

Cobalt-Catalyzed Allylic Substitution Reaction of Allylic Ethers with Phenyl and Trimethylsilylmethyl Grignard Reagents

Keiya Mizutani, Hideki Yorimitsu, and Koichiro Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510

(Received April 6, 2004; CL-040375)

Treatment of cinnamyl methyl ether with phenylmagnesium bromide in ether in the presence of CoCl_2 [1,5-bis(diphenylphosphino)pentane] affords 1,3-diphenylpropene in good yield. Similar allylic substitution reaction with trimethylsilylmethylmagnesium chloride proceeded smoothly to yield homoallylsilanes. α,β -Unsaturated aldehyde acetal also underwent allylic substitution.

Palladium-catalyzed allylic substitution is recognized as one of the most useful reactions catalyzed by transition metal complexes.¹ On the other hand, cobalt-catalyzed allylic substitutions have scarcely been studied, where enolates were employed as nucleophiles.^{2,3} We have been interested in cobalt-phosphine complexes-catalyzed reactions.⁴ During the course of our study, we felt that the combination of cobalt salts, phosphine ligands, and Grignard reagents deserves further investigation and that allylic substitution reaction is a suitable probe. Here we report the reaction of allylic ether with phenyl and trimethylsilylmethyl Grignard reagents in the presence of cobalt-phosphine complexes.

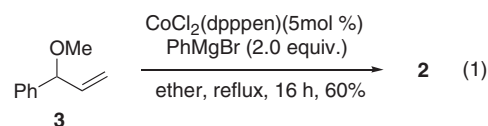
The reaction of cinnamyl methyl ether (**1**) with phenyl Grignard reagent was first examined (Table 1). In the previous report on the cross-coupling reaction of alkyl halide with ArMgBr , 1,2-bis(diphenylphosphino)ethane (DPPE) was the choice of the ligand.^{4a} For the allylic substitution reaction, DPPE was not suitable and linear product **2** was obtained in only 15% yield (Entry 1). A variety of ligands were surveyed and 1,5-bis(diphenylphosphino)pentane (DPPPEN) was found to be the most effective for this reaction. 3,3-Diphenyl-1-propene was not detected in every experiment.

Table 1. Reaction of cinnamyl ether **1** with PhMgBr

$\text{Ph}-\text{CH}=\text{CH}-\text{CH}_2-\text{OMe} \xrightarrow[\text{ether, reflux, 16 h}]{\text{CoCl}_2(\text{ligand}) (5 \text{ mol } \%), \text{PhMgBr} (2.0 \text{ equiv.})} \text{Ph}-\text{CH}=\text{CH}-\text{CH}_2-\text{Ph}$		
Entry	Ligand ^a	Yield / %
1	DPPE	15
2	None	29
3	PPh_3 (10 mol %)	30
4	DPPM	24
5	DPPP	27
6	DPPB	50
7	DPPPEN	72
8	DPPH	58

^aLigands DPPM–DPPH represent $\text{Ph}_2\text{P}(\text{CH}_2)_n\text{PPh}_2$, $n = 1$, DPPM; $n = 2$, DPPE; $n = 3$, DPPP; $n = 4$, DPPB; $n = 5$, DPPPEN; $n = 6$, DPPH.

Reactions at ambient temperature decreased the yield of **2**. The choice of the solvent was essential to obtain **2** in satisfactory yield. Reaction in THF gave rise to very low conversion of **1**. It is worth noting that treatment of cinnamyl bromide under similar conditions gave a mixture of dimeric compounds such as 1,6-diphenyl-1,5-hexadiene and 3,4-diphenyl-1,5-hexadiene in addition to a trace of **2**. The formation of the dimeric products suggests that single electron transfer from a cobalt complex yields the cinnamyl radical intermediate. Starting from branched ether **3**, **2** was obtained in comparable yield (Eq 1).



Treatment of (*E*)-2-octenyl methyl ether (**4**) with phenylmagnesium bromide in the presence of CoCl_2 (dpppen) afforded a mixture of the corresponding coupling products **5**, **6**, and **7** in very poor yields (Table 2, Entry 1). Under the reaction conditions, a part of **5** was transformed into **6**. Without any phosphine ligand, coupling products were obtained in moderate yield (Entry 2). Instead, triphenylphosphine proved to be the best ligand for the reaction of **4** (Entry 4). Other monodentate phosphine ligands were inferior to triphenylphosphine (Entries 5–8).

Under the reaction conditions of Entry 4 in Table 2, **8** was also converted into **5** and **7** (Eq 2). No isomerization of **5** into **6** was observed in this reaction.

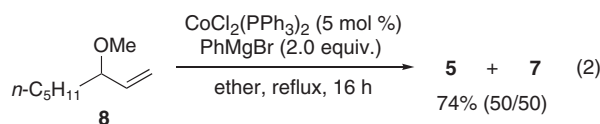


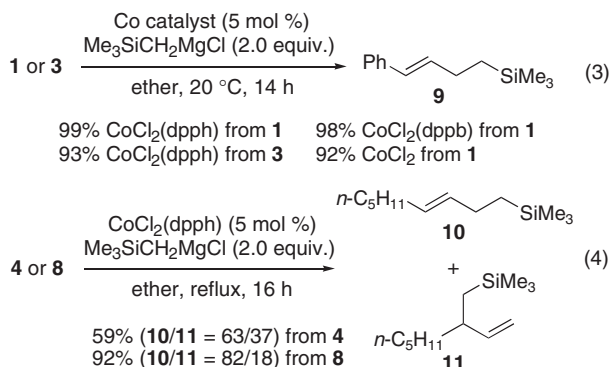
Table 2. Reaction of (*E*)-2-octenyl ether **4** with PhMgBr

$\text{R}-\text{CH}=\text{CH}-\text{CH}_2-\text{OMe} \xrightarrow[\text{ether, reflux, 16 h}]{\text{CoCl}_2(\text{ligand}) (5 \text{ mol } \%), \text{PhMgBr} (2.0 \text{ equiv.})} \begin{matrix} \text{R}-\text{CH}=\text{CH}-\text{CH}_2-\text{Ph} \\ \text{R}-\text{CH}(\text{Ph})-\text{CH}=\text{CH}_2 \end{matrix}$			
Entry	Ligand	Yield / % ^a	5/6/7
1	DPPPEN	12	N.D. ^b
2	—	47	58/10/32
3	DPPE	32	10/53/37
4	PPh_3 ^c	78	36/7/57
5	$\text{P}(2\text{-MeC}_6\text{H}_4)_3$ ^c	39	66/<1/33
6	$\text{P}(4\text{-MeC}_6\text{H}_4)_3$ ^c	49	42/6/52
7	$\text{P}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_3$ ^c	trace	N.D. ^b
8	$\text{P}(4\text{-MeOC}_6\text{H}_4)_3$ ^c	41	31/16/53

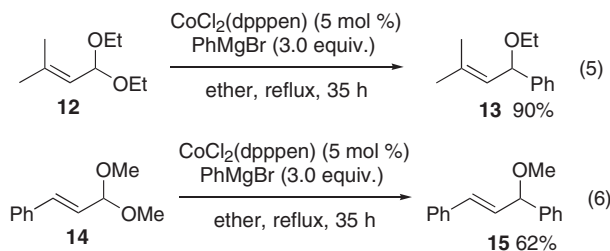
^aCombined yield of **5**, **6**, and **7**. ^bNot determined.

^c10 mol % of monodentate phosphines were used.

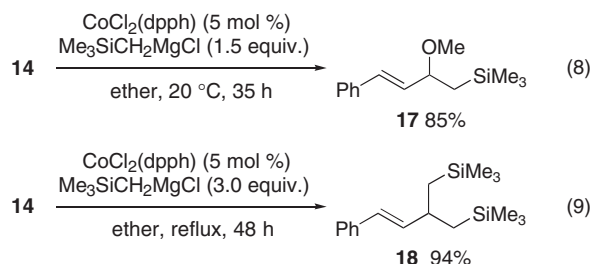
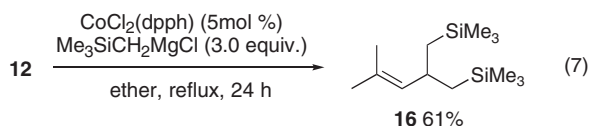
Allylic substitution reaction with $\text{Me}_3\text{SiCH}_2\text{MgCl}$ was facile. Treatment of **1** with $\text{Me}_3\text{SiCH}_2\text{MgCl}$ in the presence of $\text{CoCl}_2(\text{dppe})$ for 14 h at 20 °C afforded a linear product **9** in 99% yield (Eq 3).⁵ Whereas the choice of the ligand was crucial to establish phenylation, ligandless CoCl_2 and $\text{CoCl}_2(\text{dppe})$ also catalyzed the trimethylsilylmethylation to afford **9** in 92 and 98% yields, respectively. Reactions of **3** with $\text{Me}_3\text{SiCH}_2\text{MgCl}$ afforded **9** in excellent yield. On the other hand, alkyl-substituted allylic ethers **4** and **8** were converted into mixtures of regioisomers **10** and **11** (Eq 4). The reaction required a higher temperature to complete within a satisfactory reaction time. Trimethylsilylmethylation of branched ether **8** afforded higher yields of **10** and **11** than the reaction of **4**.



Treatment of acetals **12** and **14** with phenyl Grignard reagent in the presence of $\text{CoCl}_2(\text{dppe})$ afforded the corresponding monophenylated allylic ethers **13** and **15**, respectively (Eqs 5 and 6). The dimethyl and phenyl groups would interfere with second phenylation.



In contrast to the reaction with phenyl Grignard reagent, bis-trimethylsilylmethylation occurred in the reaction of **12** with three equimolar amounts of the Grignard reagent in refluxing ether (Eq 7). Interestingly, in the reaction of **14**, we could control the distribution of the product by changing the amount of the Grignard reagent and reaction time (Eqs 8 and 9). Reaction with 1.5 equiv. amounts of the Grignard reagent at ambient temperature for 35 h afforded monosubstituted product **17** in 85% yield. On the other hand, use of three equiv. amounts of the Grignard reagent resulted in generation of doubly substituted product **18** in 94% yield after 48 h reaction at reflux.



In summary, we have demonstrated allylic substitution reaction of allylic ethers with Grignard reagents under cobalt catalysis. The cobalt-catalyzed reaction with phenyl Grignard reagent proved to be a function of a substrate as well as of solvent and ligand. To attain high yields in the phenylation reaction, intensive tunings of variants are essential. In contrast, introduction of a trimethylsilylmethyl group was facile and clean under cobalt catalysis.

References and Notes

- a) J. Tsuji, *Acc. Chem. Res.*, **2**, 144 (1969). b) J. Tsuji, *Pure Appl. Chem.*, **54**, 197 (1982). c) B. M. Trost and D. L. Van Vranken, *Chem. Rev.*, **96**, 395 (1996). d) J. Tsuji, *J. Organomet. Chem.*, **300**, 281 (1986).
- a) B. Bhatia, M. M. Reddy, and J. Iqbal, *Tetrahedron Lett.*, **34**, 6301 (1993). b) P. A. Grieco, W. J. DuBay, and L. J. Todd, *Tetrahedron Lett.*, **37**, 8707 (1996).
- Cobalt-mediated direct electrochemical coupling of aryl halides with allylic esters was reported. P. Gomes, C. Gosmini, and J. Périchon, *J. Org. Chem.*, **68**, 1142 (2003).
- a) K. Wakabayashi, H. Yorimitsu, and K. Oshima, *J. Am. Chem. Soc.*, **123**, 5374 (2001). b) Y. Ikeda, H. Yorimitsu, and K. Oshima, *J. Am. Chem. Soc.*, **124**, 6514 (2002). c) T. Fujioka, T. Nakamura, H. Yorimitsu, and K. Oshima, *Org. Lett.*, **4**, 2257 (2002). d) T. Tsuji, H. Yorimitsu, and K. Oshima, *Angew. Chem., Int. Ed.*, **41**, 4137 (2002). e) K. Mizutani, H. Shinokubo, and K. Oshima, *Org. Lett.*, **5**, 3959 (2003).
- Experimental Procedure:** Anhydrous CoCl_2 (7 mg, 0.05 mmol) was placed in a 50-mL two-necked flask and heated with a hair dryer in vacuo for 3 min. DPPH (27 mg, 0.06 mmol) and ether (1 mL) were sequentially added under argon. After the mixture was stirred for 30 min to obtain blue suspension, cinnamyl methyl ether (**1**, 0.15 g, 1.0 mmol) and $\text{Me}_3\text{SiCH}_2\text{MgCl}$ (1.0 M in ether, 2.0 mL, 2.0 mmol) were successively added to the reaction mixture at 0 °C. After being stirred for 14 h at 20 °C, the reaction mixture was poured into saturated NH_4Cl solution. The products were extracted with ethyl acetate (20 mL $\times$ 3) and the combined organic layer was dried over sodium sulfate and concentrated. Silica gel column purification of the crude product provided **9** (0.20 g, 0.99 mmol) in 99% yield as colorless oil.