
Received 15 August 2009
Revised 14 September 2009
Accepted 18 September 2009
Available online 25 September 2009

Keywords:
Homo-coupling
Biaryls
Symmetric dienes
Cobalt
Grignard reagents

ABSTRACT

An efficient procedure for the synthesis of symmetric biphenyl and olefinic compounds was reported by cobalt-catalyzed direct homo-coupling reaction of aryl and alkenyl bromide in the presence of metallic magnesium using atmospheric oxygen as the oxidant. All tested aromatic bromides could give corresponding biaryls in good yields (up to 85%). Moreover, under the same conditions, β-bromostyrene could also afford the corresponding conjugated dienes in moderate yields, and the coupling is highly stereoselective to give trans-products. This mild and practicable method opened a new way to the preparation of symmetric biaryls and conjugated dienes.

The biaryl motif plays a considerable role in organic chemistry by its common presence in a vast array of natural products, pharmaceuticals, agrochemicals, and materials.[1] Increasing attentions have been paid to the development of efficient synthetic methods for biaryl formation. Homo- and cross-coupling are most commonly used methods to construct biaryl structure. Historically, the copper-catalyzed coupling, known as Ullmann reaction, was the first efficient method to synthesize symmetrical biaryls.[2] Since Ullmann reaction is always performed under tough conditions, various mild methods relying on the use of nickel or palladium have been developed.[3] Many symmetrical biaryls can be obtained by the palladium- or nickel-catalyzed homo-coupling of ArX (X = I, Br, Cl, OTf) in the presence of a reducing agent. However, the metal catalysts together with the ligands are expensive and toxic. Recently, such reaction was elevated to a high plateau by Gosmini who reported an efficient procedure for reductive homo-coupling of aryl halide catalyzed by $CoBr_2$.[4] In their reactions, excessive Mn (6 equiv) was used as reducing agent, and besides, only low yields were obtained when using substrates with electron-donating substituents.

Oxidative homo-coupling of aryl-metal reagents is another efficient synthetic method for the construction of symmetrical biaryls. Although many organometallic reagents (ArM; M = B, Sn, Si, Zn, Mn, and Mg) can be used for this reaction, Grignard reagent was no doubt the best choice for large-scale preparation because of their convenient and economical preparation directly from aryl halides. However, most homo-couplings involving Grignard reagent need stoichiometric use of transition metal halides such as $TiCl_4$,[5] TlCl,[6] $VO(OEt)Cl_2$,[7] $FeCl_3$,[8] $CoCl_2$,[9] and $CuCl_2$,[10] making the reactions neither atom-economical nor green. More recently, Hayashi[11] and Cahiez[12] developed iron-catalyzed homo-couplings

Table 1
Cobalt-catalyzed homo-coupling of bromobenzene[a]

Entry	Cobalt salt	Catalyst amount (mol %)	Yield[b] (%)
1	–	–	Trace
2	Co_2O_3	10	43
3	$CoSO_4$	10	66
4	$Co(acac)_3$	10	81
5	$CoCl_2$	10	79
6	$CoCl_2$	5	81
7	$CoCl_2$	2.5	76
8[c]	$CoCl_2$	5	64
9[d]	$CoCl_2$	5	79
10[e]	$CoCl_2$	5	81
11[f]	$CoCl_2$	5	35

[a] Bromobenzene, 1 mmol; Mg turnings, 1.2 mmol; anhydrous THF, 2 mL; under dry air; and reaction time 3 h.
[b] Isolated yields after column chromatography.
[c] Mg, 0.75 equiv.
[d] Mg, 1 equiv.
[e] Mg, 2 equiv.
[f] Reaction under argon.

---

* Corresponding author. Tel.: +86 28 85460576; fax: +86 28 85415886.
E-mail address: xqyu@tfol.com (X.-Q. Yu).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.09.092

of Grignard reagents using 1, 2-dihalogenoethanes as oxidant. Such procedures may be attractive alternatives to those reactions using stoichiometric amounts of metal salts. Cahiez et al. also developed a more economical procedure for the homo-coupling catalyzed by $MnCl_2$ or $FeCl_3$ by using atmospheric oxygen as oxidant.[13] Similar reactions were performed smoothly with $FeCl_3$/bipyridine/O_2 system by Lei group.[14] However, all the above methods require the preparation of Grignard reagents, which make the reaction moisture-sensitive and not easily handled.

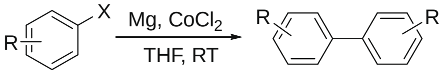
To the best of our knowledge, direct oxidative homo-coupling of aryl halide in the presence of metallic magnesium is rare, and only two examples catalyzed by $MnCl_2$ and $FeCl_3$ were reported.[15] Cobalt, as an environmental friendly and inexpensive metal like iron or manganese, has been widely used as catalyst in the coupling reactions between organomagnesium halides and organohalides.[16] Herein, we report the cobalt-catalyzed direct homo-coupling of aryl bromides in the presence of metallic magnesium using atmospheric oxygen as oxidant, and this method obviates the pre-preparation of Grignard reagents. Furthermore, we also studied the direct homo-coupling of alkenyl bromides, and the resulted conjugate olefins, which can be used in liquid crystal material,[17] were smoothly obtained.

Initially, the study was carried out by the direct homo-coupling of bromobenzene catalyzed by different cobalt salts (10 mol %) in tetrahydrofuran under dry air on 1 mmol scale at room temperature (Table 1). Only trace of the desired product was obtained in the absence of catalyst, indicating that cobalt salt is essential to this reaction (entry 1). The reactions catalyzed by $CoSO_4$ or Co_2O_3 with poor solubility led to moderate yields (entries 2 and 3). The use of $CoCl_2$ or $Co(acac)_3$ as catalysts could evidently increase the chemical yield to around 80% (entries 4 and 5). $CoCl_2$ was chosen for subsequent optimization of reaction conditions for economic consideration. It was found that the catalyst loading does not affect the yields apparently, and only slight yield differences (76–81%) were found in the reactions using 2.5–10 mol % of $CoCl_2$ (entries 5–7). 1.2 equiv of magnesium might be a proper amount for this reaction (entries 6 and 9), and the yield did not change by increasing Mg to 2 equiv (entry 10), which is the amount chosen by Xu and Yuan.[15] On the other hand, a sharp decrease of yield was found by reducing the amounts of Mg to 0.75 equiv, and only 64% yield together with 20% of recovered substrate was obtained (entry 8). These various yields caused by different Mg loadings suggest that Grignard reagent species was involved in the reaction, and at least 1 equiv of Mg is needed for complete conversion.

When the reaction was performed under argon, only 35% homo-coupling product was given (entry 11). We consider that, as Cahiez reported,[13] the atmospheric oxygen plays a key role as an oxidant in the reaction. It was known that in the absence of any transition metal salts, aryl Grignard reagents could be oxidized directly by oxygen to give ArOH. However, little amount of phenol was observed in our system. We speculate that the oxidation of Grignard reagents to biphenyl products catalyzed by cobalt salts is much faster than the oxidative formation of phenols.

When the reaction was carried out on a 5 mmol scale under same conditions, the biphenyl product increased to 85%, indicating that the reaction system may avail large-scale preparation. This result also encouraged us to extend the scope of the reaction to various bromide substrates, and the results are listed in Table 2.

Table 2
$CoCl_2$-catalyzed homo-coupling of bromide compounds[a]



1 **2**

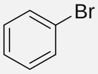
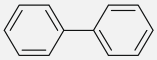
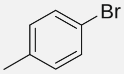
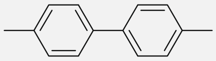
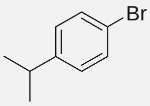
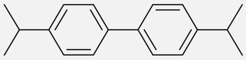
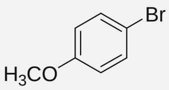
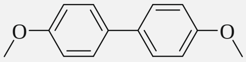
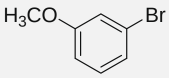
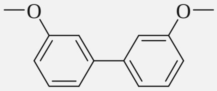
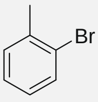
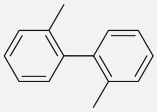
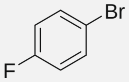
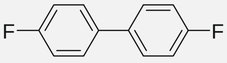
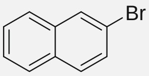
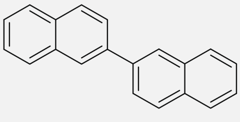
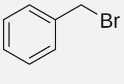
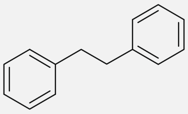
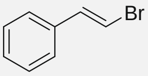
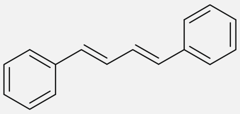
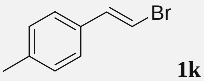
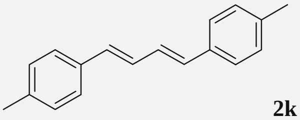
Entry	Substrate	Product	Yield[b] (%)
1	 **1a**	 **2a**	85
2	 **1b**	 **2b**	84
3	 **1c**	 **2c**	84
4	 **1d**	 **2d**	80
5	 **1e**	 **2e**	80
6	 **1f**	 **2f**	79

Table 2 (*continued*)

Entry	Substrate	Product	Yield[b] (%)
7	 **1g**	 **2g**	70
8	 **1h**	 **2h**	75[c]
9	 **1i**	 **2i**	81
10	 **1j**	 **2j**	65 *E*/*E*:*Z*/*E* = 99:1[d]
11	 **1k**	 **2k**	66 *E*/*E*:*Z*/*E* = 98.5:1.5[d]

[a] Bromobenzene, 5 mmol; cobalt salt, 5 mol %; Mg turnings, 6 mmol; anhydrous THF, 10 mL; under dry air; and reaction time 4 h.

[b] Isolated yields after column chromatography.

[c] Recrystallized from ethanol.

[d] The stereoselectivity was determined by GC–MS.

All tested aromatic bromides could give the corresponding biaryls in good yields (entries 1–7). Strong electron-donating substituent such as methoxy group on the phenyl ring has little effect on the reaction (entries 4 and 5). The substituent at *ortho*-position decreased the yield (entry 2 and 6), which might be attributed to the steric effect. For *p*-fluorophenyl bromide (entry 7), decreased yield of homo-coupling product was obtained, while some terphenyl compounds were obtained. This method also worked well in the reaction of 2-bromonaphthalene, and 2,2′-binaphthalene was obtained with 75% yield after recrystallization from ethanol (entry 8). Moreover, activated alkyl bromide such as benzyl bromide could also be converted to 1,2-diphenylethane smoothly through homo-coupling with 81% yield (entry 9). When ester or nitrile substituents were present, no obvious conversion was observed (data not shown), which was probably due to the surface deactivation of Mg caused by the substituted groups.[18] More interestingly, under the same conditions, *trans*-β-bromostyrene also afforded the corresponding conjugated dienes in moderate yields (entries 10 and 11), and the coupling is highly stereoselective to give trans-products. Such high stereoselectivity might be attributed to the fast coupling of alkenyl Grignard reagents.

In conclusion, we have developed an efficient procedure to construct C–C bond by cobalt-catalyzed direct homo-coupling of aryl bromide in the presence of magnesium using atmospheric oxygen as oxidant under mild conditions. Alkenyl bromides were also found to be suitable substrates for the reaction system with high stereoselectivity. Further studies including mechanism exploration about the cobalt-catalyzed coupling reactions are in progress.

Acknowledgments

The authors acknowledge the National Science Foundation of China (Nos. 20702034 and 20725206) for financial support. The authors also thank the Analytical & Testing Center of Sichuan University for NMR analysis.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.09.092.

References and notes

1. (a) Thomson, R. H. *The Chemistry of Natural Products*; Blackie: Glasgow, 1985; (b) Hassan, J.; Sevignon, M.; Cozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359; (c) Corbet, J. P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651.
2. (a) Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174; (b) Fanta, P. E. *Chem. Rev.* **1964**, *64*, 613.
3. (a) Mukhopadhyay, S.; Rothenberg, G.; Gitis, D.; Sasson, Y. *Org. Lett.* **2000**, *2*, 211; (b) Venkatraman, S.; Li, C. J. *Org. Lett.* **1999**, *1*, 1133; (c) Lee, K.; Lee, P. H. *Tetrahedron Lett.* **2008**, *49*, 4302; (d) Wang, L.; Zhang, Y.; Liu, L.; Wang, Y. *J. Org. Chem.* **2006**, *71*, 1284; (e) Lee, P. H.; Seommon, D.; Lee, K. *Org. Lett.* **2005**, *7*, 343; (f) Catellani, M.; Motti, E.; DellaCá, N.; Ferraccioli, R. *Eur. J. Org. Chem.* **2007**, *72*, 4153.
4. Moncomble, A.; Floch, P. L.; Gosmini, C. *Chem. Eur. J.* **2009**, *15*, 4770.
5. Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2000**, *56*, 9601.
6. (a) McKillop, A.; Elsom, L. F.; Taylor, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 2423; (b) Elsom, L. F.; McKillop, A.; Taylor, E. C.. In *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI. p 488.
7. (a) Ishikawa, T.; Ogawa, A.; Hirao, T. *Organometallics* **1998**, *17*, 5713; (b) Hirao, T. *Coord. Chem. Rev.* **2003**, *237*, 271.
8. Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264.
9. Kharasch, M. S.; Fields, E. K. *J. Am. Chem. Soc.* **1941**, *63*, 2316.
10. Sakellarios, E.; Kyrimis, T. *Ber. Dtsch. Chem. Ges.* **1924**, *57B*, 322.
11. Nagano, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 491.
12. Cahiez, G.; Chaboche, C.; Mahuteau-Betzer, F.; Ahr, M. *Org. Lett.* **2005**, *7*, 1943.
13. Cahiez, G.; Moyeux, A.; Buendia, J.; Duplais, C. *J. Am. Chem. Soc.* **2007**, *129*, 13788.
14. Liu, W.; Lei, A. W. *Tetrahedron Lett.* **2008**, *49*, 610.
15. (a) Xu, X. L.; Cheng, D. P.; Pei, W. *J. Org. Chem.* **2006**, *71*, 6637; (b) Yuan, Y.; Bian, Y. B. *Appl. Organomet. Chem.* **2008**, *22*, 15.
16. (a) Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 6514; (b) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 1866; (c) Cahiez, G.; Chaboche, C.; Duplais, C.; Giulliani, A.; Moyeuxa, A. *Adv. Synth. Catal.* **2008**, *350*, 1484; (d) Kobayashi, T.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. J. *Am. Chem. Soc.* **2008**, *130*, 11276; (e) Gosmini, C.; Bégouin, J. M.; Moncomble, A. *Chem. Commun.* **2008**, 3221; (f) Cahiez, C.; Chaboche, C.; Duplais, C.; Moyeux, A. *Org. Lett.* **2009**, *11*, 277.
17. (a) Davis, R.; Mallia, V. A.; Das, S. *Chem. Mater.* **2003**, *15*, 1057; (b) Brettle, R.; Dunmur, D. A.; Hindley, N. J.; Marson, C. M. *J. Chem. Soc., Chem. Commun.* **1992**, 411.
18. Lee, J. S.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J. R.; Rieke, R. D. *J. Org. Chem.* **2000**, *65*, 5428.