Cobalt-catalyzed Coupling of Alkenyl Triflates with Aryl and Alkenyl Grignard Reagents

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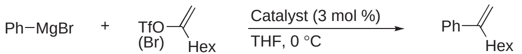
$Co(acac)_3$–PPh_3 was found to effectively catalyze the $C(sp^2)$–$C(sp^2)$ coupling of Grignard reagents to give alkenylarenes and conjugated dienes, utilizing close affinity towards alkenyl triflates.

The cobalt-catalyzed cross-coupling reaction of Grignard reagents has recently attracted considerable attention because the catalysts and the organometallic reagents are fairly inexpensive and easily available.[1] However the cobalt-catalyzed coupling shows a much limited scope compared with the palladium-catalyzed reaction, which covers a variety of cross-coupling reactions between carbon atoms in diverse hybridized states.[2] A marked difference is observed for $C(sp^2)$–$C(sp^2)$ coupling,[3,4] in particular for alkenyl–alkenyl coupling, which has only one example with cobalt catalysis.[5] In this context, we have reported that alkenyl triflates, which are easily prepared from ketones, as alkenyl electrophiles have a close affinity towards cobalt catalysts to undergo the coupling with alkynyl Grignard reagents.[6,7] In this first cobalt-catalyzed $C(sp)$–$C(sp^2)$ coupling, we used a simple catalyst system consisting merely of $Co(acac)_3$ and THF respectively as a catalyst and a solvent. Here, we report that addition of triphenylphosphine to the system makes alkenyl triflates effectively react also with aryl and alkenyl Grignard reagents to give $C(sp^2)$–$C(sp^2)$ coupling products in good to high yields.

We chose phenylmagnesium bromide (**1a**) and 1-octen-2-yl triflate (**2a**) as a substrate combination to evaluate the catalyst system for $C(sp^2)$–$C(sp^2)$ coupling. The reaction of **1a** (1.8 equiv) with **2a** (1.0 equiv) using the same catalyst system [3 mol % of $Co(acac)_3$ with no ligands in THF] as the coupling of alkynyl Grignard reagents with alkenyl triflates[6] at 0 °C for 3 h gave 2-phenyl-1-octene (**3aa**) only in 67% yield (Entry 1 of Table 1). Addition of PPh_3 (12 mol %) as a ligand increased the yield to 88% (Entry 2). Higher conversion with PPh_3 possibly shows that the main role of the ligand is stabilization of the cobalt catalyst. High activity of the cobalt catalyst was disclosed by higher conversion (83%) in a short reaction period (30 min) than that with the corresponding palladium catalyst (Entry 3 vs. 4), which though scored a high yield in a long reaction period (Entry 5). A close affinity of the cobalt catalyst towards triflates was shown in comparison with the reaction of 1-octen-2-yl bromide, which coupled with **1a** only in 60% yield (Entry 6).

Table 1. Comparison of catalysts in the coupling of phenylmagnesium bromide with 1-octen-2-yl triflate[a]



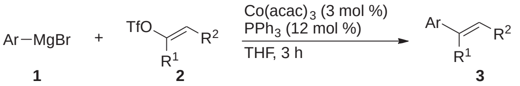
1a **2a** **3aa**

Entry	Catalyst	Time/h	Conv./%[b]	Yield/%[b]
1	$Co(acac)_3$	3	91	67
2	$Co(acac)_3/PPh_3$ (1/4)	3	>99	88 (87)[c]
3	$Co(acac)_3/PPh_3$ (1/4)	0.5	83	69
4	$Pd(acac)_2/PPh_3$ (1/4)	0.5	30	27
5	$Pd(acac)_2/PPh_3$ (1/4)	24	96	93
6[d]	$Co(acac)_3/PPh_3$ (1/4)	3	98	60

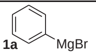
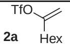
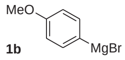
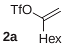
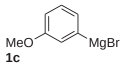
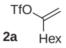
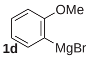
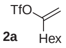
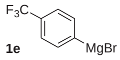
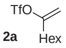
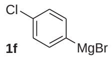
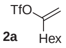
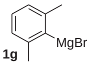
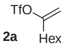
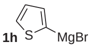
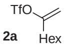
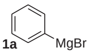
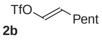
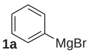
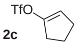
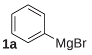
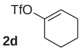
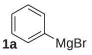
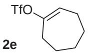
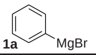
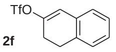
[a] The reaction was carried out in THF (1.0 mL) at 0 °C using **1a** (0.45 mmol) and **2a** (0.25 mmol) in the presence of $Co(acac)_3$ (7.5 µmol) and PPh_3 (30 µmol). [b] Determined by ^1H NMR of the crude product. [c] Isolated yield based on **2a**. [d] The corresponding bromide was used instead of **2a**.

The cobalt catalyst was applied to the coupling of alkenyl triflates not only with arylmagnesium bromides (Table 2) but also with alkenylmagnesium bromides (Table 3).[8,9] In addition to nonsubstituted phenyl Grignard reagent **1a**, those having an electron-donating methoxy group at p, m, or o position underwent the coupling with triflate **2a** in high yields (Entries 1–4 of Table 2). Introduction of an electron-withdrawing group is

Table 2. Cobalt-catalyzed coupling of aryl Grignard reagents with alkenyl triflates[a]

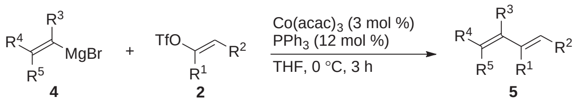


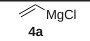
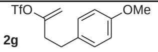
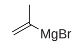
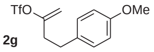
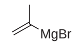
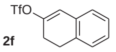
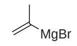
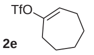
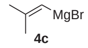
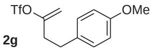
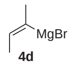
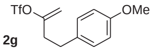
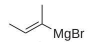
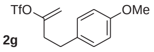
1 **2** **3**

Entry	1	2	Temp /°C	Prod	Yield /%[b]
1	 1a	 2a	0	**3aa**	87
2	 1b	 2a	0	**3ba**	80
3	 1c	 2a	0	**3ca**	87
4	 1d	 2a	20	**3da**	72
5	 1e	 2a	0	**3ea**	79
6	 1f	 2a	0	**3fa**	67
7	 1g	 2a	40	**3ga**	77
8	 1h	 2a	40	**3ha**	71
9	 1a	 2b	−20	**3ab**	78
10	 1a	 2c	0	**3ac**	40 (71)[c]
11	 1a	 2d	20	**3ad**	11 (20)[c]
12	 1a	 2e	20	**3ae**	93
13	 1a	 2f	20	**3af**	93

[a] The reaction was carried out in THF (1.0 mL) for 3 h using **1** (0.45 mmol) and **2** (0.25 mmol) in the presence of $Co(acac)_3$ (7.5 µmol) and PPh_3 (30 µmol). [b] Isolated yield based on **2**. [c] Tris(4-methoxyphenyl)phosphine was used instead of PPh_3.

Table 3. Cobalt-catalyzed coupling of alkenyl Grignard reagents with alkenyl triflates[a]



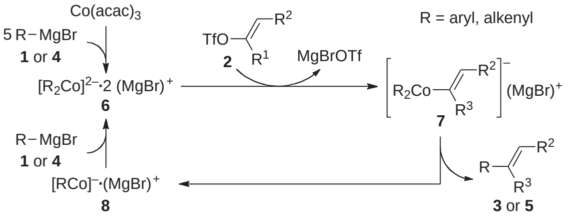
Entry	4	2	Prod	Yield /%[b]
1[c]	 4a	 2g	**5ag**	87
2	 4b	 2g	**5bg**	93
3	 4b	 2f	**5bf**	73
4	 4b	 2e	**5be**	84[d]
5	 4c	 2g	**5cg**	69
6	 4d	 2g	**5dg**	88
7	 4e	 2g	**5eg**	79

[a]The reaction was carried out in THF (1.0 mL) at 0 °C for 3 h using **4** (0.45 mmol) and **2** (0.25 mmol) in the presence of Co(acac)$_3$ (7.5 µmol) and PPh$_3$ (30 µmol). [b]Isolated yield based on **2**. [c]Reaction temperature = 40 °C. [d]Determined by ^{1}H NMR of the crude product.

compatible with the reaction (Entry 5). The chloroarene moiety of Grignard reagent **1f** did not participate in the cross-coupling (Entry 6). Bulky aryl Grignard reagent **1g** and 2-thienylmagnesium bromide (**1h**) coupled with triflate **2a** (Entries 7 and 8). The reaction is applicable also to linear and cyclic alkenyl triflates **2b**–**2f** to give the corresponding coupling products with **1a**, though a large drop of the yield was observed in the reaction of cyclopentenyl and -hexenyl triflates (Entries 9–13).[10] For the reaction of these cyclic triflates, use of tris(4-methoxyphenyl)phosphine instead of PPh$_3$ gave better results. On the other hand, conjugated dienes are obtained by the coupling of alkenyl Grignard reagents. Nonsubstituted vinyl Grignard reagent **4a** reacts with 1-alken-2-yl triflate **2g** having a methoxyphenyl moiety to give 2-substituted 1,3-butadiene **5ag** (Entry 1 of Table 3). The scope of alkenyl triflates was examined with monosubstituted vinyl Grignard reagent **4b**, which coupled with cyclic triflates **2f** and **2e** in addition to acyclic **2g** (Entries 2–4). Disubstituted vinyl Grignard reagents **4c**–**4e** also underwent the coupling reaction with triflate **2g** (Entries 5–7). During the coupling reaction, the stereochemistry of 2-buten-2-yl Grignard reagents **4d** and **4e** was retained to give (*Z*)- and (*E*)-dienes, respectively.

A plausible mechanism based on those proposed in the reports by Oshima et al.[4d,4g] and us[6] is shown in Scheme 1, though we do not have any evidence for the present C(sp^2)–C(sp^2) coupling. The catalytic cycle includes three distinct steps: 1) oxidative addition of alkenyl triflate **2** to R$_2$Co^0 di-ate complex **6**, generated through reduction of Co(acac)$_3$ by Grignard reagent **1** or **4**, giving cobalt(II) complex **7**, 2) reductive elimination of coupling product **3** or **5** to give RCo^0 ate complex **8**, 3) regeneration of di-ate complex **6** through the reaction of **8** with a Grignard reagent.

In conclusion, we have disclosed an effective catalyst consisting of Co(acac)$_3$ and PPh$_3$ for the coupling of alkenyl triflates with aryl and alkenyl Grignard reagents, where C(sp^2)–C(sp^2) coupling products are obtained in good to high yields.



Scheme 1.

References and Notes

1 For early examples, see: a) M. S. Kharasch, C. F. Fuchs, *J. Am. Chem. Soc.* **1943**, *65*, 504. b) G. Cahiez, H. Avedissian, *Tetrahedron Lett.* **1998**, *39*, 6159.

2 For a review on the palladium-catalyzed coupling of Grignard reagents, see: *Metal-catalyzed Cross-coupling Reactions*, 2nd ed., ed. by A. de Meijere, F. Diederich, Wiley-VCH, Weinheim, **2004**.

3 To the best of our knowledge, the reports on the cobalt-catalyzed C(sp^2)–C(sp^2) coupling using Grignard reagents are limited to the followings except for ref 1. a) T. J. Korn, G. Cahiez, P. Knochel, *Synlett* **2003**, 1892. b) T. J. Korn, M. A. Schade, M. N. Cheemals, S. Wirth, S. A. Guevara, G. Cahiez, P. Knochel, *Synthesis* **2006**, 3547. c) T. Hatakeyama, M. Nakamura, *J. Am. Chem. Soc.* **2007**, *129*, 9844.

4 Many reports, predominantly by Oshima and co-workers, are available for the cobalt-catalyzed coupling of Grignard reagents with C(sp^3) electrophiles. For alkyl halides: a) T. Tsuji, H. Yorimitsu, K. Oshima, *Angew. Chem., Int. Ed.* **2002**, *41*, 4137. b) H. Ohmiya, T. Tsuji, H. Yorimitsu, K. Oshima, *Chem.—Eur. J.* **2004**, *10*, 5640. c) H. Ohmiya, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2006**, *128*, 1886. d) H. Ohmiya, K. Wakabayashi, H. Yorimitsu, K. Oshima, *Tetrahedron* **2006**, *62*, 2207. e) A. Kuno, N. Saino, T. Kamachi, S. Okamoto, *Tetrahedron Lett.* **2006**, *47*, 2591. f) H. Ohmiya, H. Yorimitsu, K. Oshima, *Org. Lett.* **2006**, *8*, 3093. For the coupling of alkyl halides accompanied by insertion of a carbon–carbon unsaturated bond, see: g) K. Wakabayashi, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2001**, *123*, 5374. h) K. Mizutani, H. Shinokubo, K. Oshima, *Org. Lett.* **2003**, *5*, 3959. i) H. Someya, H. Ohmiya, H. Yorimitsu, K. Oshima, *Org. Lett.* **2007**, *9*, 1565. j) H. Someya, H. Ohmiya, H. Yorimitsu, K. Oshima, *Tetrahedron* **2007**, *63*, 8609. For allyl methoxides: k) K. Mizutani, H. Yorimitsu, K. Oshima, *Chem. Lett.* **2004**, *33*, 832. l) H. Yasui, K. Mizutani, H. Yorimitsu, K. Oshima, *Tetrahedron* **2006**, *62*, 1410.

5 The coupling of 2-methyl-1-propenylmagnesium bromide with styryl bromide in the presence of 5 mol % of Co(acac)$_2$ at 60–65 °C for 15 min gave 60% yield of the coupling product. See ref 1b.

6 E. Shirakawa, T. Sato, Y. Imazaki, T. Kimura, T. Hayashi, *Chem. Commun.* **2007**, 4513.

7 For the examples of the cobalt-catalyzed coupling of alkenyl halides, see ref 1. See also: a) T. Kamachi, A. Kuno, C. Matsuno, S. Okamoto, *Tetrahedron Lett.* **2004**, *45*, 4677. b) W. Affo, H. Ohmiya, T. Fujioka, Y. Ikeda, T. Nakamura, H. Yorimitsu, K. Oshima, Y. Imamura, T. Mizuta, K. Miyoshi, *J. Am. Chem. Soc.* **2006**, *128*, 8068.

8 Supporting Information, which contains experimental details including characterization data, is also available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

9 Under several similar conditions, *p*-tolyl triflate coupled with phenylmagnesium bromide in yields less than 15%.

10 In the reaction of the 5- and 6-membered cyclic triflates, low conversions were observed even in a longer reaction period. Cyclohexenyl triflate is a rather poor electrophile also in the cobalt-catalyzed coupling with alkynyl Grignard reagents. See ref 6.

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