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

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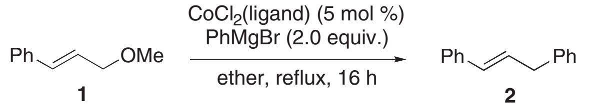
Treatment of cinnamyl methyl ether with phenylmagnesium bromide in ether in the presence of $CoCl_2$[1,5-bis(diphenylphosphino)pentane] affords 1,3-diphenylpropene in good yield. Similar allylic substitution reaction with trimethylsilylmethylmagnesium chloride proceeded smoothly to yield homoallylsilanes. $\alpha,\beta$-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.

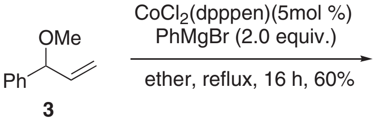
**Table 1.** Reaction of cinnamyl ether 1 with PhMgBr



| 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 |

[a] Ligands DPPM–DPPH represent $Ph_2P(CH_2)_nPPh_2$, $n = 1$, DPPM; $n = 2$, DPPE; $n = 3$, DPPP; $n = 4$, DPPB; $n = 5$, DPPPEN; $n = 6$, DPPH.

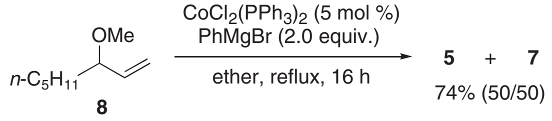
Reactions at ambient temperature decreased the yield of **2**. The choice of the solvent was essential to obtain **2** in satisfactory yield. Reaction in THF gave rise to very low conversion of **1**. It is worth noting that treatment of cinnamyl bromide under similar conditions gave a mixture of dimeric 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).



(1)

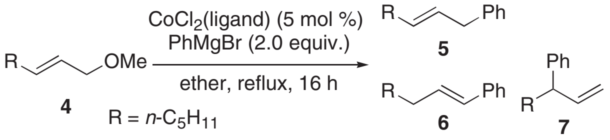
Treatment of (*E*)-2-octenyl methyl ether (**4**) with phenylmagnesium bromide in the presence of $CoCl_2$(dpppen) afforded a mixture of the corresponding coupling products **5**, **6**, and **7** in very poor yields (Table 2, Entry 1). Under the reaction conditions, a part of **5** was transformed into **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.



(2)

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



| 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 | $P(2\text{-}MeC_6H_4)_3$[c] | 39 | 66/<1/33 |
| 6 | $P(4\text{-}MeC_6H_4)_3$[c] | 49 | 42/6/52 |
| 7 | $P[3,5\text{-}(CF_3)_2C_6H_3]_3$[c] | trace | N.D.[b] |
| 8 | $P(4\text{-}MeOC_6H_4)_3$[c] | 41 | 31/16/53 |

[a] Combined yield of **5**, **6**, and **7**. [b] Not determined.
[c] 10 mol % of monodentate phosphines were used.

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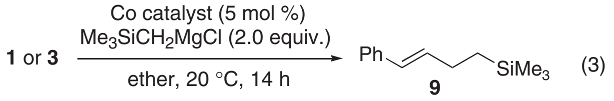
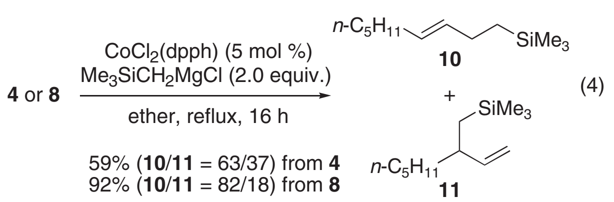
Allylic substitution reaction with $Me_3SiCH_2MgCl$ was facile. Treatment of **1** with $Me_3SiCH_2MgCl$ in the presence of $CoCl_2$(dpph) for 14 h at 20 °C afforded a linear product **9** in 99% yield (Eq 3).[5] Whereas the choice of the ligand was crucial to establish phenylation, ligandless $CoCl_2$ and $CoCl_2$(dppb) also catalyzed the trimethylsilylmethylation to afford **9** in 92 and 98% yields, respectively. Reactions of **3** with $Me_3SiCH_2MgCl$ 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**.

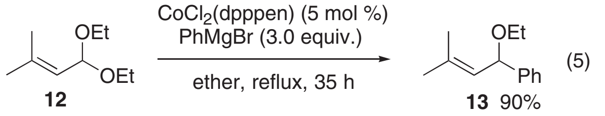


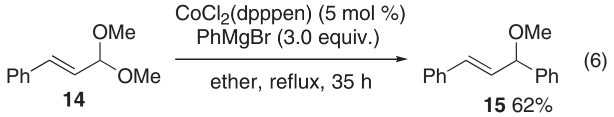
99% $CoCl_2$(dpph) from **1** 98% $CoCl_2$(dppb) from **1**
93% $CoCl_2$(dpph) from **3** 92% $CoCl_2$ from **1**



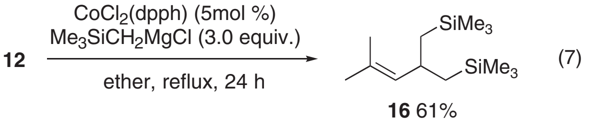
59% (**10**/**11** = 63/37) from **4**
92% (**10**/**11** = 82/18) from **8**

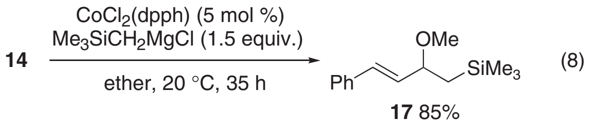
Treatment of acetals **12** and **14** with phenyl Grignard reagent in the presence of $CoCl_2$(dpppen) afforded the corresponding monophenylated allylic ethers **13** and **15**, respectively (Eqs 5 and 6). The dimethyl and phenyl groups would interfere with second phenylation.

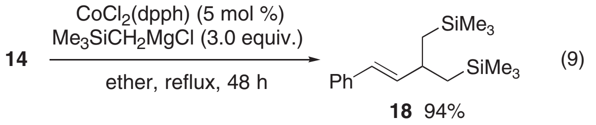




In contrast to the reaction with phenyl Grignard reagent, bistrimethylsilylmethylation occurred in the reaction of **12** with three equimolar amounts of the Grignard reagent in refluxing ether (Eq 7). Interestingly, in the reaction of **14**, we could control the distribution of the product by changing the amount of the Grignard reagent and reaction time (Eqs 8 and 9). Reaction with 1.5 equimolar 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 equimolar 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

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5 **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 $Me_3SiCH_2MgCl$ (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 × 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.

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