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Manganese-Catalyzed Cross-Coupling Reaction between Aryl Grignard Reagents and Alkenyl Halides

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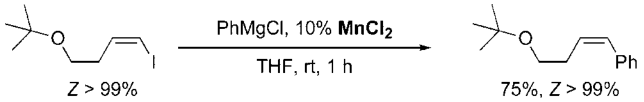
ABSTRACT



Aryl Grignard reagents react stereospecifically with alkenyl halides in the presence of manganese chloride (10%) to afford good yields of cross-coupling products.

Recently, the use of iron salts to replace palladium or nickel complexes as catalysts has emerged as a very promising area for sustainable development. During the past decade, numerous Fe-catalyzed cross-coupling reactions were reported by us[1] and others.[2] From both an economical and environmental point of view, manganese salts are a valuable alternative to iron salts. However, examples of Mn-catalyzed cross-coupling reactions are rare.[1h,3] Generally, only very reactive organic halides like activated aryl halides[3a−c] or chloroenynes[3d] have been used until now.

We report herein the first Mn-catalyzed cross-coupling reactions between aryl Grignard reagents and simple alkenyl halides. Our first attempts were performed with various 2-bromostyrenes in the presence of 10% $MnCl_2$ (Table 1, entries 1−7). At room temperature the reaction is slow, but satisfactory yields were obtained. In some case, it is necessary to accelerate the reaction by heating at 50 °C (entries 5−7). Some other reactive alkenyl bromides were coupled under similar conditions (entries 8−10). The coupling reaction is always stereospecific (entries 1−7, 9, and 10) except in the case of the (*Z*)-3-(2-bromoethenyl)pyridine (entry 8). Surprisingly, a complete inversion of configuration of the double bond is then observed. As a rule, the slow reaction rate is

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(1) Selected references: (a) Cahiez, G.; Marquais, S. *Pure Appl. Chem.* **1996**, *68*, 53. (b) Cahiez, G.; Avedissian, H. *Synthesis* **1998**, 1199. (c) Dohle, W.; Kopp, F.; Cahiez, G.; Knochel, P. *Synlett* **2001**, 1901. (d) Duplais, C.; Bures, F.; Korn, T.; Sapountzis, I.; Cahiez, G.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2968. (e) Cahiez, G.; Chaboche, C.; Mahuteau-Betzer, F.; Ahr, M. *Org. Lett.* **2005**, *7*, 1943. (f) Cahiez, G.; Habiak, V.; Duplais, C.; Moyeux, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4364. (g) Cahiez, G.; Duplais, C.; Moyeux, A. *Org. Lett.* **2007**, *9*, 3253. (h) Cahiez, G.; Moyeux, A.; Buendia, J.; Duplais, C. *J. Am. Chem. Soc.* **2007**, *129*, 13788.

(2) Selected references: (a) Fürstner, A.; Leitner, A.; Méndez, M.; Krause, H. *J. Am. Chem. Soc.* **2002**, *124*, 13856. (b) Fürstner, A.; Leitner, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 609. (c) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686. (d) Nagano, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 1297. (e) Bedford, R. B.; Bruce, D. W.; Frost, R. M.; Goodby, J. W.; Hird, M. *Chem. Commun.* **2004**, 2822. (f) Martin, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3955. (g) Nagano, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 491. (h) Bedford, R. B.; Bruce, D. W.; Frost, R. M.; Hird, M. *Chem. Commun.* **2005**, 4161. (i) Guerinot, A.; Reymond, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6521. (j) Taillefer, M.; Xia, N.; Ouali, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 934. (k) Hatakeyama, T.; Nakamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 9844. See also: Cahiez, G.; Duplais, C. Iron-Catalyzed Reactions of Grignard Reagents. In *The Chemistry of Organomagnesium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley VCH: Weinheim, 2008; Chapter 13, p 595.

(3) For Mn-catalyzed reactions of activated aryl halides with RMgX: (a) Cahiez, G.; Lepifre, F.; Ramiandrasoa, P. *Synthesis* **1999**, 2138. (b) Cahiez, G.; Luart, D.; Lecomte, F. *Org. Lett.* **2004**, *6*, 4395. (c) Rueping, M.; Ieawsuwan, W. *Synlett* **2007**, 247. For a Mn-catalyzed reaction of RMgX with 1-chloro-1,3-dienes and 1-chloro-1,3-enynes, see: (d) Alami, M.; Ramiandrasoa, P.; Cahiez, G. *Synlett* **1998**, 325. (e) For a Mn-catalyzed reaction with aryl or alkynyltin, see: Kang, S.-K.; Kim, J.-S.; Choi, S.-C. *J. Org. Chem.* **1997**, *62*, 4208. For a Mn-catalyzed reaction with organoalanes, see: (f) Fugami, K.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1987**, *16*, 2203. For various Mn-catalyzed homocoupling reactions, see: (g) Cahiez, G.; Bernard, D.; Normant, J. F. *J. Organomet. Chem.* **1976**, *113*, 99. (h) Kang, S.-K.; Baik, T.-G.; Jiao, X. H.; Lee, Y.-T. *Tetrahedron Lett.* **1999**, *40*, 2383.

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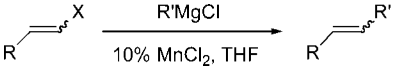
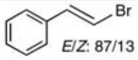
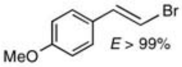
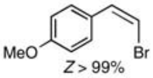
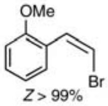
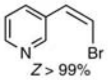
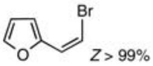
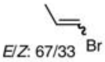
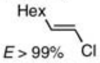
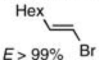
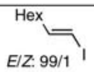
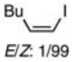
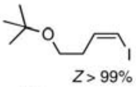
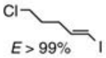
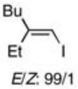
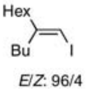
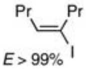
Table 1. Mn-Catalyzed Arylation of Alkenyl Halides



entry	alkenyl halide	R from RMgCl	reaction conditions	yield (*E*/*Z*)[a]
1	 Br *E*/*Z*: 87/13	Ph	rt, 3 h	83% (88/12)
2	"	*o*-Tol	rt, 18 h	49% (63%)[b] (82/18)
3	"	*p*-MeOPh	"	81% (84/16)
4	"	*p*-F-Ph[c]	"	50% (82/18)
5	 MeO, Br *E* > 99%	Ph	50 °C, 6 h	65% (96/4)
6	 MeO, Br *Z* > 99%	Ph	"	69% (4/96)
7	 OMe, Br *Z* > 99%	Ph	50 °C, 4 h	79% (5/95)
8	 N, Br *Z* > 99%	Ph	0 °C, 1 h	71% (99/1)
9	 O, Br *Z* > 99%	Ph	rt, 6 h	55% (4/96)
10	 Br *E*/*Z*: 67/33	*p*-Tol	rt, 3 h	66% (88%)[b] (69/31)
11	 Hex, Cl *E* > 99%	Ph	reflux, 18 h	(20%)[b] (99/1)
12	 Hex, Br *E* > 99%	"	rt, 18 h	75% (87%)[b] (*E* > 99)
13	 Hex, I *E*/*Z*: 99/1	"	rt, 3 h	79% (99/1)
14	"	*p*-MeOPh	50 °C, 18 h	72% (98/2)
15	"	*p*-(Me)$_2$NPh	"	61% (99/1)
16	"	2-Naphtyl[c]	rt, 18 h	69% (96/4)
17	 Bu, I *E*/*Z*: 1/99	Ph	rt, 4 h	75% (87%)[b] (2/98)
18	"	*p*-MeOPh	"	85% (1/99)
19	 O, I *Z* > 99%	Ph	rt, 1 h	75% (*Z*> 99)
20	 Cl, I *E* > 99%	Ph	"	69% (97/3)
21	 Bu, Et, I *E*/*Z*: 99/1	Ph	50 °C, 18 h	65% (96/4)
22	"	*p*-MeOPh	"	52% (93/7)
23	 Hex, Bu, I *E*/*Z*: 96/4	Ph	"	56% (94/6)
24	 Pr, Pr, I *E* > 99%	Ph	rt, 4 h	59% (84/16)

[a] Ratio *E*/*Z* determined by GC on the crude product. [b] GC yield. [c] ArMgBr was used

probably due to the reductive elimination step. Indeed, Mn(II) species like Ar$_2$Mn are generally stable at room temperature.[4]

The reaction was extended to less reactive alkenyl halides (entries 11−24). Alkenyl bromides and iodides were coupled successfully (entries 12 and 13); however, the corresponding chlorides led to poor yields (entry 11). It should be noted that β-monosubstituted alkenyl iodides often react at room temperature (entries 13−20), whereas the less reactive β,β-disubstituted analogues slowly lead to the coupling product at 50 °C (entries 21−23). The reaction is stereospecific, except with the α-substituted alkenyl halides (entry 24). It should be noted that, in some cases, alkyl Grignard reagents can also be used successfully.[5]

In conclusion, we described the first Mn-catalyzed coupling reaction of aryl Grignard reagents with alkenyl halides. These results demonstrate the feasibility of Mn-catalyzed cross-coupling reactions with nonactivated organic halides. Such reactions could be complementary and/or competitive to the Fe-catalyzed coupling procedures recently described.[1,2] It is important to note that Mn catalysis is an interesting field of investigation for sustainable development.

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Supporting Information Available: Detailed experimental procedures and complete compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) See ref 3h and the Supporting Information.
(5) See the Supporting Information.