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Cobalt-Catalyzed Three-Component Coupling Reaction of Alkyl Halides, 1,3-Dienes, and Trimethylsilylmethylmagnesium Chloride

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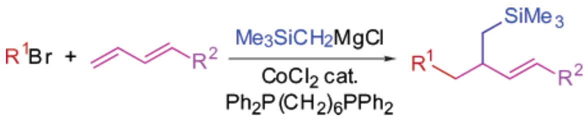
ABSTRACT



A combination of $CoCl_2$ and 1,6-bis(diphenylphosphino)hexane catalyzes a novel three-component coupling reaction of alkyl bromides, 1,3-dienes, and silylmethylmagnesium chloride, yielding homoallylsilanes in good to excellent yields. The reaction involves a radical species from alkyl halides.

In recent years, cobalt-catalyzed carbon−carbon bond formation with organometallic reagents has received increasing attention.[1] Cahiez and Knochel have demonstrated the ability of cobalt complexes as a catalyst in the cross-coupling reaction between aryl halides and organomagnesium and organozinc species. We have also reported that a cobalt−phosphine complex catalyzes a Heck-type reaction of alkyl halides with styrenes in the presence of trimethylsilylmethylmagnesium chloride.[2] During the course of our research on cobalt-catalyzed novel reactions, we have found that the use of 1,3-dienes in place of styrene resulted in a formation of unexpected three-component coupling products.[3] Herein we wish to describe a synthesis of homoallylsilanes from 1,3-dienes, alkyl halides, and a silylmethylmagnesium Grignard reagent under cobalt catalysis.

Trimethylsilylmethylmangnesium chloride (1.0 M ether solution, 1.0 mL, 1.0 mmol) was added to a mixture of cyclohexyl bromide (0.75 mmol) and 1-phenyl-1,3-butadiene (**1a**, 0.5 mmol)[4] in ether (3 mL) in the presence of $CoCl_2$ (0.025 mmol) and 1,6-bis(diphenylphosphino)hexane ($Ph_2P(CH_2)_6PPh_2$ (dpph) 0.025 mmol) at 0 °C. The resulting mixture was then stirred for 5 h at 25 °C. After aqueous workup, silica gel column purification afforded (*E*)-4-cyclohexyl-1-phenyl-3-trimethylsilylmethyl-1-butene (**2a**) in 87% yield with high regio- and stereoselectivity (E/Z = >99/1).

The choice of the phosphine ligand is crucial for the successful reaction. The use of 1,6-bis(diphenylphosphino)hexane (dpph) provided the best result among phosphine ligands we examined. Other diphosphines, 1,5-bis(diphenylphosphino)pentane and 1,4-bis(diphenylphosphino)butane (dppb) afforded **2a** in 75% and 65% yield, respectively. In contrast, 1,3-bis(diphenylphosphino)propane (dppp) gave only a trace amount of the desired coupling product **2a** under

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(1) (a) Cahiez, G.; Avedissian, H. *Tetrahedron Lett.* **1998**, *39*, 6159. (b) Avedissian, H.; Berillon, L.; Cahiez, G.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 6163. (c) Nishii, Y.; Wakasugi, K.; Tanabe, Y. *Synlett* **1998**, 67. (d) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc*. **2001**, *123*, 5374. (e) Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 4137. (f) Clark, A. J.; Davies, D. I.; Jones, K.; Millbanks, C. *J. Chem. Soc., Chem. Commun.* **1994**, 41. (g) Uemura, S.; Fukuzawa, S.; Patil, S. R. *J. Organomet. Chem*. **1983**, *243*, 9. (h) Kneisel, F. F.; Monguchi, Y.; Knapp, K. M.; Zipse, H.; Knochel, P. *Tetrahedron Lett.* **2002**, *43*, 4875. (i) Holzer, B.; Hoffmann, R. W. *Chem. Commun.* **2003**, 732.

(2) (a) Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc*. **2002**, *124*, 6514. (b) Fujioka, T.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *Org. Lett*. **2002**, *4*, 2257.

(3) For reviews on multicomponent-coupling reactions, see: (a) Weber, L.; Illgen, K.; Almetetter, M. *Synlett* **1999**, 366. (b) Bienaymé, H.; Hulme, C.; Oddon, G.; Schmitt, P. *Chem. Eur. J*. **2000**, *6*, 3321. (c) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed*. **2000**, *39*, 3168.

(4) A mixture of stereoisomer (E/Z = 40/60) was employed. The geometry of the starting material seems not to be essential. The use of the pure *E*-isomer provided almost the same result.

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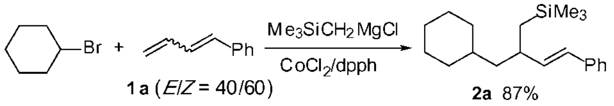
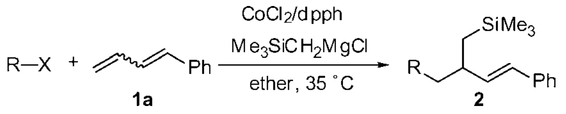
the same reaction conditions. 1,2-Bis(diphenylphosphino)ethane and bis(diphenylphosphino)methane afforded a complex mixture. The reaction did not take place at all in the presence of monophosphine ligands such as PPh_3 or in the absence of ligands.[5] Whereas it took 5 h for completion of the reaction with dpph at 25 °C, full conversion was accomplished within 30 min at 35 °C (ether reflux).

Scheme 1



Next we examined the use of various alkyl halides in the three-component coupling reaction using 1-phenyl-1,3-butadiene and trimethylsilylmethylmagnesium chloride in the presence of the $CoCl_2/Ph_2P(CH_2)_6PPh_2$ catalyst combination. The results are summarized in Table 1. Several characteristics of this reaction are noteworthy. Not only secondary bromides but also primary and tertiary bromides provided the corresponding coupling products in good to excellent yields. As for halides, bromides are the choice. The use of cyclohexyl iodide instead of bromide yielded **2a** in rather reduced yield. Furthermore, alkyl chlorides such as cyclohexyl chloride did not react at all under the same reaction conditions, and the chloride was recovered unchanged completely. Another silylmethyl Grignard reagent, $PhMe_2SiCH_2MgCl$, also effected the three-component coupling reaction, yielding the corresponding product **2f** (entry 7). Unfortunately, the use of other alkyl and aryl Grignard reagents provided none of the desired three-component coupling products[6]

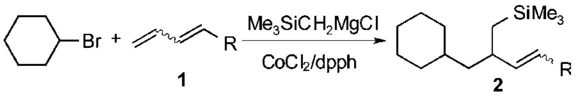
Table 1. Three-Component Coupling Reaction with Various Alkyl Halides[a]



entry	R−X	time (h)	product	yield (%)
1	n-$C_9H_{19}Br$	2	**2b**	84
2	2-bromooctane	0.5	**2c**	87
3	t-BuBr	0.5	**2d**	87
4	1-bromoadamantane	0.5	**2e**	93
5	c-$C_6H_{11}I$	2	**2a**	60
6	c-$C_6H_{11}Cl$	2	**2a**	nr[b]
7	c-$C_6H_{11}Br$	0.5	**2f**	91[c]

[a] RX (0.75 mmol), **1a** (0.5 mmol), $CoCl_2$ (0.025 mmol), dpph (0.025 mmol), Me_3SiCH_2MgCl (1.0 mmol), and ether (3.0 mL) were employed. [b] No reaction proceeded and cyclohexyl chloride was recovered. [c] $PhMe_2SiCH_2MgCl$ was used instead of Me_3SiCH_2MgCl.

Table 2. Three-Component Coupling Reaction with Various 1,3-Dienes[a]

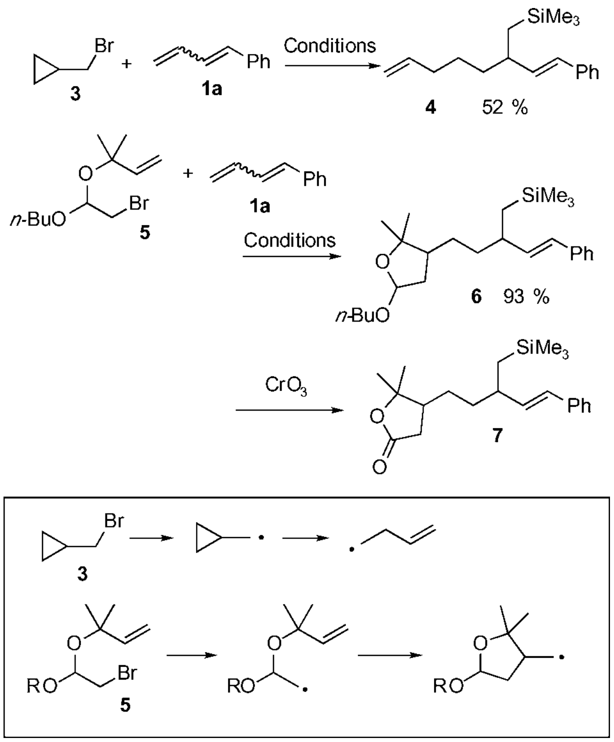


entry	R	product	yield (%) (selectivity)
1	p-$MeOC_6H_4$	**2g**	99 (E/Z = >99/1)
2	o-BrC_6H_4	**2h**	72 (E/Z = >99/1)
3	m-ClC_6H_4	**2i**	78 (E/Z = >99/1)
4	n-C_9H_{19}	**2j**	(85)[b]
5	c-$C_6H_{11}CH_2$	**2k**	85 (57/43)[c]
6	n-$C_9H_{19}CH{=}CH$	**2l**	93 (58/42)[c]
7	$PhMe_2Si$	**2m**	97 (E/Z = 92/8)

[a] Cyclohexyl bromide (0.75 mmol), 1,3-diene (0.5 mmol), $CoCl_2$ (0.025 mmol), dpph (0.025 mmol), Me_3SiCH_2MgCl (1.0 mmol), and ether (3.0 mL) were employed. [b] The product was obtained as a mixture of isomers of which the ratio could not be determined. [c] The stereochemistry of the isomers could not be assigned.

We next examined several 1,3-dienes to clarify the scope and limitations of this reaction (Table 2). 1-Aryl-1,3-dienes that have an electron-donating group or an electron-withdrawing group on the benzene ring worked equally well to provide **2** in good to excellent yields. In addition, the reaction tolerates chloride and bromide in the substrates (entries 2 and 3). An aliphatic diene, trideca-1,3-diene,

Scheme 2[a]



[a] Conditions: RX (0.75 mmol), **1a** (0.5 mmol), $CoCl_2$ (0.025 mmol), dpph (0.025 mmol), Me_3SiCH_2MgCl (1.0 mmol), and ether (3.0 mL) were employed.

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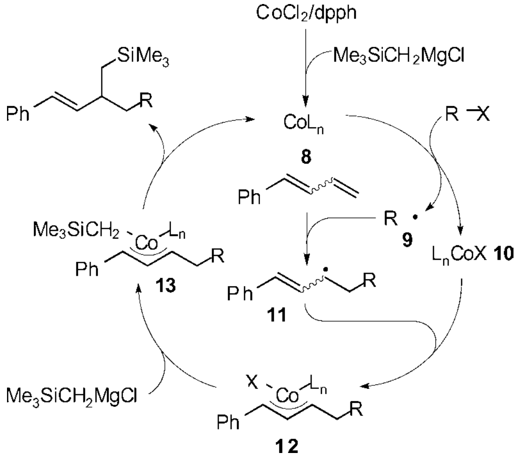
[5] At the present time, we do not know the exact nature of the catalyst combination of $CoCl_2$/dpph, i.e., whether dpph acts as a bidentate or monodentate ligand to the cobalt center.

yielded an inseparable mixture of regioisomers in 85% yield (entry 4). The use of 2,4-pentadienylcyclohexane as a substrate, which does not give rise to a problem associated with regioisomerism, furnished the expected homoallylsilane **2k** in good yield (entry 5). Pentadeca-1,3,5-triene provided the corresponding coupling product **2l** in excellent yield without the formation of its regioisomer (entry 6). The reaction with 1-aryl-1,3-dienes exhibited high stereoselectivity with regard to the newly formed double bond, and the (*E*)-isomers were formed exclusively. In contrast, the formation of the *Z*-isomer in addition to the *E*-isomer was observed in other cases.

To elucidate the reaction mechanism, the following two reactions were carried out (Scheme 2). Treatment of cyclopropylmethyl bromide **3** with 1-phenyl-1,3-butadiene **1a** exclusively yielded 1-phenyl-3-trimethylsilylmethyl-1,7-octadiene **4**, which was derived via the cleavage of the cyclopropane ring. In addition, starting from bromo acetal **5**, the cyclization-coupling product **6**, which has a tetrahydrofuran ring, was obtained in excellent yield. These experimental results strongly suggest that the reaction involves some radical species from the alkyl halides employed.[7] Now we propose the following reaction mechanism depicted in Scheme 3. An addition of trimethylsilylmethylmagnesium chloride to the mixture of $CoCl_2$ and $Ph_2P(CH_2)_6PPh_2$ provides low valent cobalt species **8**. Single electron transfer from cobalt complex **8** to an alkyl halide yields L_nCoX and an alkyl radical **9**, which then attacks to 1-phenyl-1,3-butadiene, yielding allylic radical **10**. Recombination of the radical **11** with cobalt species **10** affords π-allylcobalt complex **12**.[8] Allylcobalt **12** is alkylated with Me_3SiCH_2MgCl. The complex **13** eventually collapses to the coupling product via reductive elimination on the cobalt center and regenerates low valent cobalt complex **8**.[9]

Scheme 3. Proposed Reaction Pathway



In conclusion, we have developed a cobalt-catalyzed novel three-component coupling reaction of alkyl bromides, 1,3-dienes, and trimethylsilylmethylmagnesium chloride. The reaction requires the use of 1,6-bis(diphenylphosphino)-hexane as the phosphine ligand.

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

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[6] We examined the reaction with PhMgBr, MeMgI, EtMgBr, *n*-BuMgBr, and $CH_2{=}CHCH_2MgCl$ and could not obtain the corresponding coupling products.

[7] (a) Newcomb, M. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 1, Chapter 3.1. (b) Newcomb, M.; Choi, S. Y.; Horner, J. H. *J. Org. Chem.* **1999**, *64*, 1225. (c) Beckwith, A. L. J.; Glover, S. A. *Aust. J. Chem.* **1987**, *40*, 157.

[8] For the formation of allylmetals via the addition of alkyl radicals to 1,3-dienes, see: (a) Takai, K.; Matsukawa, N.; Takahashi, A.; Fujii, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 152. (b) Terao, J.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1998**, *39*, 9697. (c) Nii, S.; Terao, J.; Kambe, N. *J. Org. Chem.* **2000**, *65*, 5291.

[9] For coupling reactions involving allylcobalt species, see: (a) Gomes, P.; Gosmini, C.; Périchon, J. *J. Org. Chem.* **2003**, *68*, 1142. (b) Gomes, P.; Gosmini, C.; Périchon, J. *Org. Lett.* **2003**, *5*, 1043. See also ref 1e.