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# Studies on Synthetic Methods of Grignard Reagents Involving C-C Bond Formation by Using Transition Metal Catalysts

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Osaka University

2009

# Studies on Synthetic Methods of Grignard Reagents Involving C-C Bond Formation by Using Transition Metal Catalysts

(遷移金属触媒を用いた炭素－炭素結合形成を伴うグリニャール試薬の合成法に関する研究)

**Yuuki Fujii**

**Osaka University**

**2009**

# Preface

The study described in this thesis have been carried out (2003-2009) under the direction of Professor Nobuaki Kambe at Department of Applied Chemistry, Graduate School of Engineering, Osaka University. The objective of this thesis is concerned with studies on synthetic methods of Grignard reagents involving C-C bond formation by using transition metal catalysts.

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Chapter 4 Titanocene-Catalyzed Alkylative Dimerization of Vinyl Grignard Reagents Using Alkyl Halides

# General Introduction

The first organomagnesium compounds (Grignard reagents) were synthesized by Grignard in 1900 by a reaction of organic halides with metallic magnesium.[1] This simple and efficient method for the synthesis of Grignard reagents has been still widely employed in synthetic practice.[2] The Grignard reagents are used to create new C-C bonds for the syntheses of various classes of organic compounds. The preparation of Grignard reagents has been subjects of numerous publications.[2-7]

One of novel non-traditional approach to the synthesis of organomagnesium reagents is addition of ordinary Grignard reagents to unsaturated compounds (carbomagnesiation). However, it has been known that carbomagnesiation requires particular substrates and harsh conditions.[6] During the last quarter century, transition-metal catalysts have been found to facilitate this type reaction under mild conditions.[7]

This thesis describes transition-metal catalyzed carbomagnesiation using substrates which had rarely been employed in conventional catalytic system (chapters 1 and 2) and new type carbomagnesiation that carbon moieties derived from electrophiles are introduced to butadiene formed by vinyl Grignard reagents and transition-metal catalysts (chapters 3 and 4). In chapter 1, palladium catalyzed regioselective carbomagnesiation of aryl allenes is described. In chapter 2, silver-catalyzed carbomagnesiation of terminal aryl and silyl alkynes and enynes in the presence of 1,2-dibromoethane is described. In chapter 3, nickel-catalyzed dimerization coupling reactions of vinyl Grignard reagents with 3,4-membered cyclic ethers. In chapter 4, titanocene-catalyzed alkylative dimerization of vinyl Grignard reagents using alkyl halides is described.

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# Chapter 1

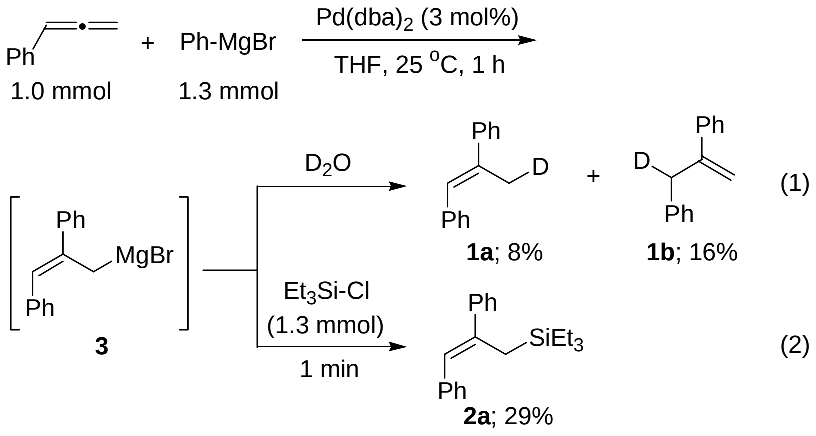
# Palladium-Catalyzed Regioselective Carbomagnesiation of Aryl Allenes

## 1-1. Introduction

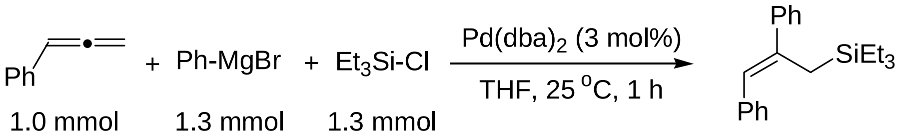
The addition of Grignard reagents across carbon-carbon unsaturated bond is a principal and important reaction in organic syntheses for the generation of Grignard reagents having desired carbon skeletons. It have been known that alkenes and alkynes undergo carbomagnesiation in the presence of various transition-metal catalysts.[1] On the contrary, there have been only few reports for transition-metal catalyzed carbomagnesiation of allenes.[2] Oshima *et al.* have reported that manganese catalyzes regioselective allylmagnesiation of allenes to form vinyl Grignard reagents.[2a] However, to date, carbomagnesiation of allenes leading to allyl Grignard reagents has not been achieved. Here, I report that carbomagnesiation of aryl allenes proceeded regioselectively to form allyl Grignard reagents by the aid of palladium catalyst.

## 1-2. Results and Discussion

To a mixture of phenylallene (1.0 mmol), Ph-MgBr (1.3 mmol) in THF (1.3 mL) was added Pd(dba)$_2$ (dba = dibenzylideneacetone) (0.03 mmol) at 25 $^{o}$C under nitrogen, and the resulting mixture was stirred for 1 hour at the same temperature. Quenching the reaction mixture with $D_2O$ gave a 30:70 mixture of arylated compounds **1a** and **1b** which contain a deuterium at an allylic position in 27% total yield (Eq. 1). When the same reaction mixture was treated with $Et_3SiCl$ instead of $D_2O$, carbosilylated product **2** was obtained in 29% with high regio- and stereoselectivities (Eq. 2). These results suggest the formation of carbomagnesation product **3** in the present reaction.



When I carried out this reaction in the presence $Et_3SiCl$ under the same condition, yield of **2a** dramatically increased to 92% (Eq. 3). The product was obtained in pure form in 67% yield by column chlomatography with hexane as an eluent. In this reaction, only a trace amount of $Et_3SiPh$ (2%) was formed as a byproduct probably through the direct reaction of $Et_3SiCl$ and PhMgBr.

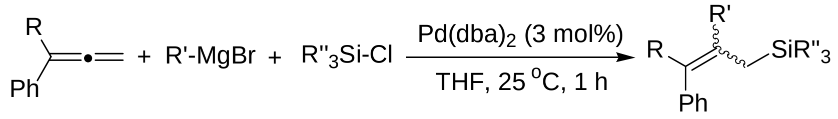


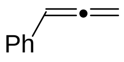
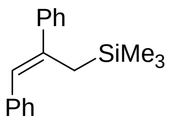
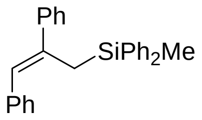
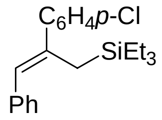
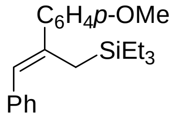
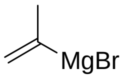
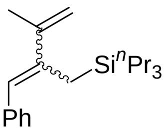
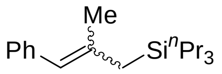
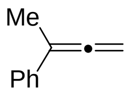
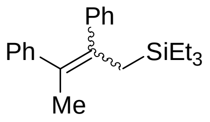
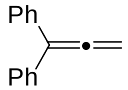
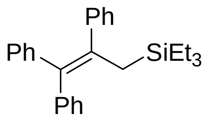
(3)

**2a**; 92% [*E*/*Z* = 1/99]

Carbosilylation also proceeded efficiently when $Me_3SiCl$ and $Ph_2MeSiCl$ were used (Table 1, entries 1 and 2). Chloro and methoxy substituents on the aryl ring remained intact in this reaction system (entries 3 and 4). The use of vinyl and methyl Grignard reagents also afforded the corresponding coupling products **2e** and **2f** in 72% and 51% yield, respectively (entries 5 and 6) although the stereoisomers were obtained. $\alpha$-Methyl and phenyl substituted phenylallenes also underwent present coupling reaction (entries 7 and 8). The reaction was sluggish with respect to alkylallenes.

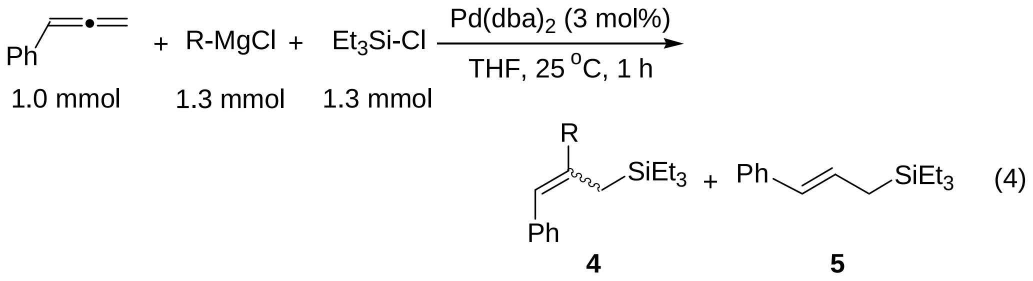
**Table 1**: Palladium-catalyzed carbosilylation of aryl allenes with Grignard reagents and chlorosilanes[a]



| Entry | Allene | R'-MgBr | R"$_3$Si-Cl | Product | | Yield (%)[d] | *E/Z*[e] |
|---|---|---|---|---|---|---|---|
| 1 |  | Ph-MgBr | $Me_3Si$-Cl |  | **2b** | 89 | 2/98 |
| 2 | | Ph-MgBr | $Ph_2MeSi$-Cl |  | **2c** | 82 (68) | 2/98 |
| 3 | | *p*-Cl-$C_6H_4$-MgBr | $Et_3Si$-Cl |  | **2d** | 90 (80) | 1/99 |
| 4 | | *p*-OMe-$C_6H_4$-MgBr | $Et_3Si$-Cl |  | **2e** | 87 (75) | 1/99 |
| 5[b] | |  | $^nPr_3Si$-Cl |  | **2f** | (72) | 30/70 |
| 6[b] | | Me-MgBr | $^nPr_3Si$-Cl |  | **2g** | 53 (51) | 84/16 |
| 7[c] |  | Ph-MgBr | $Et_3Si$-Cl |  | **2h** | 84 (72) | 93/7 |
| 8 |  | Ph-MgBr | $Et_3Si$-Cl |  | **2i** | 50 (38) | |

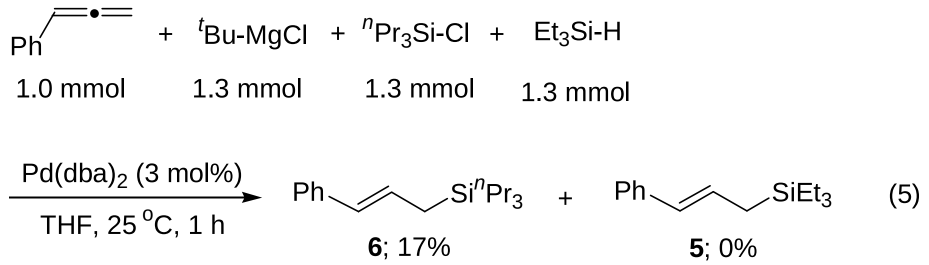
[a] The reaction was carried out unless otherwise stated in THF at 25 °C for 1 h using arylallene (1.0 mmol), Grignard reagent (1.3 mmol), chlorosilane (1.3 mmol), and $Pd(dba)_2$ (0.03 mmol). [b] Grignard reagent and chlorosilane were used in 1.5 mmol. [c] The reaction was carried out for 9 h. [d] NMR yield. Isolated yield is in parentheses. [e] Determined by GC.

When *n*-butyl Grignard reagent was used, expected carbosilylated product **4a** was obtained in 76% yield along with 8% yield of hydrosilylated product **5** (Eq. 4). *s*-Butyl Grignard reagent gave nearly 1:1 mixure of **4b** and **5**. Hydrosilylated product was predominantly obtained when *t*-butyl Grignard reagent was employed. The yields of **5** increase in the order of primary < secondary < tertiary reflecting the number of *β*-hydrogens.

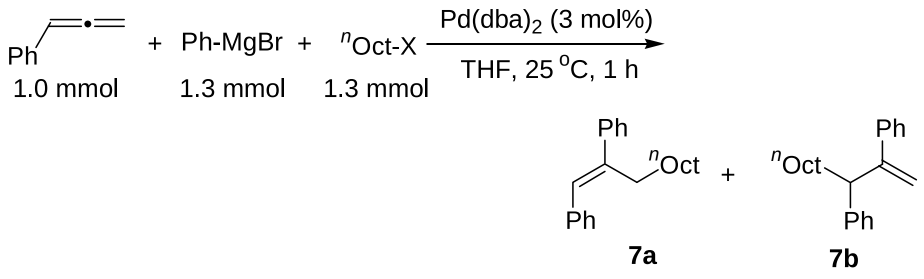


| Entry | R | Yield (%) |  |
|---|---|---|---|
|  |  |  | **5** |
| 1 | $^n$Bu | **4a**; 76 [*E*/*Z* = 4/96] | 8 |
| 2 | $^s$Bu | **4b**; 30 [E/Z = 0/100] | 36 |
| 3 | $^t$Bu | **4c**; 2 | 62 |

I carried out control experiments in order to prove the hydrogen source for the formation of **5**. When the reaction mixture of eq. 4 using *t*-BuMgCl was quenched with $D_2O$ before work-up, deuterated **5** was not obtained at all. This result would rule out the formation of silylmagnesation intermediate. Since it is known that a palladium complex catalyzes hydrosilylation of allenes to give allylsilanes,[3] I next examined whether a similar hydrosilylation process is involved in the present reaction. When a reaction similar to that in entry 3 of eq. 4 was carried out in the presence of $^n\mathrm{Pr_3SiCl}$ and $\mathrm{Et_3SiH}$, only **6** having $^n\mathrm{Pr_3Si}$ group was obtained as silylated product and 84% of $\mathrm{Et_3SiH}$ was recovered (Eq. 5). These results suggest that hydrogen would be derived from alkyl group of Grignard reagents.



Use of 1-bromooctane instead of chlorosilanes yielded three component coupling products **7a** and **7b** in 24% and 51% yields, respectively (Eq. 6). Under the same conditions, 1-chlorooctane gave low yields of coupling products. It should be noted that the present reaction proceeds efficiently in the case of alkyl fluorides with superior yields and regioselectivities compared with other halides.[4]

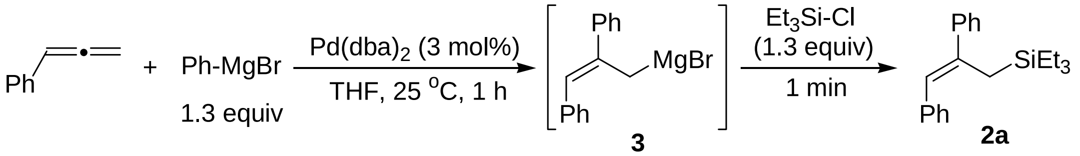


(6)

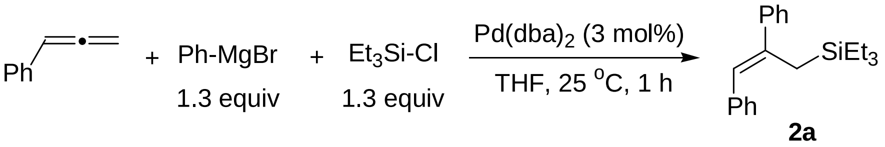
| | 7a | 7b |
|---|---|---|
| X = Br | 24% | 51% |
| X = Cl | 6% | 19% |
| X = F | 11% | 73% |

To investigate reaction mechanism, I examined the time course of the Pd-catalyzed reaction of phenylallene with phenyl Grignard reagent in the absence (Eq. 7) and presence (Eq. 8) of $Et_3SiCl$. Into a mixture of phenylallene (0.5 mmol) and PhMgBr (0.65 mmol) was added Pd(dba)$_2$ (0.015 mmol) and the mixture was stirred for 1, 3, 5, 7, 10 or 15 min. After trapping the formed product with $Et_3SiCl$ at 25 °C for 1 min, the reaction was quenched with 1N HCl. The yield of **2a** for the reaction of eq 7 was plotted in Figure 1 together with the result of the catalytic reaction depicted in eq 8 where the reaction was carried out in the presence of $Et_3SiCl$ and quenched directly with 1N HCl. The evidence that the yield of **2a** increases linearly indicates that the rate of formation of **2a** is independent on the concentration of substrates. On the other hand, forming rate of **2a** in eq 7 decreased against reaction time. At any stage of the reaction, **2a** was formed more efficiently in the catalytic system than in eq 7. These results would indicate that more reactive species than **3** are formed in catalytic system.

Plausible reaction pathways are shown in Scheme 1. The reaction of Pd(dba)$_2$ with aryl allenes affords allene-palladium complexes **8**,[5] which reacts with Grignard reagents to give palladate complexes **9**.[6] Direct reaction of palladate complexes **9** with chrolosilanes or alkyl halides at terminal or benzylic carbon leads to palladium (II) complexes **10** (*Path A*). The subsequent reductive coupling of these palladium (II) complexes **10** gives silylated or alkylated products **11** and regenerates Pd(0) to complete the catalytic cycle. The result of Figure 1 indicates that reductive elimination from **10** is the rate determining step. Alternatively, transmetalation of **8** with Grignard reagents via **9** gives carbomagnesation product **12**, which is trapped with chlorosilanes or alkyl halides to afford **11** (*Path B*). Silyl groups are introduced regioselectively at the terminal position of intermediates **9** or **12** due probably to the steric effect. When highly branched alkyl Grignard reagents are used, $\beta$-hydrogen elimination of **10** leading to hydrosilylation products predominates over the reductive coupling to form **11**.



(7)



(8)

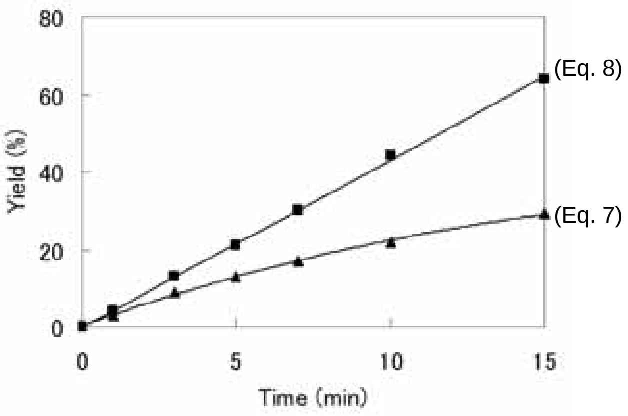
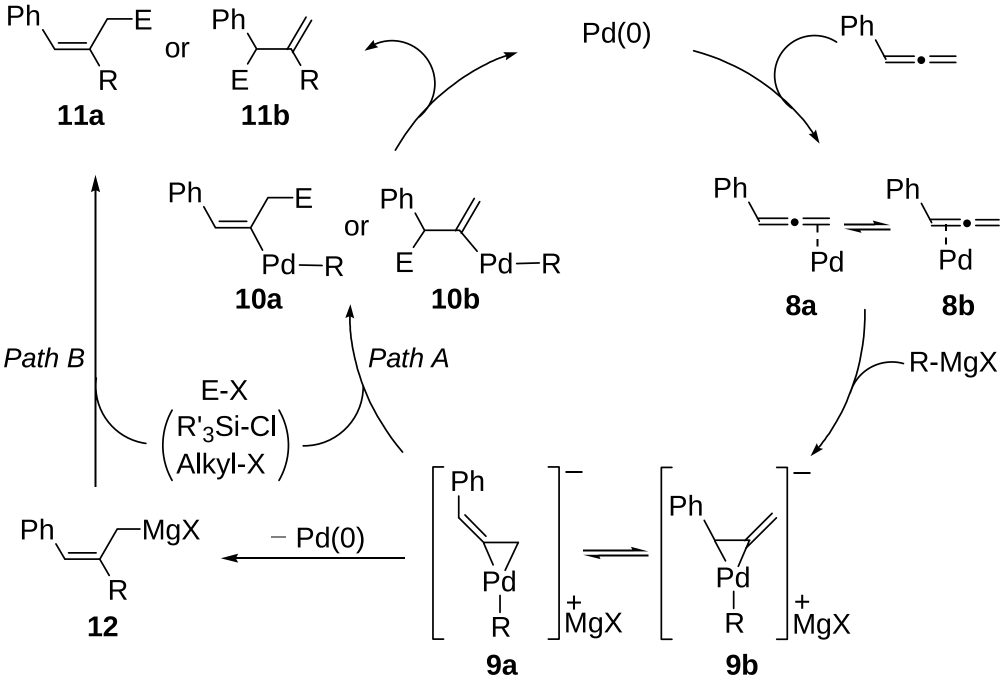


**Figure 1**. Time course of the formation of **2a** in Eq. 7 and 8



**Scheme 1**. Plausible reaction pathways

## 1-3. Conclusion

In conclusion, I have disclosed that palladium catalyzes regioselective carbomagnesiation of allenes to form allyl Grignard reagents. In the presence of chlorosilanes and alkyl halides, silylation and alkylation of allenes proceeded efficiently via the formation of palladate complexes or allyl Grignard reagents.

## 1-4. Experimental Section

### General Comments

$^1$H NMR and $^{13}$C NMR spectra were recorded with a JEOL JNM-Alice 400 (400 MHz and 100 MHz, respectively) spectrometer. Chemical shifts are reported in parts per million ($\delta$) downfield from internal tetramethylsilane. Infrared spectra were recorded with a Perkin-Elmer FT-IR (Model 1600). Both conventional and high resolution mass spectra were recorded with a JEOL JMS-DX303HF spectrometer. GC Mass spectra (EI) were obtained using a JMS-mate operating in the electron impact mode (70 eV) equipped with a RTX-5 30MX.25MMX.25U column. HPLC separations were performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using $CHCl_3$ as an eluent. Column chromatography was conducted using Kanto Chemical Co., Inc. silica gel 60 (63-210 $\mu$m). Elemental analyses were performed on a Perkin Elmer 240C apparatus. GC yields were determined using decane as an internal standard. Grignard reagents (Kanto Chemical Company), triethylchlorosilane, triethylsilane (Shin-Etsu Chemical Company), trimethylchlorosilane, tripropylchlorosilane, methyldiphenylchlorosilane, octyl fluoride (Aldrich Chemical Company), octyl chloride, octyl bromide, $D_2O$ (Wako Pure Chemical Industries), $Pd(dba)_2$ (Tokyo Chemical Industry Company) were purchased and used as received. Arylallenes were prepared according to the literature.[7]

### Procedures and Characterization of Reaction Products

### General procedure

To a mixture of aryl allenes (1.0 mmol), chlorosilanes or alkyl halides (0.22 mL, 1.3 mmol) and Grignard reagent (1.3 mmol) was added $Pd(dba)_2$ (0.03 mmol) at 25 $^{o}$C under nitrogen. After stirring for 1 h, aqueous 1N HCl was added and the products were extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to give crude products. Purification by column chromatography on silica gel with hexane as the eluent afforded the corresponding products.

**(*Z*)-1,2-Diphenyl-3-triethylsilyl-1-propene (2a)**

IR(NaCl): 3055, 3022, 2952, 2874, 1598, 1494, 1456, 1446, 1414, 1237, 1156, 1004, 822 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.46-7.19 (m, 10H), 6.51 (s, 1H), 2.33 (s, 2H), 0.76 (t, *J* = 8.0 Hz, 9H), 0.34 (q, *J* = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): 145.1, 141.5, 138.7, 128.6, 128.0, 126.9, 126.7, 125.9, 125.52, 125.50, 17.0, 7.4, 4.1; MS (EI) *m*/*z* (relative intensity, %): 308 ($M^+$, 38), 279 (6), 116 (11), 115 (100), 107 (6), 88 (7), 87 (70), 59 (22); HRMS calcd for $C_{21}H_{28}Si$: 308.1960, found 308.1965; Anal. Calcd for $C_{21}H_{28}Si$: C, 81.75; H, 9.15. Found: C, 81.48; H, 9.21.

**(*Z*)-3-Methyldiphenylsilyl-1,2-diphenyl-1-propene (2c)**

IR(KBr): 3051, 3023, 2959, 1612, 1598, 1491, 1445, 1427, 1254, 1151, 1110, 989, 833, 789, 766, 735, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.53-7.09 (m, 20H), 6.57 (s, 1H), 2.84 (s, 2H), 0.23 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): 144.2, 139.9, 138.2, 136.5, 134.3, 129.0, 128.5, 127.96, 127.95, 127.5, 127.0, 126.81, 126.75, 126.0, 19.5, -3.5; MS (EI) *m*/*z* (relative intensity, %): 390 ($M^+$, 10), 199 (5), 198 (19), 197 (100), 181 (2), 165 (2), 119 (2), 105 (4); HRMS calcd for $C_{28}H_{26}Si$: 390.1804, found 390.1801; Anal. Calcd for $C_{28}H_{26}Si$: C, 86.10; H, 6.71. Found: C, 85.81; H, 6.63.

**(*Z*)-2-(4-Chlorophenyl)-1-phenyl-3-triethylsilyl-1-propene (2d)**

IR(NaCl): 3055, 3024, 2953, 2874, 1618, 1598, 1494, 1456, 1414, 1237, 1156, 1093, 1014, 818, 747, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40-7.20 (m, 9H), 6.49 (s, 1H), 2.29 (s, 2H), 0.77 (t, *J* = 8.0 Hz, 9H), 0.34 (q, *J* = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): 143.5, 140.3, 138.4, 132.6, 128.6, 128.12, 128.07, 127.9, 126.1, 126.0, 16.9, 7.4, 4.1; MS (EI) *m*/*z* (relative intensity, %): 342 ($M^+$, 19), 313 (3), 117 (4), 116 (13), 115 (100), 88 (7), 87 (74), 59 (25); HRMS calcd for $C_{21}H_{27}ClSi$: 342.1571, found 342.1568; Anal. Calcd for $C_{21}H_{27}ClSi$: C, 73.54; H, 7.93. Found: C, 73.47; H, 7.89.

**(*Z*)-2-(4-Methoxyphenyl)-1-phenyl-3-triethylsilyl-1-propene (2e)**

IR(NaCl): 3021, 2952, 2874, 1607, 1510, 1464, 1415, 1285, 1247, 1179, 1038, 1004, 824, 749, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39-7.34 (m, 6H), 7.22-7.16 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.47 (s, 1H), 3.83 (s, 3H), 2.30 (s, 2H), 0.77 (t, *J* = 8.0 Hz, 9H), 0.35 (q, *J* = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): 158.6, 140.9, 138.9, 137.5, 128.6, 128.0, 127.7, 125.7, 124.4, 113.3, 55.3, 16.9, 7.4, 4.1; MS (EI) *m*/*z* (relative intensity, %): 338 ($M^+$, 52), 310 (2), 309 (7), 137 (6), 117 (7), 116 (12), 115 (100), 88 (8), 87 (86), 59 (29); HRMS calcd for $C_{22}H_{30}OSi$: 338.2066, found 338.2068.

### (*Z*)-3-Methyl-1-phenyl-2-[(tripropylsilyl)methyl]-1,3-butadiene (2f)

IR(NaCl): 3023, 2954, 2924, 2867, 1603, 1460, 1409, 1373, 1332, 1203, 1150, 1068, 1005, 888, 840, 743, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.34-7.14 (m, 5H), 6.50 (s, 1H), 5.12 (s, 1H), 5.04 (s, 1H), 2.07 (s, 2H), 2.03 (s, 3H), 1.21-1.11 (m, 6H), 0.86 (t, *J* = 7.2 Hz, 9H), 0.43-0.39 (m, 6H); NOE difference measurement: irradiation of vinyl proton at δ 6.50 caused 8.5% enhancement of methyl protons at δ 2.03, irradiation of methyl protons at δ 2.03 caused 5.2 % enhancement of vinyl proton at δ 6.50; $^{13}$C NMR (100 MHz, $CDCl_3$): 145.2, 140.7, 139.1, 128.8, 127.9, 125.8, 124.0, 113.2, 21.8, 20.2, 18.8, 17.4, 16.2; MS (EI) *m*/*z* (relative intensity, %): 314 (M$^+$, 26), 158 (11), 157 (84), 145 (8), 116 (14), 115 (100), 87 (21), 73 (38), 59 (11), 45 (16); HRMS calcd for $C_{21}H_{34}Si$: 314.2430, found 314.2437.

### (*E*)-2-Methyl-1-phenyl-3-tripropylsilyl-1-propene (2g)

IR(NaCl): 3022, 2954, 2925, 2868, 1640, 1493, 1454, 1409, 1374, 1333, 1202, 1158, 1068, 1008, 816, 743, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.30-7.12 (m, 5H), 6.13 (s, 1H), 1.87 (d, *J* = 1.2 Hz, 3H), 1.84 (d, *J* = 0.8 Hz, 2H), 1.30-1.20 (m, 6H), 0.90 (t, *J* = 7.2Hz, 9H), 0.52-0.48 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): 139.2, 137.7, 128.4, 127.9, 125.2, 122.6, 27.6, 19.7, 18.8, 17.5, 16.3; MS (EI) *m*/*z* (relative intensity, %): 288 (M$^+$, 17), 245 (4), 161 (5), 159 (6), 158 (12), 157 (82), 116 (12), 115 (100), 87 (21), 73 (39), 59 (13), 45 (15); HRMS calcd for $C_{19}H_{32}Si$: 288.2273, found 288.2283; Anal. Calcd for $C_{19}H_{32}Si$: C, 79.09; H, 11.18. Found: C, 79.01; H, 11.26.

### (*E*)-2,3-Diphenyl-1-triethylsilyl-2-butene (2h)

IR(NaCl): 3055, 3019, 2952, 2874, 1599, 1489, 1442, 1414, 1236, 1159, 1017, 967, 762, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.06-6.91 (m, 10H), 2.13 (s, 3H), 2.10 (s, 2H), 0.82 (t, *J* = 0.8 Hz, 9H), 0.40 (t, *J* = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): 144.9, 144.3, 135.8, 129.7, 129.3, 129.2, 127.22, 127.16, 125.4, 125.0, 21.9, 21.7, 7.4, 4.2; MS (EI) *m*/*z* (relative intensity, %): 322 (M$^+$, 29), 293 (7), 116 (12), 115 (100), 107 (5), 88 (8), 87 (78), 59 (26); HRMS calcd for $C_{22}H_{30}Si$: 322.2117, found 322.2112; Anal. Calcd for $C_{22}H_{30}Si$: C, 81.92; H, 9.37. Found: C, 81.92; H, 9.28.

**3-Triethylsilyl-1,1,2-triphenyl-1-propene (2i)**

IR(KBr): 3053, 3020, 2950, 2873, 1598, 1492, 1442, 1413, 1237, 1191, 1072, 1019, 762, 701 cm$^{-1}$; $^{1}$H NMR (400 MHz, CDCl$_3$): δ 7.35-6.88 (m, 15H), 2.04 (s, 2H), 0.77 (t, $J$ = 8.0 Hz, 9H), 0.33 (q, $J$ = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): 143.6, 143.5, 143.1, 138.6, 136.2, 130.6, 129.6, 129.5, 128.0, 127.4, 127.1, 126.1, 126.0, 125.2, 22.0, 7.5, 4.2; MS (EI) *m*/*z* (relative intensity, %): 384 (M$^+$, 34), 355 (4), 191 (5), 116 (11), 115 (100), 107 (7), 91 (6), 88 (6), 87 (66), 59 (22); HRMS calcd for $C_{27}H_{32}Si$: 384.2273, found 384.2282.

**(*Z*)-1-Phenyl-2-[(triethylsilyl)methyl]-1-hexene (4a)**

IR (NaCl): 3055, 3022, 2952, 2930, 2873, 1636, 1598, 1492, 1465, 1414, 1238, 1156, 1016, 750 cm$^{-1}$; $^{1}$H NMR (400 MHz, CDCl$_3$): δ 7.30-7.22 (m, 4H), 7.15-7.12 (m, 1H), 6.12 (s, 1H), 2.11 (t, $J$ = 7.2 Hz, 2H), 1.86 (s, 2H), 1.55-1.47 (m, 2H), 1.37 (qt, $J$ = 7.2 Hz, 2H), 0.94 (t, $J$ = 7.2 Hz, 3H), 0.86 (t, $J$ = 8.0 Hz, 9H), 0.51 (q, $J$ = 8.0 Hz, 6H); NOE difference measurement: irradiation of vinyl proton at δ 6.12 caused 5.4% enhancement of methylene protons at δ 2.11 (-$CH_2$-$^n$Pr), irradiation of methylene protons at δ 2.11 (-$CH_2$-$^n$Pr) caused 5.3% enhancement of vinyl proton at δ 6.12; $^{13}$C NMR (100 MHz, CDCl$_3$): δ 141.7, 139.3, 128.5, 127.9, 125.2, 121.8, 40.1, 30.8, 22.7, 16.8, 14.3, 7.5, 4.4; MS (EI) *m*/*z* (relative intensity, %): 288 (M$^+$, 16), 259 (4), 117 (4), 116 (11), 115 (100), 88 (6), 87 (68), 59 (19); HRMS calcd for $C_{19}H_{32}Si$: 288.2273, found 288.2277; Anal. Calcd for $C_{19}H_{32}Si$: C, 79.09; H, 11.18. Found: C, 78.80; H, 11.03.

**(*Z*)-3-Methyl-1-phenyl-2-[(triethylsilyl)methyl]-1-pentene (4b)**

IR(NaCl): 3056, 3022, 2956, 2874, 1636, 1598, 1494, 1460, 1415, 1377, 1238, 1154, 1017, 749, 698 cm$^{-1}$; $^{1}$H NMR (400 MHz, CDCl$_3$): δ 7.30-7.22 (m, 4H), 7.14-7.11 (m, 1H), 6.09 (s, 1H), 2.01-1.91 (m, 2H), 1.78 (d, $J$ = 13.2 Hz, 1H), 1.68-1.58 (m, 1H), 1.46-1.35 (m, 1H), 1.12 (d, $J$ = 6.8 Hz, 3H), 0.93 (t, $J$ = 7.2 Hz, 3H), 0.85 (t, $J$ = 8.0 Hz, 9H), 0.85 (q, $J$ = 8.0 Hz, 6H); NOE difference measurement: irradiation of vinyl proton at δ 6.09 caused 5.7% enhancement of methyl protons at δ 1.12 ($CH_3$-CH), irradiation of methyl protons at δ 1.12 ($CH_3$-CH) caused 2.7 % enhancement of vinyl proton at δ 6.09; $^{13}$C NMR (100 MHz, CDCl$_3$): 146.7, 139.5, 128.6, 127.8, 125.1, 119.5, 42.9, 29.3, 19.4, 17.7, 12.2, 7.5, 4.4; MS (EI) *m*/*z* (relative intensity, %): 288 (M$^+$, 16), 259 (4), 117 (4), 116 (11), 115 (100), 88 (6), 87 (65), 59 (19); HRMS calcd for $C_{19}H_{32}Si$: 288.2273, found 288.2280; Anal. Calcd for $C_{19}H_{32}Si$: C, 79.09; H, 11.18. Found: C, 78.80; H, 11.15.

**(*E*)-1-phenyl-3-tripropylsilyl-1-propene (6)**

IR (NaCl): 2954, 2867, 1641, 1599, 1496, 1460, 1408, 1332, 1146, 1067, 960, 738 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.33-7.10 (m, 5H), 6.24-6.21 (m, 2H), 1.68 (m, 2H), 1.36 (tq, *J* = 7.3, 7.1 Hz, 6H), 0.96 (t, *J* = 7.1 Hz, 9H), 0.58-0.54 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.4, 128.3, 128.0, 127.9, 126.0, 125.3, 20.2, 18.8, 17.6, 15.3; MS (EI) *m*/*z* (relative intensity, %): 274 (M$^+$, 13), 157 (90), 115 (100), 87 (24), 73 (43); HRMS calcd for $C_{18}H_{30}Si$: 274.2117, found 274.2108; Anal. Calcd for $C_{18}H_{30}Si$: C, 78.75; H, 11.02. Found: C, 78.58; H, 10.92.

**(*E*)-1,2-Diphenyl-1-undecene (7a)**

IR (NaCl): 3053, 3021, 2954, 2854, 1598, 1494, 1465, 1443, 1074, 1029, 918, 759, 696 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.47-7.23 (m, 10H), 6.69 (s, 1H), 2.69 (t, *J* = 7.6 Hz, 2H), 1.45-1.38 (m, 2H), 1.28-1.21 (m, 12H), 0.87 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 143.2, 142.9, 138.2, 128.6, 128.2, 128.1, 127.9, 126.9, 126.4, 126.3, 32.0, 30.3, 29.8, 29.6, 29.5, 29.4, 28.8, 22.8, 14.3; MS (EI) *m*/*z* (relative intensity, %): 306 (M$^+$, 100), 194 (93), 193 (84), 179 (43), 178 (38), 129 (14), 117 (21), 116 (40), 115 (70), 103 (13), 91 (68); HRMS calcd for $C_{23}H_{30}$: 306.2348, found 306.2352.

**2,3-Diphenyl-1-undecene (7b)**

IR (NaCl): 3080, 3023, 2924, 2852, 1626, 1600, 1493, 1451, 1074, 1028, 899, 777, 697 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.38-7.13 (m, 10H), 5.37 (s, 1H), 5.17 (s, 1H), 3.75 (t, *J* = 7.6 Hz, 1H), 1.93-1.85 (m, 1H), 1.81-1.73 (m, 1H), 1.43-1.22 (m, 12H), 0.86 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 151,7, 143.5, 142.5, 128.03, 127.95, 127.8, 126.9, 126.6, 125.9, 113,0 50.5, 35.3 32.0, 29.8, 29.6, 29.4, 28.1, 22.8, 14.3; MS (EI) *m*/*z* (relative intensity, %): 306 (M$^+$, 10), 195 (16), 194 (100), 193 (45), 179 (14), 178 (14), 117 (9), 115 (31), 105 (9), 103 (9), 91 (45); HRMS calcd for $C_{23}H_{30}$: 306.2348, found 306.2343; Anal. Calcd for $C_{23}H_{30}$: C, 90.13; H, 9.87. Found: C, 89.88; H, 9.60.

**CAS registry numbers of other compounds known in the literature.**

**2b**, 221280-63-3; **5**, 63522-98-5.

## 1-5. References

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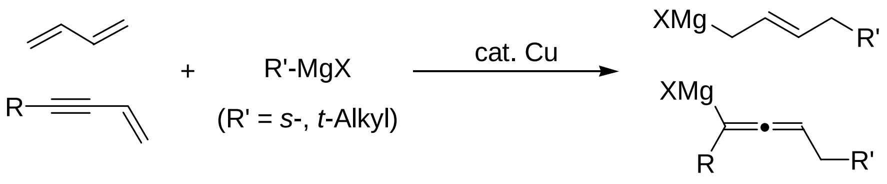
# Chapter 2

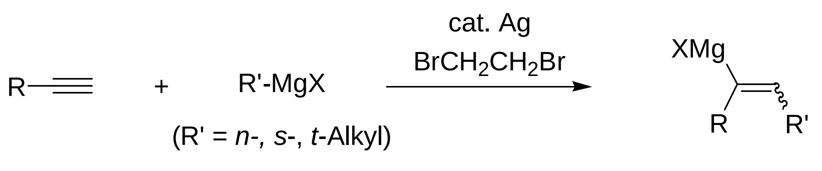
## Silver-Catalyzed Carbomagnesiation of Terminal Aryl and Silyl Alkynes and Enynes in the Presence of 1,2-Dibromoethane

### 2-1. Introduction

Transition-metal catalyzed carbomagnesiation of carbon-carbon multiple bonds is a useful and attractive method for the preparation of Grignard reagents with concomitant construction of the desired carbon skeletons via new carbon-carbon bond formation.[1] To date, addition of aryl,[2] vinyl,[3] allyl,[4] and primary-alkyl[5] magnesium compounds toward carbon-carbon unsaturated bonds have been accomplished by the aid of various transition-metal catalysts. However, the use of secondary and tertiary-alkyl Grignard reagents had so far been limited mostly to the reaction of activated alkynes or the ones having a hetero atom directing group[6] until our discovary that Cu catalyzes carbomagnesiation of unfunctionalized dienes and enynes with secondary and tertiary alkyl Grignard reagents giving rise to conjugated allyl or allenyl Grignard reagents (Eq 1).[7] If the similar addition to alkynes proceeds, vinyl Grignard reagents can be formed. However, the Cu-catalyzed system was not effective toward such transformation. Here, I disclose silver catalyzed regioselective carbomagnesiation of terminal alkynes with alkyl Grignard reagents in the presence of 1,2-dibromoethane (Eq 2). This reaction can also be applied to enynes.



(1)



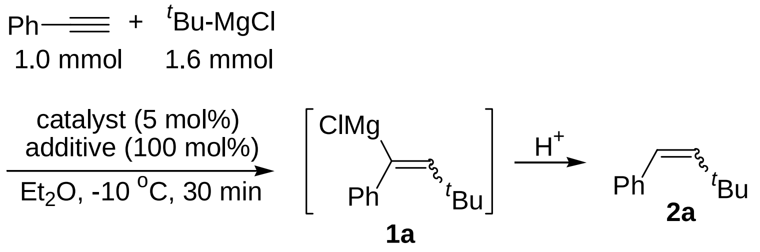
(2)

### 2-2. Results and Discussion

When the reaction of phenylacetylene (1.0 mmol) with $^t$Bu-MgCl (1.6 mmol) was conducted in the presence of AgOTs (0.05 mmol) in $Et_2O$ at –10 °C for 30 min and the reaction was quenched by aqueous HCl, the hydroalkylation product **2a** was obtained in

28% yield ($E/Z$ = 1/99) (Table 1, entry 1). Addition of $PPh_3$ or $P(p\text{-}C_6H_4Cl)_3$ increased the yield of **2a** and gave a byproduct $^t$Bu-$^t$Bu in 4% yield (entries 2 and 3). The latter may be formed by reductive coupling of *tert*-alkyl silver complex intermediates.[8] This process reduces Ag(I) to Ag(0) and may terminate the catalytic cycle. Hayashi *et al.* have reported that 1,2-dibromoethane acts as reoxidizing reagent of Ag(0) complex to Ag(I) in the silver catalyzed homo-coupling reaction of alkyl Grignard reagents.[9] So I reexamined the reaction in the presence of 1,2-dibromoethane (100 mol%) under the same conditions as entries 1–3 and found that the yields of **2a** were significantly improved as shown in entries 4–6. The use of (IMes)AgCl (IMes=1,3-dimesitylimidazol-2-ylidene)[10] as a catalyst, afforded **2a** in 98% GC yield (entry 7). The product was obtained in pure form in 88% yield by silica gel column chromatography. When the amount of 1,2-dibromoethane was reduced to 50 mol%, the yield of **2a** decreased to 88% yield (entry 8). 1,2-Dichloroethane and 1,2-diiodoethane were less efficient than 1,2-dibromoethane, and formed **2a** in 34% and 17% yields, respectively (entries 9 and 10).

**Table 1**. Silver-catalyzed carbomagnesiation of phenylacetylene with $^t$Bu-MgCl[a]

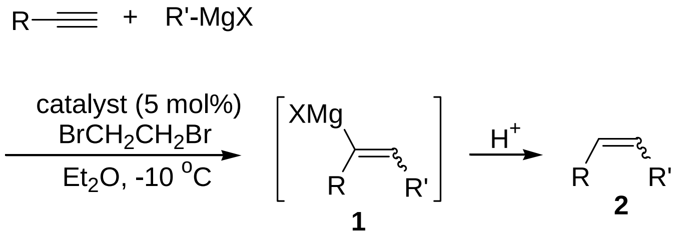


| Entry | Catalyst | Additive | Yield (%)[b] | $E/Z$ |
|---|---|---|---|---|
| 1 | AgOTs | none | 28 | 1/99 |
| 2 | AgOTs + $PPh_3$ | none | 59 | 2/98 |
| 3 | AgOTs + $P(p\text{-}C_6H_4Cl)_3$ | none | 58 | 3/97 |
| 4 | AgOTs | $BrCH_2CH_2Br$ | 76 | 2/98 |
| 5 | AgOTs + $PPh_3$ | $BrCH_2CH_2Br$ | 79 | 6/94 |
| 6 | AgOTs + $P(p\text{-}C_6H_4Cl)_3$ | $BrCH_2CH_2Br$ | 86 | 4/96 |
| 7 | (IMes)AgCl | $BrCH_2CH_2Br$ | 98 (88) | 2/98 |
| 8[c] | (IMes)AgCl | $BrCH_2CH_2Br$ | 88 | 1/99 |
| 9 | (IMes)AgCl | $ClCH_2CH_2Cl$ | 34 | 1/99 |
| 10 | (IMes)AgCl | $ICH_2CH_2I$ | 17 | 8/92 |

[a] Condition: Ag catalyst (0.05 mmol), phenylacetylene (1.0 mmol), Additive (100 mol%), $^t$Bu-MgCl (1.6 mmol), -10 $^oC$, 30 min. [b] GC yield. Isolated yield is in parentheses. [c] Additive (50 mol%) was used.

Results of the present silver catalyzed carbomagnesiation using other substrates are shown in Table 2. The present carbomagnesiation was applicable to *p*-, *m*- and *o*-methyl substituted phenylacetylene under the conditions of (IMes)AgCl/Br$(CH_2)_2$Br catalytic system (condition A) (Table 2, entries 1–3). Methoxy and trifluoromethyl group on aryl ring did not affect the yield of products significantly (entries 4–5). Thienyl alkyne also underwent carbomagnesiation giving rise to the corresponding alkenes in 65% isolated yield (entry 6). $^s$Bu-MgCl also added to phenylacetylene to give **2h** in 59% yield under the same conditions (entry 7). Combined use of AgOTs (5 mol%) and P(*p*-$C_6H_4Cl)_3$ (5 mol%) was more suitable for *sec*-butylmagnesiation than (IMes)AgCl and gave **2h** in 81% yield (entry 8, Condition B). Under the identical conditions, $^c$Hex-MgCl also smoothly underwent carbomagnesiation to afford **2i** in 83%

**Table 2**. Silver-catalyzed carbomagnesiation of terminal alkynes



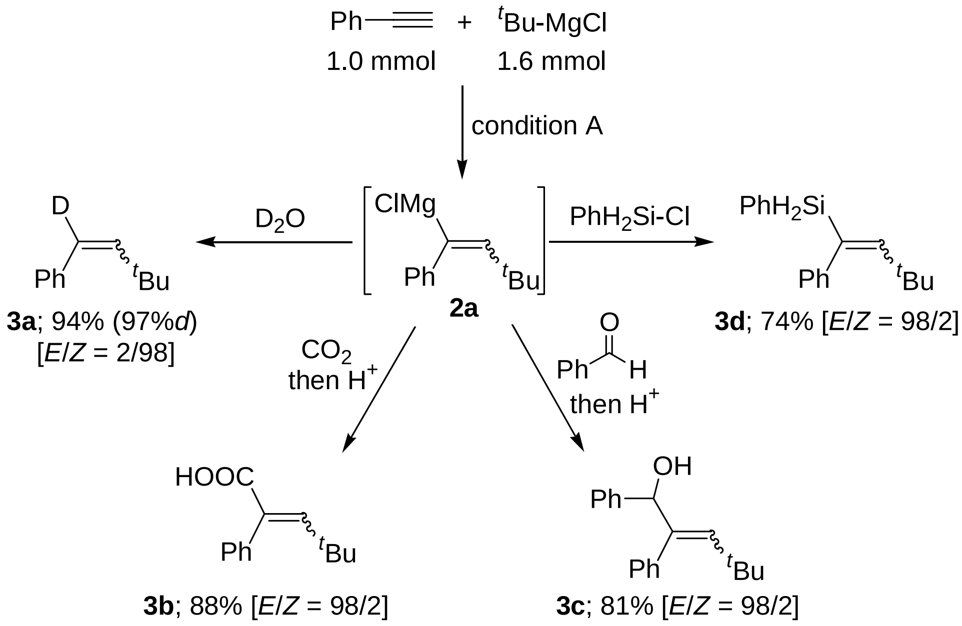
| Entry | R | R'-MgX | Condition[a] | Product | Yield (%)[b] | *E*/*Z* |
|---|---|---|---|---|---|---|
| 1 | 4-Me$C_6H_4$ | $^t$Bu-MgCl | A | **2b** | 88 (80) | 2/98 |
| 2 | 3-Me$C_6H_4$ | $^t$Bu-MgCl | A | **2c** | 90 (83) | 2/98 |
| 3 | 2-Me$C_6H_4$ | $^t$Bu-MgCl | A | **2d** | 91 (81) | 7/93 |
| 4 | 4-MeO$C_6H_4$ | $^t$Bu-MgCl | A | **2e** | (70) | 2/98 |
| 5 | 4-$CF_3C_6H_4$ | $^t$Bu-MgCl | A | **2f** | (81) | 1/99 |
| 6 | 3-thienyl | $^t$Bu-MgCl | A | **2g** | (65) | 3/97 |
| 7 | Ph | $^s$Bu-MgCl | A | **2h** | 59 (43) | 12/88 |
| 8 | Ph | $^s$Bu-MgCl | B | **2h** | 81 (68) | 14/86 |
| 9 | Ph | $^c$Hex-MgCl | B | **2i** | 83 (71) | 20/80 |
| 10 | Ph | $^n$Bu-MgCl | A | **2j** | 64 (49) | 42/58 |
| 11 | Ph | $^n$Bu-MgCl | C | **2j** | 73 (58) | 43/57 |
| 12 | Ph | $^n$Oct-MgBr | C | **2k** | 89 (73) | 42/58 |
| 13 | Ph$Me_2$Si | $^t$Bu-MgCl | C | **2l** | (66) | 8/92 |

[a] Condition A: (IMes)AgCl (5 mol%), phenylacetylene (1.0 mmol), 1,2-dibromoethane (100 mol%), R'-MgX (1.6 mmol), -10 °C, 30 min. B: AgOTs (5 mol%), P(p-$C_6H_4Cl)_3$ (5 mol%), phenylacetylene (1.0 mmol), 1,2-dibromoethane (200 mol%), R'-MgX (1.6 mmol), -10 °C, 30 min. C: (IMes)AgCl (5 mol%), phenylacetylene (1.0 mmol), 1,2-dibromoethane (200 mol%), R'-MgX (2.0 mmol), -10 °C, 3 h.

[b] GC yield. Isolated yield is in parentheses.

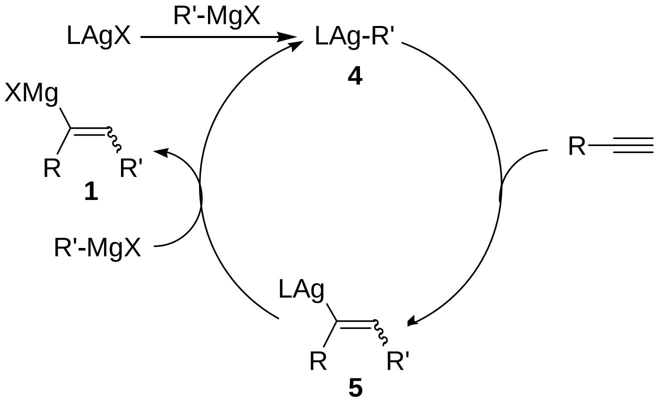
yield (Entry 9). Primary-alkyl Grignard reagents also gave hydroalkylated product **2j** and **2k** in moderate to good yields when the reaction was conducted for 3 h in the presence of large amount of 1,2-dibromoethane (Entries 10–12, condition C). No reaction took place with methyl, benzyl and phenyl Grignard reagents. As for the alkynes, dimethylphenylsilyl alkyne gave **2l** in 66% isolated yield (Entry 13). Aliphatic alkynes and internal alkynes, however, did not undergo carbomagnesiation under the conditions examined.

Vinyl Grignard reagents formed by the present carbomagnesiation can be trapped with various electrophiles (Scheme 1). For example, quenching of **1a** with $D_2O$ gave deuterated product **3a** in 94% yield (97% *d*). Electrophilic trapping of **1a** with $CO_2$, benzaldehyde, and chlorophenylsilane afforded **3b**, **3c,** and **3d** in 88%, 81%, and 74% yield, respectively.



**Scheme 1**. Electrophilic trap of vinyl Grignard reagent **2a**

A plausible reaction mechanism is outlined in Scheme 2. The reaction of silver complex with alkyl Grignard reagent forms alkyl silver complex **4**.[11] Then, **4** reacts with terminal alkyne to afford vinyl silver complex **5** which undergoes transmetallation with alkyl Grignard reagents to give vinyl Grignard reagent **1** and regenerate **4**.



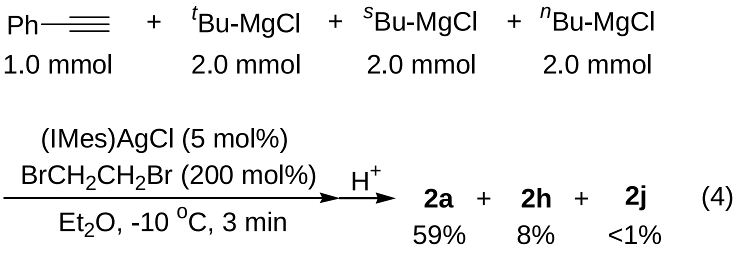
**Scheme 2**. A Plausible Reaction Pathway

It has been known that alkyl silver ate complexes are formed from silver (I) complexes and alkyl lithium or Grignard reagents.[11] To confirm whether silver ate complexes rather than neutral complexes are active species toward terminal acetylenes in the present reaction, I carried out the reactions using stoichiometric amounts of (IMes)AgCl, ${}^{t}$Bu-MgCl, and phenylacetylene. As shown in Eq 3, desired product **2a** was obtained in 40% yield. The use of 2.0 equiv. of ${}^{t}$Bu-MgCl which may generate alkyl silver ate complexes, would gave the identical result. These results may indicate that alkyl silver ate complexes would not play important role in the present reaction.

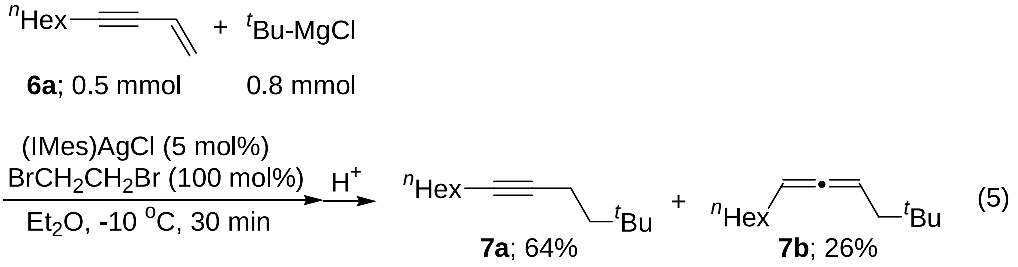
$$\underset{0.2\ \text{mmol}}{\text{(IMes)AgCl}} + {}^{t}\text{Bu-MgCl} \xrightarrow[\substack{\text{Et}_2\text{O, -78 }^{o}\text{C} \\ \text{5 min}}]{} \xrightarrow[\text{-10 }^{o}\text{C, 30 min}]{\substack{\text{Ph}\!-\!\!\equiv \\ \text{(0.2 mmol)}}} \xrightarrow{\text{H}^+} \mathbf{2a} \qquad (3)$$

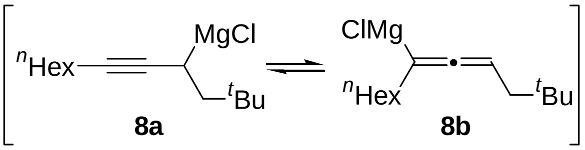
| ${}^{t}$Bu-MgCl | GC yield (%) **2a** |
|---|---|
| 0.2 mmol | 40 [*E*/*Z* = 4/96] |
| 0.4 mmol | 41 [*E*/*Z* = 1/99] |

To examine reactivities of the alkyl Grignard reagents in this catalytic system, I performed the following competitive experiments: a $Et_2O$ solution of (IMes)AgCl, phenylacetylene, and 1,2-dibromoethane was added to a mixture of equimolar amounts of ${}^{t}$Bu-MgCl, ${}^{s}$Bu-MgCl, and ${}^{n}$Bu-MgCl. Quenching the reaction with $H_2O$ afforded hydroalkylation products **2a**, **2h** and **2j** in 59%, 8%, and <1% yields, respectively (Eq 4). Preferable formation of the products having highly branched butyl group may suggest that the addition of alkyl silver complexes toward phenylacetylene proceeds via a radical mechanism.



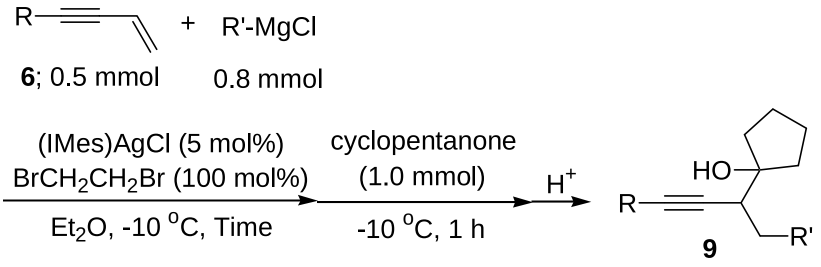
It is known that alkyl silver complexes add to enyne derivatives to give allenyl silver complexes.[11a, 12] I then applied the present carbomagnesiation to enynes. The reaction of hexyl substituted enyne **6a** with ${}^{t}$Bu-MgCl under condition A followed by hydrolysis gave a mixture of **7a** and **7b** in 64% and 26% (Eq 5). This result indicates the formation of propargyl and/or allenyl Grignard reagents **8**.[13]





When **8** was trapped with cyclopentanone, **9a** was obtained regioselectively in 85% yield as a single isomer (Table 4, entry 1). The use of ${}^{s}$Bu-MgCl also afforded the corresponding coupling product **9b** in 81% yield (entry 2). On the other hand, carbomagnesiation using ${}^{n}$Bu-MgCl failed to give **9c** (entry 3). Phenyl and silyl substituted enyne **6b** and **6c** underwent carbomagnesiation and successive electrophilic traping afforded coupling product **9d** and **9e** in good yields (entries 4–5).

**Table 3**. Silver-catalyzed carbomagnesiation of enynes and quenching with cyclopentanone



| Entry | Enyne | Time | R' | Yield (%) |
|---|---|---|---|---|
| 1 | **6a** (R = $^{n}$Hex) | 30 min | $^{t}$Bu | **9a**; 85 |
| 2 | **6a** | 3 h | $^{s}$Bu | **9b**; 81 |
| 3 | **6a** | 3 h | $^{n}$Bu | **9c**; <1 |
| 4 | **6b** (R = Ph) | 30 min | $^{t}$Bu | **9d**; 87 |
| 5 | **6c** (R = TMS) | 30 min | $^{t}$Bu | **9e**; 85 |

## 2-3. Conclusion

In conclusion, regioselective carbomagnesiation of terminal alkynes with various alkyl Grignard reagents was found to proceed using silver catalyst such as (IMes)AgCl or AgOTs, in the presence of 1,2-dibromoethane as a reoxidizing reagents. Vinyl Grignard reagents generated by the present method were successfully trapped with various electrophiles. This catalytic system could also be applicable to the regioselective carbomagnesiation of enynes.

## 2-4. Experimental Section

### General Comments

$^1$H NMR and $^{13}$C NMR spectra were recorded with a JEOL JNM-Alice 400 (400 MHz and 100 MHz, respectively) spectrometer. Chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were recorded with a Perkin-Elmer FT-IR (Model 1600). Both conventional and high resolution mass spectra were recorded with a JEOL JMS-DX303HF spectrometer. GC Mass spectra (EI) were obtained using a JMS-mate operating in the electron impact mode (70 eV) equipped with a RTX-5 30MX.25MMX.25U column. HPLC separations were performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using $CHCl_3$ as an eluent. Column chromatography was conducted using Kanto Chemical Co., Inc. silica gel 60 (63-210 μm). Elemental analyses were performed on a Perkin Elmer 240C apparatus. GC yields were determined using octane as an internal standard. $^t$Bu-MgCl, $^s$Bu-MgCl, $^n$Bu-MgCl, $^c$Hex-MgCl, $^n$Oct-MgCl, phenylacetylene, 2-ethynyltoluene, 3-ethynyltoluene 4-ethynyltoluene, 4-ethynylanisole, 4-ethynyltrifluorotoluene, 3-ethynylthiophene, dimethylphenylsilylacetylene, benzaldehyde and chlorophenylsilane (Aldrich Chemical Company), 1,2-dibromoethane and cyclopentanone (Tokyo Chemical Industry Company), AgOTs, $D_2O$ (Wako Pure Chemical Industries) were purchased and used as received. (IMes)AgCl was prepared according to the literature (ref. [10]). Enynes **6a**–**c** were synthesized by Sonogashira coupling reactions of vinyl bromide with corresponding terminal alkynes.

### Procedures and Characterization of Reaction Products

### 3,3-Dimethyl-1-phenyl-1-butene (2a)

To a mixture of phenyl acetylene (101.9 mg, 1.0 mmol), 1,2-dibromoethane (185 mg, 1.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 138 mg (88%) of **2a** as a mixture of stereoisomers (*E*/*Z* = 2/98). IR(NaCl): 3078, 3057, 2959, 2903, 2867, 1600, 1492, 1476, 1461, 1360, 1202, 1072, 1028, 918, 754, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.30-7.16 (m, 5H), 6.41 (d, $J$ = 12.7 Hz, 1H), 5.60 (d, $J$ = 12.7 Hz, 1H), 0.98 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.6, 139.4, 128.9, 127.5, 127.1, 126.1, 34.2, 31.2; MS (EI) *m/z* (relative intensity, %): 160 (M, 28), 146 (11), 145 (100), 130 (11), 129 (8), 128 (8), 117 (19), 115 (8), 105 (9), 91 (21), 77 (6); HRMS (EI) calcd for $C_{12}H_{16}$: 160.1252, found 160.1255. Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. found: C, 89.76; H, 10.27.

### 3,3-Dimethyl-1-(4-methylphenyl)-1-butene (2b)

To a mixture of 4-ethynyltoluene (114.5 mg, 0.99 mmol), 1,2-dibromoethane (187 mg, 1.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 138 mg (80%) of **2b** as a mixture of stereoisomers (*E*/*Z* = 2/98). IR(NaCl): 2958, 2866, 1510, 1475, 1462, 1360, 1200, 1108, 1022, 902, 849, 775, 740 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.07 (s, 4H), 6.37 (d, *J* = 12.7 Hz, 1H), 5.57 (d, *J* = 12.7 Hz, 1H), 2.33 (s, 3H), 0.98 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.5, 136.3, 135.7, 128.8, 128.2, 127.1, 34.1, 31.2, 21.1; MS (EI) *m*/*z* (relative intensity, %): 174 (M, 30), 160 (12), 159 (100), 144 (13), 131 (11), 129 (9), 128 (8), 117 (8), 115 (8), 105 (16), 91 (6), 77 (3); HRMS (EI) calcd for $C_{13}H_{18}$: 174.1409, found 174.1413. Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. found: C, 89.30; H, 10.27.

### 3,3-Dimethyl-1-(3-methylphenyl)-1-butene (2c)

To a mixture of 3-ethynyltoluene (114.2 mg, 0.98 mmol), 1,2-dibromoethane (185 mg, 1.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 141 mg (83%) of **2c** as a mixture of stereoisomers (*E*/*Z* = 2/98). IR(NaCl): 2958, 2866, 1602, 1583, 1476, 1461, 1360, 1218, 812, 764, 738, 703 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.15 (t, *J* = 7.4 Hz, 1H), 7.02-6.97 (m, 3H), 6.37 (d, *J* = 12.7 Hz, 1H), 5.57 (d, *J* = 12.7 Hz, 1H), 2.33 (s, 3H), 0.98 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.4, 139.3, 137.0, 129.6, 127.4, 127.2, 126.8, 126.0, 34.2, 31.2, 21.4; MS (EI) *m*/*z* (relative intensity, %): 174 (M, 31), 160 (14), 159 (100), 144 (12), 131 (12), 129 (9), 128 (9), 119 (4), 117 (7), 115 (7), 105 (15), 91 (6), 77 (4); HRMS (EI) calcd for $C_{13}H_{18}$: 170.1409, found 174.1398. Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. found: C, 89.40; H, 10.31.

### 3,3-Dimethyl-1-(2-methylphenyl)-1-butene (2d)

To a mixture of 2-ethynyltoluene (114.9 mg, 0.99 mmol), 1,2-dibromoethane (188 mg, 1.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 140 mg (81%) of **2d** as a mixture of stereoisomers (*E*/*Z* = 7/93). IR(NaCl): 2958, 2866, 1475, 1461, 1360, 1234, 1205, 901, 752, 738 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.14-7.08 (m, 4H), 6.26 (d, *J* = 12.7 Hz, 1H), 5.61 (d, *J* = 12.7 Hz, 1H), 2.24 (s, 3H), 0.93 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.1, 138.9, 125.7, 129.5, 129.2, 126.6, 126.2, 124.8, 34.3, 30.8, 20.3; MS (EI) *m*/*z* (relative intensity, %): 174 (M, 36), 160 (14), 159 (100), 145 (5), 144 (13), 131 (14), 129 (10), 128 (9), 117 (11), 115 (10), 105 (16), 104 (7), 91 (7), 77 (4); HRMS (EI) calcd for $C_{13}H_{18}$: 174.1409, found 174.1405. Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. found: C, 89.50; H, 10.61.

### 3,3-Dimethyl-1-(4-methoxyphenyl)-1-butene (2e)

To a mixture of 4-ethynyanisole (132.2 mg, 1.0 mmol), 1,2-dibromoethane (187 mg, 1.00 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane/ether = 90/10) gave 133 mg (70%) of **2e** as a mixture of stereoisomers (*E*/*Z* = 2/98). IR(NaCl): 2994, 2957, 2904, 2865, 2835, 1607, 1509, 1464, 1441, 1410, 1360, 1284, 1247, 1201, 1171, 1106, 1039, 851, 816, 783, 745 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.12-7.08 (m, 2H), 6.84-6.80 (m, 2H), 6.35 (d, *J* = 12.6 Hz, 1H), 5.56 (d, *J* = 12.6 Hz, 1H), 3.80 (s, 3H), 0.99 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 158.0, 142.5, 131.6, 130.0, 126.8, 113.0, 55.2, 34.0, 31.2 MS (EI) *m*/*z* (relative intensity, %): 190 (M, 30), 176 (12), 175 (100), 160 (11), 146 (4), 145 (4), 128 (4), 121 (12), 115 (5), 91 (6), 77 (4); HRMS (EI) calcd for $C_{13}H_{18}O$: 190.1358, found 190.1360. Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. found: C, 81.77; H, 9.38.

### 3,3-Dimethyl-1-(4-trifluoromethylphenyl)-1-butene (2f)

To a mixture of 4-ethynytrifluoromethylbenzene (167.8 mg, 0.99 mmol), 1,2-dibromoethane (184.7 mg, 0.99 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 183 mg (81%) of **2f** as a mixture of stereoisomers (*E*/*Z* = 1/99). IR(NaCl): 2962, 2905, 2868, 1616, 1478, 1465, 1406, 1363, 1165, 1127, 1106, 1066, 1019, 903, 862, 814, 732 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.38 (d, *J* = 12.9 Hz, 1H), 5.68 (d, *J* = 12.9 Hz, 1H), 0.97 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 143.9, 143.3 (q, *J* = 1.4 Hz), 129.2, 128.5 (q, *J* = 32.5 Hz), 125.6, 124.5 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 270.4 Hz), 34.3, 31.2; MS (EI) *m*/*z* (relative intensity, %): 228 (M, 30), 214 (15), 213 (100), 209 (7), 185 (23), 173 (7), 165 (8), 159 (21), 144 (5), 129 (6), 128 (6); HRMS (EI) calcd for $C_{13}H_{15}F_3$: 228.1126, found 228.1140. Anal. Calcd for $C_{13}H_{15}F_3$: C, 68.41; H, 6.62. found: C, 68.70; H, 6.68.

### 3,3-Dimethyl-1-(3-thienyl)-1-butene (2g)

To a mixture of 3-ethynylthiophene (109.2 mg, 1.01 mmol), 1,2-dibromoethane (191 mg, 1.02 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 110 mg (65%) of **2g** as a mixture of stereoisomers (*E*/*Z* = 3/97). IR(NaCl): 2993, 2959, 2903, 2866, 1475, 1462, 1418, 1360, 1202, 1079, 890, 861, 836, 810, 758, 735, 683 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 5.1, 2.8 Hz, 1H), 6.98 (ddd, *J* = 2.8, 1.4, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.21 (dd, *J* = 12.4, 1.4 Hz, 1H), 5.62 (d, *J* = 12.4 Hz, 1H), 1.02 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 144.1, 139.1, 129.3, 124.2, 122.1, 121.6, 33.8, 30.9; MS (EI) *m*/*z* (relative intensity, %): 166 (M, 47), 153 (5), 152 (12), 151 (100), 136 (8), 135 (7), 134 (5), 123 (9), 118 (9), 117 (12), 111 (6), 105 (7), 97 (24), 91 (8), 77 (4), 67 (7), 65 (5), 59 (7); HRMS (EI) calcd for $C_{10}H_{14}S$: 166.0816, found 166.0812. Anal. Calcd for $C_{10}H_{14}S$: C, 72.23; H, 8.49. found: C, 72.40; H, 8.44.

### 3-Methyl-1-phenyl-1-pentene (2h)

To a mixture of phenyl acetylene (99.5 mg, 0.98 mmol), 1,2-dibromoethane (373 mg, 2.0 mmol) and AgOTs (14.0 mg, 0.05 mmol), $P(p\text{-}C_6H_4Cl)_3$ (18.3 mg, 0.05 mmol) was added *sec*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by HPLC with $CHCl_3$ as an eluent gave 106 mg (68%) of **2h** as a mixture of stereoisomers (*E*/*Z* = 14/86). IR(NaCl): 2961, 2926, 2873, 1600, 1493, 1456, 1378, 1074, 1030, 965, 916, 798, 778, 697 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.36-7.20 (m, 5H), 6.40-6.32 (m, 1H), 6.10 (dd, $J$ = 15.9, 7.6 Hz, 0.14H), 5.43 (t, $J$ = 11.1 Hz, 0.86H), 2.70-2.62 (m, 0.86H), 2.24-2.16 (m, 0.14H), 1.42-1.29 (m, 2H), 1.07 (d, $J$ = 6.8 Hz, 0.42H), 1.03 (d, $J$ = 6.6 Hz, 2.58 H), 0.92-0.84 (m, 3H);$^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 139.4, 136.8, 128.6, 128.1, 127.5, 126.3, 33.8, 30.3, 20.7, 11.8; (*E* isomer): δ 138.0, 136.8, 128.5, 128.1, 126.7, 125.9, 38.9, 29.8, 20.2, 11.9; MS (EI) *m*/*z* (relative intensity, %) (*Z* isomer): 160 (M, 25), 145 (6), 132 (12), 131 (100), 129 (7), 128 (5), 117 (5), 116 (8), 115 (9), 104 (8), 91 (23), 77 (4); HRMS (EI) calcd for $C_{12}H_{16}$: 160.1252, found 160.1243. Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. found: C, 89.54; H, 9.80.

**1-Cyclohexyl-2-phenylethene (2i)**

To a mixture of phenyl acetylene (102.4 mg, 1.0 mmol), 1,2-dibromoethane (374 mg, 2.0 mmol) and AgOTs (14.0 mg, 0.05 mmol), P(*p*-$C_6H_4Cl)_3$ (18.3 mg, 0.05 mmol) was added cyclohexyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by HPLC with $CHCl_3$ as an eluent gave 132 mg (71%) of **2i** as a mixture of stereoisomers (*E*/*Z* = 20/80). IR(NaCl): 3002, 2924, 2850, 1705, 1600, 1492, 1448, 1074, 1029, 957, 890, 788, 766, 697 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.35-7.16 (m, 5H), 6.36-6.29 (m, 1H), 6.18 (dd, $J$ = 16.0, 7.0 Hz, 0.2H), 5.48 (t, $J$ = 10.9 Hz, 0.8H), 2.61-2.54 (m, 0.8H), 2.18-2.07 (m, 0.2H), 1.82-1.65 (m, 5H), 1.36-1.12 (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 139.0, 137.9, 128.6, 128.2, 126.8, 126.4, 36.9, 33.2, 26.01, 25.7; (*E* isomer): δ 138.0, 136.9, 128.5, 127.1, 126.7, 125.9, 41.2, 32.9, 26.2, 26.04; MS (EI) *m*/*z* (relative intensity, %) (Z isomer): 186 (M, 30), 143 (9), 130 (7), 129 (22), 128 (14), 117 (9), 115 (12), 105 (12), 104 (100), 95 (8), 91 (13); HRMS (EI) calcd for $C_{14}H_{18}$: 186.1409, found 186.1413. Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. found: C, 89.98; H, 9.78.

**1-Phenyl-1-hexene (2j)**

To a mixture of phenyl acetylene (101.6 mg, 1.0 mmol), 1,2-dibromoethane (373 mg, 2.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *n*-butyl magnesium chloride (2.0 M in $Et_2O$, 1.0 mL, 2.0 mmol) at -10 °C. After stirring for 3 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by HPLC with $CHCl_3$ as an eluent gave 91 mg (58%) of **2j** as a mixture of stereoisomers (*E*/*Z* = 43/57). IR(NaCl): 3026, 2957, 2929, 2903, 2872, 2859, 1706, 1600, 1494, 1455, 1378, 1272, 1072, 1027, 965, 748, 699 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.35-7.16 (m, 5H), 6.41-6.36 (m, 1H), 6.22 (dt, *J* = 15.6, 6.8 Hz, 0.43H), 5.66 (dt, *J* = 11.7, 7.4 Hz, 0.57H), 2.36-2.30 (m, 1.14H), 2.24-2.18 (m, 0.86H), 1.49-1.30 (m, 4H), 0.94-0.88 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 137.8, 133.2, 128.7, 128.6, 128.1, 126.4, 32.1, 28.3, 22.4, 14.0; (*E* isomer): δ 137.9, 131.2, 129.7, 128.4, 126.7, 125.9, 32.7, 31.5, 22.3, 14.0; MS (EI) *m*/*z* (relative intensity, %) (*Z* isomer): 160 (M, 41), 131 (5), 118 (12), 117 (100), 116 (8), 115 (28), 105 (6), 104 (59), 92 (4), 91 (22), 77 (4); (*E* isomer): 160 (M, 40), 131 (5), 118 (11), 117 (100), 116 (8), 115 (26), 105 (6), 104 (54), 91 (21), 77 (4); HRMS (EI) calcd for $C_{12}H_{16}$: 160.1252, (*Z* isomer): found 160.1234; (*E* isomer): found 160.1235. Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. found: C, 89.70; H, 9.77.

### 1-Phenyl-1-decene (2k)

To a mixture of phenyl acetylene (103.5 mg, 1.0 mmol), 1,2-dibromoethane (373 mg, 2.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *n*-octyl magnesium bromide (2.0 M in $Et_2O$, 1.0 mL, 2.0 mmol) at -10 °C. After stirring for 3 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) and HPLC with $CHCl_3$ as an eluent gave 158 mg (73%) of **2k** as a mixture of stereoisomers (*E*/*Z* = 42/58). IR(NaCl): 3025, 2924, 2854, 1600, 1494, 1466, 1448, 963, 768, 742, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.35-7.16 (m, 5H), 6.41-6.35 (m, 1H), 6.23 (dt, *J* = 15.6, 6.8 Hz, 0.42H), 5.66 (dt, *J* = 11.7, 7.3 Hz, 0.58H), 2.35-2.29 (m, 1.16H), 2.22-2.17 (m, 0.84H), 1.48-1.40 (m, 2H), 1.35-1.26 (m, 10H), 0.90-0.86 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 137.8, 133.3, 128.7, 128.6, 128.1, 126.4, 31.9, 30.0, 29.5, 29.4, 29.3, 28.6, 22.7, 14.1; (*E* isomer): δ 137.9, 131.3, 129.6, 128.4, 126.7, 125.9, 33.1, 31.9, 29.5, 29.4, 29.3, 29.2, 22.7, 14.1; MS (EI) *m*/*z* (relative intensity, %) (*Z* isomer): 216 (M, 23), 131 (5), 118 (12), 117 (74), 116 (5), 115 (16), 105 (11), 104 (100), 92 (6), 91 (23), 77 (3); (*E* isomer): 216 (M, 26), 131 (5), 118 (11), 117 (79), 116 (6), 115 (17), 105 (10), 104 (100), 92 (5), 91 (21), 77 (2); HRMS (EI) calcd for $C_{16}H_{24}$: 216.1878, (*Z* isomer): found 216.1866; (*E* isomer): found 216.1876. Anal. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18. found: C, 88.56; H, 10.98.

### 3,3-Dimethyl-1-dimethylphenylsilyl-1-butene (2l)

To a mixture of dimethylphenylsilyl acetylene (158.5 mg, 0.99 mmol), 1,2-dibromoethane (376 mg, 1.0 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 1.0 mL, 2.0 mmol) at -10 °C. After stirring for 3 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by HPLC with $CHCl_3$ as an eluent gave 142 mg (66%) of **2l** as a mixture of stereoisomers (*E*/*Z* =

8/92). IR(NaCl): 3051, 2956, 2905, 2867, 1596, 1476, 1464, 1428, 1360, 1248, 1112, 822, 786, 731, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.56-7.52 (m, 2H), 7.36-7.30 (m, 3H), 6.48 (d, *J* = 15.6 Hz, 1H), 5.51 (d, *J* = 15.6 Hz, 1H), 0.96 (s, 9H), 0.41 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 161.7, 140.9, 133.7, 128.6, 127.6, 122.6, 35.6, 30.0, 0.83; MS (EI) *m*/*z* (relative intensity, %): 218 (M, 5), 204 (8), 203 (40), 162 (9), 161 (60), 149 (6), 148 (10), 145 (6), 136 (13), 135 (100), 125 (10), 121 (31), 119 (5), 107 (6), 105 (12), 91 (4), 73 (30), 59 (9); HRMS (EI) calcd for $C_{14}H_{22}Si$: 218.1491, found 218.1501. Anal. Calcd for $C_{14}H_{22}Si$: C, 76.99; H, 10.15. found: C, 76.72; H, 10.10.

**1-Deuterio-3,3-dimethyl-1-phenyl-1-butene (3a)**

To a mixture of phenyl acetylene (100 mg, 0.98 mmol), 1,2-dibromoethane (185.4 mg, 0.99 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, $D_2O$ was added to the solution at -10 °C. After stirring for 3 h at 25 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 146 mg (94%) of **3a** as a mixture of stereoisomers (*E*/*Z* = 2/98). IR(NaCl): 3020, 2959, 2904, 2867, 1599, 1492, 1475, 1461, 1442, 1361, 1202, 1028, 918, 744, 721, 697 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.29-7.17 (m, 5H), 5.60 (t, *J* = 1.8 Hz, 1H), 0.98 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.6, 139.3, 129.0, 127.5, 126.8 (t, *J* = 23.6 Hz), 126.2, 34.1, 31.2; MS (EI) *m*/*z* (relative intensity, %): 161 (M, 27), 147 (12), 146 (100), 131 (10), 130 (7), 129 (7), 118 (13), 106 (6), 92 (15), 91 (7); HRMS (EI) calcd for $C_{12}H_{15}D$: 161.1314, found 161.1315. Anal. Calcd for $C_{12}H_{15}D$: C, 89.38; H and D, 10.62. found: C, 89.17; H and D, 10.83.

**4,4-Dimethyl-2-phenyl-2-pentenoic acid (3b)**

To a mixture of phenyl acetylene (100.7 mg, 0.99 mmol), 1,2-dibromoethane (187 mg, 1.00 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, dry $Et_2O$ (0.8 mL) and $CO_2$ was added to the solution at -10 °C. Aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (hexane/ether = 1/2) gave 178 mg (88%) of **3b** as a mixture of stereoisomers (*E*/*Z* = 98/2). Mp: 129-133 °C; IR(KBr): 2965, 1674, 1423, 1268, 922, 784, 702 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.33-7.29 (m, 3H), 7.16-7.13 (m, 3H), 0.92 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 173.2, 155.8, 135.6, 130.6, 130.1, 127.6, 127.5, 34.4, 30.2; MS (EI) *m*/*z* (relative intensity, %): 204 (M, 100), 189 (30), 186 (11), 171 (14), 161 (14), 159 (21), 146 (37), 145 (16), 144 (14), 143 (82), 129 (21), 128 (41), 127 (11), 118 (18), 117 (52), 116 (9), 115 (20), 103 (12), 102 (9), 91 (16), 77 (16), 59 (37); HRMS (EI) calcd for $C_{13}H_{16}O_2$: 204.1150, found 204.1154. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. found: C, 76.23; H, 7.65.

### 4,4-Dimethyl-1,2-diphenyl-2-pentene-1-ol (3c)

To a mixture of phenyl acetylene (105.5 mg, 1.03 mmol), 1,2-dibromoethane (189 mg, 1.01 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, dry $Et_2O$ (0.8 mL) and benzaldehyde (212 mg, 2.0 mmol) was added to the solution at -10 °C. After stirring for 3 h at 25 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (hexane/ether = 90/10) gave 223 mg (81%) of **3c** as a mixture of stereoisomers (*E*/*Z* = 98/2). IR(NaCl): 3391, 3058, 3029, 2957, 2901, 2866, 1600, 1574, 1493, 1475, 1452, 1360, 1220, 1190, 1069, 1029, 1005, 916, 775, 763 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.29-7.12 (m, 8H), 6.80-6.77 (m, 2H), 5.90 (s, 1H), 5.26 (d, $J$ = 4.9 Hz, 1H), 1.96 (d, $J$ = 4.9 Hz, 1H), 0.88 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 142.1, 140.1, 138.7, 137.7, 130.3, 128.0, 127.25, 127.21, 126.8, 126.5, 80.2, 33.4, 31.2; MS (EI) *m*/*z* (relative intensity, %): 266 (M, 1), 209 (20), 208 (10), 161 (10), 160 (69), 146 (12), 145 (100), 131 (5), 129 (8), 128 (7), 117 (17), 107 (32), 105 (13), 103 (8), 91 (9), 79 (14), 77 (15), 57 (23); HRMS (EI) calcd for $C_{19}H_{22}O$: 266.1671, found 266.1674. Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. found: C, 85.38; H, 8.26.

### 3,3-Dimethyl-1-phenyl-1-phenylsilyl-1-butene (3d)

To a mixture of phenyl acetylene (101 mg, 0.99 mmol), 1,2-dibromoethane (188 mg, 1.01 mmol) and (IMes)AgCl (22.4 mg, 0.05 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.8 mL, 1.6 mmol) at -10 °C. After stirring for 30 min, dry THF (1.2 mL) and chlorophenylsilane (0.27 mL, 2.0 mmol) was added to the solution at -10 °C. After stirring for 1 h at 25 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give a crude product. Purification by column chromatography on silica gel (pentane) and HPLC with $CHCl_3$ as an eluent gave 194 mg (74%) of **3d** as a mixture of stereoisomers (*E*/*Z* = 98/2). IR(NaCl): 3053, 2958, 2901, 2867, 2134, 1608, 1592, 1490, 1494, 1462, 1429, 1360, 1205, 1115, 1071, 951, 924, 890, 839, 732, 712, 699 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (*Z* isomer): δ 7.47-7.45 (m, 2H), 7.38-7.29 (m, 3H), 7.21-7.10 (m, 3H), 6.96-6.94 (m, 2H), 6.18 (s, 1H), 4.59 (s, 2H), 0.91 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) (*Z* isomer): δ 154.9, 141.5, 135.6, 134.5, 132.0, 129.6, 128.2, 127.8, 127.6, 125.3, 36.6, 30.9; MS (EI) *m*/*z* (relative intensity, %): 266 (M, 44), 224 (21), 223 (53), 209 (32), 207 (12), 197 (19), 196 (68), 195 (15), 184 (18), 183 (100), 181 (14), 173 (15), 159 (54), 158 (14), 157 (20), 143 (13), 131 (37), 128 (10), 121 (15), 117 (24), 107 (32), 105 (58), 57 (15); HRMS (EI) calcd for $C_{18}H_{22}Si$: 266.1491, found 266.1493. Anal. Calcd for $C_{18}H_{22}Si$: C, 81.14; H, 8.32. found: C, 80.99; H, 8.33.

### 2,2-Dimethyl-dodec-5-yne (7a) and 2,2-Dimethyl-dodeca-4,5-diene (7b)

To a mixture of dec-1-en-3-yne **6a** (66 mg, 0.49 mmol), 1,2-dibromoethane (93.2 mg, 0.50 mmol) and (IMes)AgCl (11.2 mg, 0.025 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.4 mL, 0.8 mmol) at -10 °C. After stirring for 30 min, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give crude product. Purification by column chromatography on silica gel (pentane) gave 60 mg (64%) of **7a** and 24 mg (26%) of **7b**. **7a**: IR(NaCl): 2955, 2932, 2859, 1467, 1365, 1248 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$): δ 2.15-2.08 (m, 4H), 1.49-1.26 (m, 10H), 0.90-0.87 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 80.9, 79.8, 43.5, 31.4, 30.3, 29.1, 29.0, 28.6, 22.6, 18.8, 14.3, 14.1; MS (EI) *m*/*z* (relative intensity, %): 194 (M, 4), 179 (10), 165 (11), 151 (9), 123 (19), 110 (13), 109 (67), 97 (8), 96 (26), 95 (64), 83 (15), 82 (18), 81 (64), 71 (19), 70 (12), 69 (29), 68 (19), 67 (39), 57 (100), 55 (20), 43 (28), 41 (28); HRMS (EI) calcd for $C_{14}H_{26}$: 194.2035, found 194.2040. Anal. Calcd for $C_{14}H_{26}$: C, 86.52; H, 13.48. found: C, 86.28; H, 13.60. **7b**: IR(NaCl): 2956, 2928, 2858, 1963, 1467, 1378, 1242, 1199, 883 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$): δ 5.05-5.00 (m, 2H), 2.01-1.94 (m, 2H), 1.89-1.86 (m, 2H), 1.43-1.24 (m, 8H), 0.94-0.87 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 205.2, 89.5, 87.6, 44.0, 31.7, 31.2, 29.3, 29.04, 29.00, 28.8, 22.6, 14.1; MS (EI) *m*/*z* (relative intensity, %): 194 (M, 0.3), 124 (29), 109 (11), 96 (6), 95 (12), 81 (13), 69 (6), 68 (36), 67 (12), 57 (100), 54 (8), 41 (15); HRMS (EI) calcd for $C_{14}H_{26}$: 194.2035, found 194.2049. Anal. Calcd for $C_{14}H_{26}$: C, 86.52; H, 13.48. found: C, 86.25; H, 13.45.

### 1-[1-(2,2-Dimethyl-propyl)-non-2-ynyl]-cyclopentanol (9a)

To a mixture of dec-1-en-3-yne **6a** (66 mg, 0.49 mmol), 1,2-dibromoethane (92.6 mg, 0.50 mmol) and (IMes)AgCl (11.2 mg, 0.025 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.4 mL, 0.8 mmol) at -10 °C. After stirring for 30 min, dry $Et_2O$ (1.2 mL) and cyclopentanone (83.2 mg, 0.99 mmol) was added to the solution at -10 °C. After stirring for 1 h at -10 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give a crude product.

Purification by column chromatography on silica gel (hexane/$Et_2O$ = 95/5) gave 114 mg (85%) of **9a**. IR(NaCl): 3461, 2956, 2861, 1468, 1394, 1365, 1328, 1247, 1197, 999, 909, 884 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.39 (tt, *J* = 4.9, 2.2 Hz, 1H), 2.15 (td, *J* = 6.8, 2.2 Hz, 2H), 1.86-1.58 (m, 11H), 1.52-1.24 (m, 8H), 0.96 (s, 9H), 0.89 (t, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 84.5, 82.9, 82.8, 44.6, 38.8, 38.5, 37.2, 31.3, 30.6, 29.8, 29.0, 28.6, 24.4, 24.3, 22.6, 18.8, 14.0; MS (CI) *m*/*z* (relative intensity, %): 279 (M+1, 6), 262 (21), 261 (100), 205 (22), 191 (23), 177 (11), 165 (5), 151 (5), 124 (7), 109 (8); HRMS (CI) calcd for $C_{19}H_{35}O$: 279.2688, found 279.2687. Anal. Calcd for $C_{19}H_{34}O$: C, 81.95; H, 12.31. found: C, 81.62; H, 12.30.

### 1-[1-(2-Methyl-butyl)-non-2-ynyl]-cyclopentanol (9b)

To a mixture of dec-1-en-3-yne **6a** (67.5 mg, 0.50 mmol), 1,2-dibromoethane (91.3 mg, 0.49 mmol) and (IMes)AgCl (11.2 mg, 0.025 mmol) was added *sec*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.4 mL, 0.8 mmol) at -10 °C. After stirring for 3 h, dry $Et_2O$ (1.2 mL) and cyclopentanone (84.4 mg, 1.0 mmol) was added to the solution at -10 °C. After stirring for 1 h at -10 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give a crude product. Purification by column chromatography on silica gel (pentane/$Et_2O$ = 95/5) gave 113 mg (81%) of **9b** as a mixture of diastereomers with ca. 1:1 ratio indicated by $^1H$, $^{13}C$ NMR and GC. A 1:1 mixture of diastereomers; IR(NaCl): 3454, 2958, 2872, 1463, 1378, 1328, 1272, 1196, 1066, 998, 906 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.50-2.44 (m, 1H), 2.19-2.15 (m, 2H), 1.83-1.57 (m, 11H), 1.52-1.23 (m, 10H), 1.10-0.99 (m, 1H), 0.94-0.85 (m, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 83.85, 83.81, 83.3, 83.2, 80.9, 80.7, 40.9, 40.8, 39.41, 39.35, 37.2, 37.10, 37.05, 37.0, 32.6, 32.3, 31.3, 30.7, 29.0, 28.49, 28.47, 27.3, 24.29, 24.28, 23.91, 23.90, 22.6 (2C), 20.1 (2C), 18.7, 18.3, 14.0 (2C), 11.5 (2C), 10.8 (2C); MS (CI) *m*/*z* (relative intensity, %): 279 (M+1, 13), 262 (22), 261 (100), 192 (6), 191 (54), 179 (8), 177 (8), 165 (8), 138 (9), 123 (8), 109 (14), 95 (7), 85 (5); HRMS (CI) calcd for $C_{19}H_{35}O$: 279.2688, found 279.2684. Anal. Calcd for $C_{19}H_{34}O$: C, 81.95; H, 12.31. found: C, 81.66; H, 12.42.

### 1-[1-(2,2-Dimethyl-propyl)-3-phenyl-prop-2-ynyl]-cyclopentanol (9d)

To a mixture of but-3-en-1-ynyl-benzene **6b** (63.1 mg, 0.49 mmol), 1,2-dibromoethane (91.6 mg, 0.50 mmol) and (IMes)AgCl (11.2 mg, 0.025 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.4 mL, 0.8 mmol) at -10 °C. After stirring for 30 min, dry $Et_2O$ (1.2 mL) and cyclopentanone (84.4 mg, 1.0 mmol) was added to the solution at -10 °C. After stirring for 1 h at -10 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give a crude product. Purification by column chromatography on silica gel (hexane/$Et_2O$ = 9/1) gave 115 mg (87%) of **9d**. IR(NaCl): 3452, 3055, 2955, 2868, 2228, 1699, 1634, 1598, 1489, 1472, 1442, 1365, 1245, 1197, 1070, 999, 911, 755, 691 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.39-7.36 (m, 2H), 7.29-7.26 (m, 3H), 2.66 (dd, *J* = 8.8, 3.4 Hz, 1H), 1.90-1.61 (m, 11H), 1.02 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 131.4, 128.2, 127.7, 123.8, 92.9, 84.5, 82.9, 44.4, 39.2, 38.8, 37.7, 30.7, 29.8, 24.4, 24.3; MS (CI) *m*/*z* (relative intensity, %): 271 (M+1, 6), 254 (22), 253 (100), 197 (8), 186 (4), 130 (5); HRMS (CI) calcd for $C_{19}H_{27}O$: 271.2062, found 271.2067.

**1-[1-(2,2-Dimethyl-propyl)-3-trimethylsilyl-prop-2-ynyl]-cyclopentanol (9e)**

To a mixture of but-3-en-1-ynyl-trimethylsilane **6c** (63 mg, 0.51 mmol), 1,2-dibromoethane (91.3 mg, 0.49 mmol) and (IMes)AgCl (11.2 mg, 0.025 mmol) was added *tert*-butyl magnesium chloride (2.0 M in $Et_2O$, 0.4 mL, 0.8 mmol) at -10 °C. After stirring for 30 min, dry $Et_2O$ (1.2 mL) and cyclopentanone (81.8 mg, 0.97 mmol) was added to the solution at -10 °C. After stirring for 1 h at -10 °C, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$ and evaporated to give a crude product. Purification by column chromatography on silica gel (pentane/$Et_2O$ = 95/5) gave 115 mg (85%) of **9e**. IR(NaCl): 3458, 2956, 2869, 2165, 1475, 1394, 1366, 1250, 1197, 1066, 1000, 976, 874, 842, 759, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.45 (dd, *J* = 9.6, 2.4 Hz, 1H), 1.86-1.45 (m, 11H), 0.96 (s, 9H), 0.13 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 110.2, 87.1, 84.1, 44.3, 39.5, 38.7, 37.3, 30.7, 29.8, 24.4, 24.3, 0.03; MS (CI) *m*/*z* (relative intensity, %): 267 (M+1, 2), 251 (6), 250 (23), 249 (100), 193 (9), 182 (5), 177 (7), 175 (7), 157 (7), 85 (5), 73 (7); HRMS (CI) calcd for $C_{16}H_{31}OSi$: 267.2144, found 267.2132. Anal. Calcd for $C_{16}H_{30}OSi$: C, 72.11; H, 11.35. found: C, 72.27; H, 11.28.

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# Chapter 3

## Nickel-Catalyzed Dimerization Coupling Reactions of Vinyl Grignard Reagents with 3,4-Membered Cyclic Ethers

### 3-1. Introduction

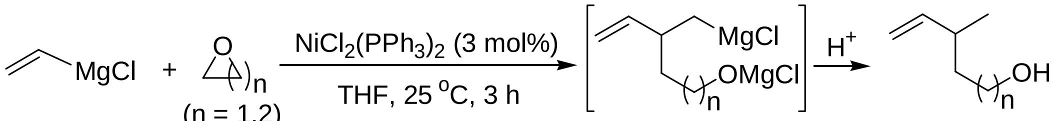
Since the discovery of the formation of Grignard reagents by the reaction of organic halides with magnesium metal in 1901,[1a] numerous efforts have been devoted to developing new synthetic applications especially to carbon-carbon bond forming reactions.[1] Epoch-making in this field was the introduction of transition metal catalysts in Grignard chemistry that provided novel synthetic methodologies by cross-coupling reactions.[1e-h] We have been working on C-C bond forming reactions using Grignard reagents catalyzed by Zr, Ti, Ni, or Pd involving ate-complex intermediates.[2] During the course of these studies, we have recently found that nickel catalyzes the alkylative dimerization of vinyl Grignard reagents with alkyl fluorides giving rise to 2-alkyl-3-butenyl Grignard reagents.[3] As an extension of this work, I report herein nickel catalyzed regioselective coupling of vinyl Grignard reagents with cyclic ethers to give 2-alkyl-3-butenyl Grignard reagents.

### 3-2. Results and Discussion

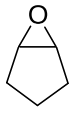
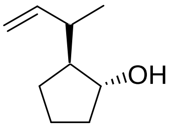
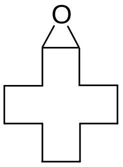
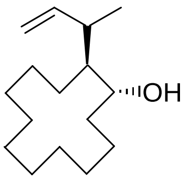
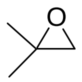
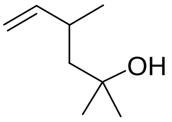
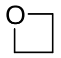
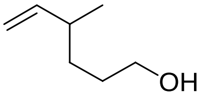
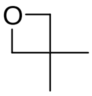
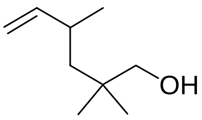
A typical example is as follows. To a mixture of cyclopentene oxide (1.0 mmol) and $NiCl_2(PPh_3)_2$ (0.03 mmol) was added vinyl magnesium chloride (2.2 mmol) in THF (1.7 mL) at 25 °C under nitrogen, and the resulting mixture was stirred for 3 hours at the same temperature. The NMR analysis of the crude mixture indicated the formation of *trans*-2-(1-Methyl-2-propenyl)cyclopentanol **2a** in 79% yield. The product was obtained as 1:1.3 mixture of diastereomers in 66% yield by column chromatography with pentane/ether = 6/4 as the eluent (Table 1, entry 1). On a 50 mmol scale, **2a** was also obtained in 72% isolated yield by reduced-pressure distillation (entry 2). When $NiCl_2$ was used instead of $NiCl_2(PPh_3)_2$, **2a** was obtained in 62% NMR yield (entry 3). When cyclododecene oxide (*trans/cis* = 33/67) was used, only *cis*-cyclododecene oxide reacted with vinyl Grignard reagent to afford coupling product **2b** as 1:1 mixture of diastereomers (entry 4).[4] Isobutylene oxide gave coupling product **2c** in poor yield (20%) (entry 5). The use of oxetanes also afforded the corresponding 2:1 coupling products **2d** and **2e** in 62% and 50% isolated yield, respectively (entries 6 and 7).

However, no reaction took place with substituted vinyl Grignard reagents such as MeCH=CHMgBr, $CH_2$=CMeMgBr and PhCH=CHMgBr.

**Table 1**. Nickel-catalyzed coupling reaction of vinyl Grignard reagent with cyclic ethers[a]



**1** **2**

| Entry | Epoxide (Oxetane) | Product | | Yield (%)[b] |
|---|---|---|---|---|
| 1<br>2[c]<br>3[d] |  |  | **2a** | 79 (66)<br>(72)<br>62 |
| 4 | <br>(*trans*/*cis* = 33/67) |  | **2b** | 66 (61) |
| 5[e] |  |  | **2c** | 25 (20) |
| 6 |  |  | **2d** | 73 (62) |
| 7 |  |  | **2e** | 64 (50) |

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[a] The reaction was carried out in THF at 25 °C for 3 h using epoxide/oxetane (1.0 mmol), vinyl Grignard reagent (2.2 mmol) and $NiCl_2(PPh_3)_2$ (0.03 mmol).

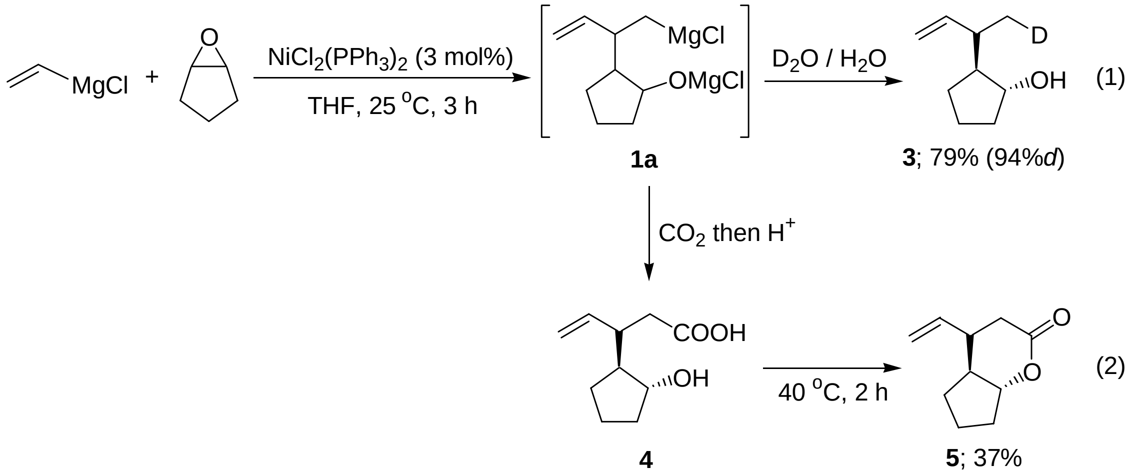
[b] NMR yield. Isolated yield is in parentheses.

[c] Reaction was carried out on a 50 mmol scale.

[d] $NiCl_2$ was used.

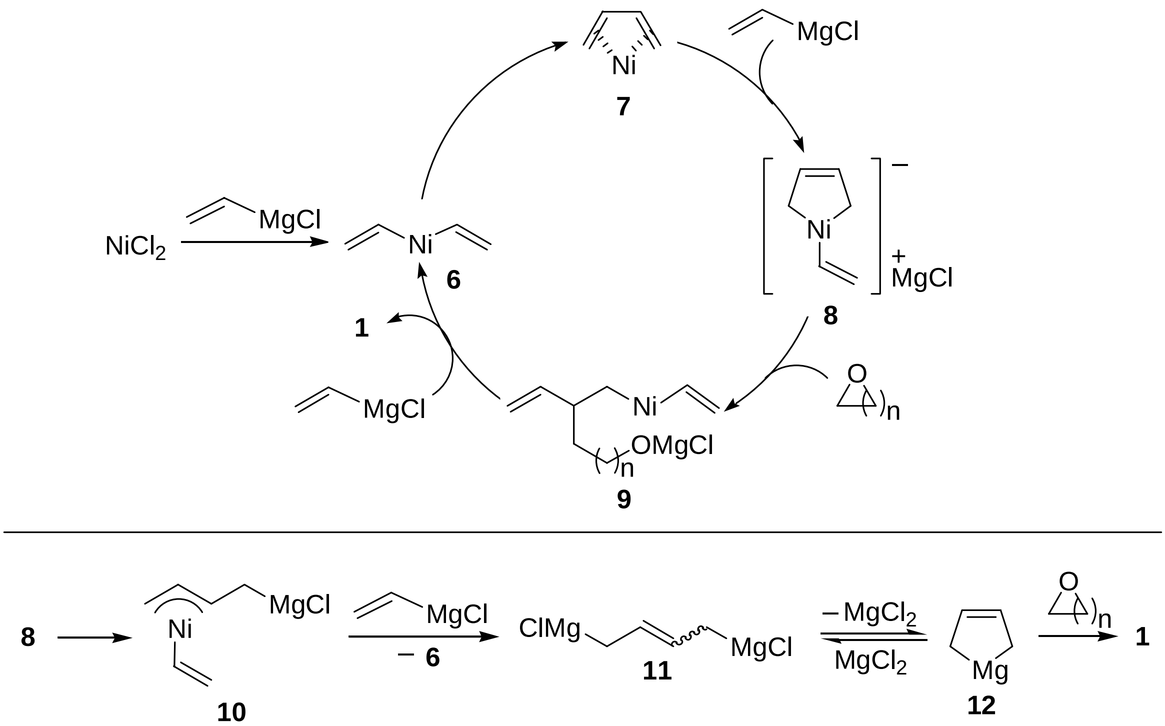
[e] Reaction was carried out on a 3.0 mmol scale.

When a reaction of cyclopentene oxide with vinyl Grignard reagent was quenched with $D_2O$, 64% yield of monodeuterated compound **3** (*d*-content 94%) as 1:1.3 mixture of diastereomers was isolated after purification by column chromatography (Eq. 1). As a synthetic application of thus-formed **1a**, I attempted to synthesize bicyclic ester **5** via intramolecular esterification of **4** formed by the reaction of **1a** with $CO_2$. Into a solution of **1a** prepared in situ under similar conditions of entry 1 in Table 1, dry ice was added at 25 °C. After treating with 3 N HCl and stirring at 40 °C for 2 h, the desired bicyclic ester **5** was obtained in 37% yield (Eq. 2).

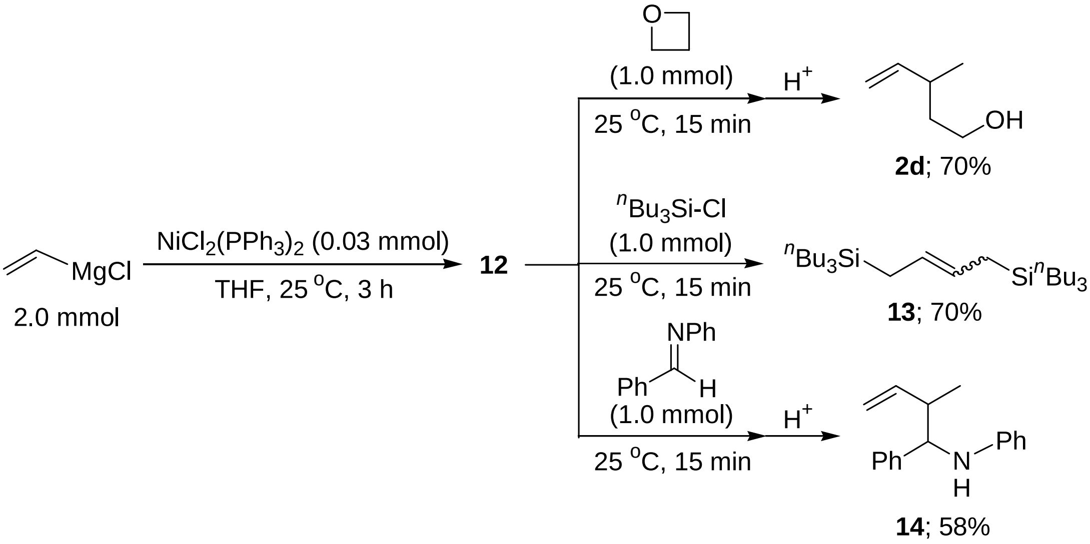


Plausible reaction pathways for the present reaction are outlined in Scheme 1. Nickel(II) is reduced by vinyl Grignard reagent to afford butadiene-nickel complex **7** via the divinylnickel complex **6**.[5] Thus formed **7** reacts with another vinyl Grignard reagent to afford nickelate complex **8**.[6] Direct reaction of **8** with epoxides/oxetanes at β-carbon leading to butenyl nickel complex **9** followed by transmetalation with vinyl Grignard reagent affords **1** along with **6**. Alternatively, π-allylnickel complex **10** which would be generated from **8**, undergoes transmetallation with vinyl Grignard reagent to afford (2-butene-1,4-diyl)magnesium **12** via diallyl Grignard reagent **11**. **12** reacts with cyclic ethers at an internal carbon to give **1**.[7]

In order to confirm the intermediary of **12** in the present reaction system, I conducted the reaction of $NiCl_2(PPh_3)_2$ (0.03 mmol) with vinyl magnesium chloride (1.5 mmol) at 25 °C in the absence of cyclic ethers. After stirring for 3 h, the reaction mixture was treated at 25 °C for 15 min with oxetane and tributylchlorosilane. GC analysis of the resulting reaction mixture showed the formation of **2d** and **13** in 70% yield (Eqs. 3 and 4). The elongation of reaction time to 3 h did not improve the products yields at all. These results suggest that **12** is formed from vinyl Grignard reagents in the presence of nickel catalyst.[8] Although these yields were slightly lower than the results of one pot reaction system as shown in Table 1, this method can be applied to more reactive electrophiles that cannot be tolerant to vinyl Grignard reagent. For example, homoallylic amine **14** was obtained as a mixture of diastereomers (threo/erythro = 94/6) by the reaction of thus-formed **12** with imine[9], which cannot be used in one pot reaction system since the direct reaction of vinyl Grignard reagent with imine predominates (Eqs. 5 and 6).



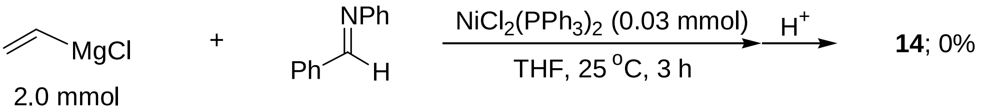
**Scheme 1**. Plausible reaction pathways



(3)

(4)

(5)



(6)

### 3-3. Conclusion

In conclusion, I have developed nickel catalyzed regioselective coupling of vinyl Grignard reagents with cyclic ethers to give 2-alkyl-3-butenyl Grignard reagents. The present reaction may proceed via the formation of nickelate complex **8** or (2-butene-1,4-diyl)magnesium **12**. From the investigation of reaction mechanism, it has been disclose that the reaction of vinyl Grignard reagents with nickel catalyst forms **12** which can be trapped with various electrophiles.

## 3-4. Experimental Section

### General Comments

$^1$H NMR and $^{13}$C NMR spectra were recorded with a JEOL JNM-Alice 400 (400 MHz and 100 MHz, respectively) spectrometer. Chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were recorded with a Perkin-Elmer FT-IR (Model 1600). Both conventional and high resolution mass spectra were recorded with a JEOL JMS-DX303HF spectrometer. GC Mass spectra (EI) were obtained using a JMS-mate operating in the electron impact mode (70 eV) equipped with a RTX-5 30MX.25MMX.25U column. HPLC separations were performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using $CHCl_3$ as an eluent. Column chromatography was conducted using Kanto Chemical Co., Inc. silica gel 60 (63-210 μm). Elemental analyses were performed on a Perkin Elmer 240C apparatus. GC yields were determined using octane as an internal standard. Vinyl Grignard reagent (Kanto Chemical Company), chlorotriethylsilane (Shin-Etsu Chemical Company), chlorotriphenylsilane, chlorotributylsilane, chlorotripropylsilane, (Aldrich Chemical Company), cyclopentene oxide, isobutylene oxide, oxetane, 3,3-dimethyl oxetane, diphenylmethylchlorosilane, benzylideneaniline, $NiCl_2(PPh_3)_2$ (Tokyo Chemical Industry Company) were purchased and used as received.

### Procedures and Characterization of Reaction Products

### General procedure (Table 1)

To a mixture of cyclic ethers (1.0 mmol) and $NiCl_2(PPh_3)_2$ (19.6 mg, 0.03 mmol) was added vinyl magnesium chloride (1.30 M in THF, 1.7 mL, 2.2 mmol) at 25 °C. After stirring for 3 h, aqueous 1N HCl was added and the products were extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to give crude products. Purification by column chromatography on silica gel gave the corresponding products (**2a**-**2e**).

### *trans*-2-(1-Methyl-2-propenyl)cyclopentanol (2a)

Purification by column chromatography on silica gel (pentane/ether = 6/4) gave 90 mg (66%) of **2a**. The following spectra and analytical data were obtained from 1:1.3 mixture of diastereomers; IR(NaCl): 3344, 2957, 2876, 1639, 1452, 1343, 1027, 996, 911 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 5.87-5.69 (m, 1H), 5.10-4.95 (m, 2H), 3.99-3.90 (m, 1H), 2.25-2.16 (m, 0.6H), 2.08-1.99 (m, 0.4H), 1.93-1.53 (m, 6H), 1.31-1.20 (m, 2H), 1.08 (d, $J$ = 6.8 Hz, 1.7H), 1.01 (d, $J$ = 6.6 Hz, 1.3H); $^{13}$C NMR (100 MHz, $CDCl_3$) (major and minor): δ (142.2, 144.2), (113.64, 113.62), (76.5, 77.3), (53.5, 53.4), (40.1, 42.8), (35.4, 34.4), (27.6, 28.9), (22.4, 21.7), (18.6, 18.9); MS (CI) *m*/*z* (relative intensity, %): 141 (M+1, 14), 124 (9), 123 (100), 84 (3), 81 (9), 67 (3); HRMS (CI) calcd for $C_9H_{17}O$ (M+1): 141.1201, found 141.1264.

### *trans*-2-(1-Methyl-2-propenyl)cyclododecanol (2b)

Purification by column chromatography on silica gel (hexane/ether = 9/1) gave 145 mg (61%) of **2b** as a mixture of diastereomers derived from *cis*-1,2-epoxycyclododecane with ca. 1:1 ratio indicated by $^1$H and $^{13}$C NMR. A 1:1 mixture of diastereomers; IR(NaCl): 3382, 2932, 2863, 1636, 1469, 1445, 1001, 907 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 6.05-5.92 (m, 1H), 5.10-4.98 (m, 2H), 3.79-3.72 (m, 1H), 2.68-2.58 (m, 0.5H), 2.58-2.50 (m, 0.5H), 1.74-1.25 (m, 22H), 1.08 (d, $J$ = 7.1 Hz, 1.5H), 1.05 (d, $J$ = 7.1 Hz, 1.5H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 144.7, 143.9, 113.8, 112.6, 72.0, 71.7, 43.6, 43.5, 37.6, 37.0, 32.9, 32.6, 25.2, 24.8, 24.6, 24.53, 24.50, 24.33, 24.27, 24.13, 24.11, 24.06, 23.99 (2 C), 23.92, 23.7, 23.6, 23.4, 21.2, 21.1, 18.0, 16.5; MS (EI) *m*/*z* (relative intensity, %): 238 (M$^+$, 12), 123 (10), 121 (12), 111 (16), 110 (10), 109 (33), 108 (10), 107 (13), 98 (15), 97 (25), 96 (24), 95 (55), 94 (18), 93 (17), 84 (27), 83 (54), 82 (25), 81 (53), 80 (11), 79 (16), 71 (19), 70 (76), 69 (60), 68 (25), 67 (45), 57 (23), 56 (40), 55 (100), 53 (11), 43 (17), 41 (40); HRMS calcd for $C_{16}H_{30}O$: 238.2297, found 238.2294; Anal. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68. Found: C, 80.50; H, 12.85.

### 2,4-Dimethyl-5-pentene-2-ol (2c)

This reaction was carried out on a 3.0 mmol scale. Purification by column chromatography on silica gel (pentane/ether = 6/4) gave 78 mg (20%) of **2c**. IR(NaCl): 3404, 2970, 2926, 1640, 1456, 1378, 1159, 908 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 5.81 (ddd, $J$ = 8.8 Hz, 10.0 Hz, 17.2 Hz, 1H), 5.09-4.94 (m, 2H), 2.50-2.39 (m, 1H), 1.74 (s, 1H), 1.60 (dd, $J$ = 9.6 Hz, 14.2 Hz, 1H), 1.49 (dd, $J$ = 4.0 Hz, 14.2 Hz 1H), 1.24 (s, 3H), 1.20 (s, 3H), 1.03 (d, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 146.2, 113.2, 71.5, 50.1, 35.2, 30.4, 29.4, 22.7; MS (CI) *m*/*z* (relative intensity, %): 129 (M+1, 0.8), 112 (9), 111 (100), 95 (1), 69 (4); HRMS (CI) calcd for $C_8H_{17}O$ (M+1): 129.1201, found 129.1277.

### 4-Methyl-5-hexen-1-ol (2d)

Purification by column chromatography on silica gel (pentane/ether = 6/4) gave 70 mg (62%) of **2d**. IR(NaCl): 3324, 3077, 2936, 1640, 1420, 1374, 1058, 910, 682 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 5.69 (ddd, *J* = 7.2 Hz, 10.1 Hz, 17.2 Hz, 1H), 4.99-4.92 (m, 2H), 3.64 (t, *J* = 7.2 Hz, 2H), 2.14 (qtd, *J* = 7.2 Hz, 7.2 Hz, 7.2 Hz, 1H), 1.62-1.51 (m, 2H), 1.40-1.31 (m, 3H), 1.00 (d, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 144.2, 112.7, 63.1, 37.7, 32.7, 30.6, 20.4; MS (EI) *m*/*z* (relative intensity, %): 114 (M$^+$, 0.1), 113 (0.1), 96 (9), 95 (6), 83 (12), 82 (8), 81 (100), 71 (27), 70 (86), 69 (15), 68 (77), 67 (30), 58 (11), 57 (27), 56 (22), 55 (95), 54 (17), 53 (19), 42 (14), 41 (37), 39 (20); HRMS calcd for $C_7H_{14}O$: 114.1045, found 114.1042; Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.35; H, 12.08.

### 2,2,4-Trimethyl-5-hexen-1-ol (2e)

Purification by column chromatography on silica gel (pentane/ether = 7/3) gave 70 mg (50%) of **2e**. IR(NaCl): 3334, 2955, 2244, 1643, 1456, 1365, 1040, 908 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 5.69 (ddd, *J* = 8.6 Hz, 10.3 Hz, 17.2 Hz, 1H), 5.02-4.87 (m, 2H), 3.36 (d, *J* = 11.0 Hz, 1H), 3.28 (d, *J* = 11.0 Hz, 1H), 2.35-2.25 (m, 1H), 1.42-1.36 (m, 2H), 1.22 (dd, *J* = 14.0 Hz, 3.6 Hz, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 3H), 0.89 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 146.5, 112.0, 71.7, 45.4, 35.9, 34.6, 25.2, 24.4, 23.9; MS (CI) *m*/*z* (relative intensity, %): 143 (M+1, 100), 126 (3), 125 (32), 83 (7), 69 (19); HRMS (CI) calcd for $C_9H_{19}O$ (M+1): 143.1358, found 143.1437.

### ***trans*-2-(1-Deuteriomethyl-2-propenyl)cyclopentanol (3)**

To a mixture of cyclopentene oxide (84.0 mg, 1.00 mmol) and $NiCl_2(PPh_3)_2$ (19.6 mg, 0.03 mmol) was added vinyl magnesium chloride (1.35 M in THF, 1.6 mL, 2.2 mmol) at 25 °C. After stirring for 3 h, $D_2O$ was added and the products were extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to give yellow crude products (79% NMR yield). Purification by column chromatography on silica gel (pentane/ether = 6/4) gave 90 mg (64%) of **3**. The following spectra and analytical data were obtained from 1:1.3 mixture of diastereomers; IR(NaCl): 3354, 2956, 2873, 1639, 1450, 1435, 1419, 1344, 1301, 1027, 996, 910 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 5.87-5.69 (m, 1H), 5.09-4.95 (m, 2H), 4.00-3.91 (m, 1H), 2.32-2.16 (m, 0.6H), 2.07-1.99 (m, 0.4H), 1.93-1.50 (m, 6H), 1.31-1.20 (m, 2H), 1.08-1.04 (m, 1.2H), 1.02-0.98 (m, 0.8H); $^{13}$C NMR (100 MHz, CDCl$_3$) (major and minor): δ (142.4, 144.4), (113.76, 113.75), (76.7, 77.5), (53.6, 53.5), (40.1, 42.7), (35.5, 34.5), (27.7, 28.9), (22.4, 21.8), (18.3, 18.6) (t, *J* = 19.3 Hz); MS (CI) *m*/*z* (relative intensity, %): 142 (M+1, 16), 125 (10), 124 (100), 123 (4), 82 (5), 67 (2); HRMS (CI) calcd for $C_9H_{16}DO$ (M+1): 142.1263, found 142.1337.

### *trans*-4-Vinyl-hexahydro-cyclopenta[*b*]pyran-2-one (5)

To a mixture of cyclopentene oxide (85.1 mg, 1.01 mmol) and $NiCl_2(PPh_3)_2$ (19.6 mg, 0.03 mmol) was added vinyl magnesium chloride (1.30 M in THF, 1.7 mL, 2.2 mmol) at 25 °C. After stirring for 3 h, $CO_2$ was added to the solution. After stirring for 30 min, aqueous 3N HCl (2 mL) was added to the solution and the mixture was stirred for 2 h at 40 °C. The product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. The NMR and GC analysis of the crude mixture indicated the formation of **5** as 1:1.3 mixture of diastereomers. Purification by HPLC afforded 62 mg (37%) of **5** as a mixture of diastereomers with ca. 5:1 retio. Major diastereomer; IR(NaCl): 3436, 2957, 2874, 1732, 1640, 1438, 1418, 1256, 1187, 918 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.67 (ddd, *J* = 7.2 Hz, 10.0 Hz, 17.2 Hz, 1H), 5.10-5.03 (m, 2H), 4.10 (td, *J* = 10.2 Hz, 7.6 Hz, 1H), 2.89-2.81 (m, 1H), 2.44-2.35 (m, 2H), 2.18-2.10 (m, 1H), 1.96-1.60 (m, 4H), 1.29-1.20 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 171.6, 139.1, 115.2, 84.0, 46.1, 41.5, 35.3, 29.2, 25.0, 19.3; MS (EI) *m*/*z* (relative intensity, %): 166 ($M^+$, 5), 138 (10), 124 (28), 95 (26), 82 (16), 81 (18), 80 (100), 79 (31), 68 (10), 67 (21), 54 (11), 53 (10), 41 (10); HRMS (EI) calcd for $C_{10}H_{14}O_2$: 166.0994, found 166.0995; Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.35; H, 8.65.

### 1,4-Bis(tributylsilyl)-2-butene (13)

Vinyl magnesium chloride (1.30 M in THF, 1.5 mL, 2.0 mmol) was added to $NiCl_2(PPh_3)_2$ (19.6 mg, 0.03 mmol) at 25 °C. After stirring for 3 h, tributylchlorosilane (234 mg, 1.00 mmol) was added to the solution at 25 °C. After stirring for 15 min, aqueous 1N HCl was added and the products were extracted with ether. The product was extracted with ether, dried over $MgSO_4$, and evaporated to give an orange crude product. Purification by HPLC with $CHCl_3$ as eluent afforded 316 mg (70%) of **13**. IR (NaCl): 2957, 2921, 2872, 2857, 1464, 1376, 1194, 1082, 886, ,789, 762, 728 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.29-5.18 (m, 2H), 1.43-1.39 (m, 4H), 1.36-1.22 (m, 24H), 0.88 (t, *J* = 6.8 Hz, 18H), 0.54-0.47 (m, 12H); $^{13}C$ NMR (100 MHz, $CDCl_3$): (*trans* isomer) δ 124.5, 26.8, 26.1, 18.4, 13.8, 11.9 (*cis* isomer) δ 123.2, 26.8, 26.2, 13.8, 13.6, 12.2; MS (EI) m/z (relative intensity, %) 452 ($M^+$, 11), 199 (94), 143 (100), 101 (12), 87 (13), 59 (14); HRMS calcd for $C_{28}H_{60}Si_2$ 452.4233, found 452.4224; Anal. Calcd for $C_{28}H_{60}Si_2$: C, 74.25; H, 13.35. Found: C, 74.26; H, 13.07.

### *N*-(2-Methyl-1-phenyl-3-butenyl)phenylamine (14)

### [CAS Registry Number 80188-13-2]

Vinyl magnesium chloride (1.30 M in THF, 1.5 mL, 2.0 mmol) was added to $NiCl_2(PPh_3)_2$ (19.6 mg, 0.03 mmol) at 25 °C. After stirring for 3 h, benzylideneaniline (181.2 mg, 1.00 mmol) was added to the solution at -78 °C. After stirring for 30 min, the solution was warmed to 0 °C and stirred at 0 °C for an additional 30 min. The product was extracted with ether, dried over $MgSO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 8/2) gave 137 mg (58%) of **14** as a mixture of diastereomers (threo/erythro = 94/6). Erythro isomer: $^1$H NMR (400 MHz, $CDCl_3$): δ 7.36-7.20 (m, 5H), 7.06-7.02 (m, 2H), 6.62-6.58 (m, 1H), 6.46 (d, *J* = 7.8 Hz, 2H), 5.75 (ddd, *J* = 7.6 Hz, 10.1 Hz, 17.5 Hz, 1H), 5.20-5.15 (m, 2H), 4.22 (br, 1H), 4.07 (d, *J* = 7.1 Hz, 1H), 2.56-2.47 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 147.6, 142.6, 140.5, 129.0, 128.3, 127.2, 127.0, 117.1, 116.2, 113.3, 62.3, 45.2, 17.3.

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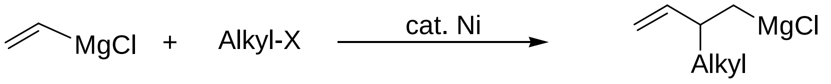
# Chapter 4

## Titanocene-Catalyzed Alkylative Dimerization of Vinyl Grignard Reagents Using Alkyl Halides

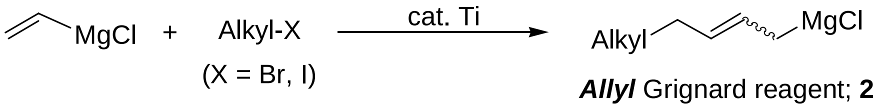
### 4-1. Introduction

In the past decade, the remarkable progress was made in the C–C forming reactions using non-activated alkyl halides, which had rarely been employed as carbon sources in conventional transition-metal-catalyzed systems.[1] We have recently developed cross-coupling reactions[2] and regioselective alkylation reactions of C–C unsaturated compounds[3] using alkyl halides and shown that the ate complexes of transition metals formed using Grignard reagents play an important role as active catalytic species. During the course of these studies, we have observed that Ni catalyzes regioselective 2:1 coupling reaction of vinyl Grignard reagents with alkyl halides or cyclic ethers to afford alkylated homoallylic Grignard reagents **1** (Eq. 1).[4] Here, I reveal that the alkylative dimerization of vinyl Grignard reagents proceeds regioselectively in the presence of a titanocene catalyst, resulting in allyl Grignard reagents **2** having an alkyl group at the terminal carbon (Eq. 2).



(1)

***Homoallyl*** Grignard reagent; **1**

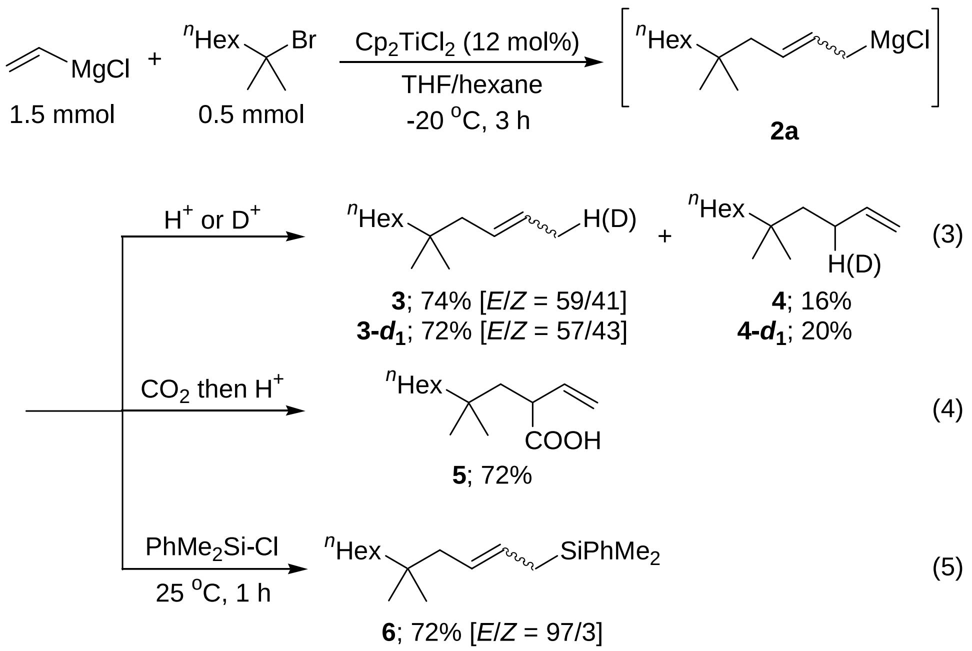


(2)

***Allyl*** Grignard reagent; **2**

### 4-2. Results and Discussion

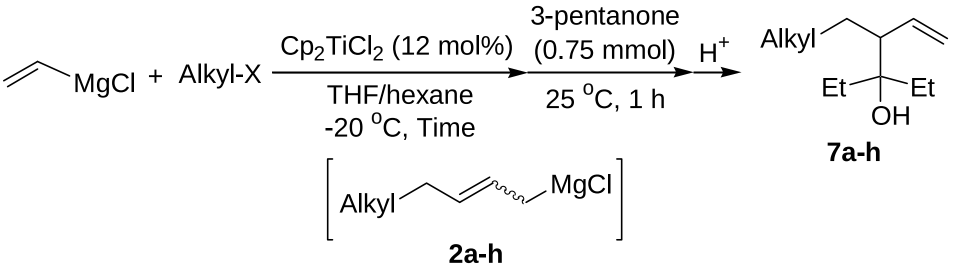
When vinyl magnesium chloride (1.5 mmol, 1.4 M in THF) was reacted with 2-bromo-2-methyloctane (0.5 mmol) in the presence of $Cp_2TiCl_2$ (0.06 mmol) and hexane (0.22 ml) at –20 °C under nitrogen, a mixture of coupling products **3** and **4** was obtained (Eq. 3). When the reaction mixture was quenched with $D_2O$, deuterated compounds **3-*d*₁** (*d*-content > 98%) and **4-*d*₁** (*d*-content > 98%) were formed in 72% and 20% yields, respectively. This result implies that the allyl Grignard reagent **2a** was formed in this reaction. The quenching of the resulting mixture with $CO_2$ or chlorosilane yielded the single regioisomers. For example, $CO_2$ reacted with the allylic Grignard reagents **2a** via a six-membered cyclic transition state to form **5** (Eq. 4). On the other hand, the silylation of the terminal carbon of **2a** yielded **6** probably due to the steric hindrance of the silyl group (Eq. 5).

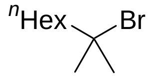


The results obtained using various alkyl halides, along with 3-pentanone as an electrophile, are summarized in Table 1. The use of 2-bromo-2-methyloctane yielded tertiary alcohol **7a** in 87% yield (Table 1, entry 1). Tertiary, secondary, and primary alkyl bromides afforded corresponding products in moderate to good yields (entries 2–5). Under similar conditions, alkyl iodides afforded corresponding alkylated products (entries 6–8); however, no reaction occurred when we used alkyl chlorides and fluorides. The present reaction was sluggish toward substituted vinyl Grignard reagents, such as MeCH=CHMgBr, $CH_2$=CMeMgBr, and PhCH=CHMgBr.

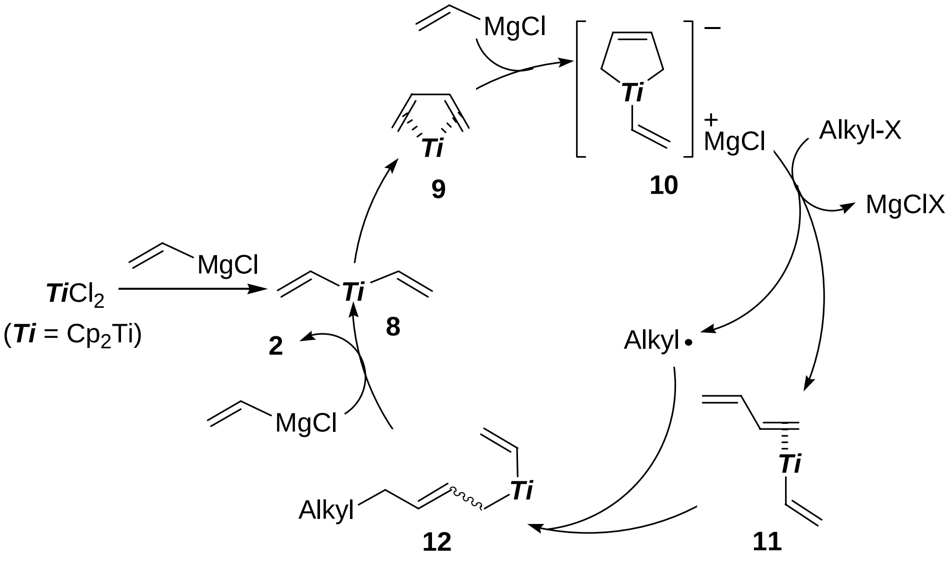
A plausible reaction pathway is shown in Scheme 1. First, titanocene dichloride reacts with two equivalents of vinyl magnesium chlorides to afford divinyl titanocene **8**, which undergoes reductive coupling to afford a titanocene-butadiene complex **9**.[5, 6] Then, **9** reacts with vinyl magnesium chloride to afford a titanate complex **10**.[7] Subsequent one electron transfer from **10** to alkyl halides yields alkyl radicals along with a titanocene (III) complex **11**.[8] Finally the addition of the alkyl radicals to a coordinated butadiene ligand of **11**, or to free butadiene followed by recombination with $Cp_2Ti$(vinyl), leads to the formation of an $\eta^1$-allyltitanocene complex **12**[9], which undergoes transmetallation with vinyl magnesium chloride to yield allyl Grignard reagent **2** and regenerate **8**.[10]

**Table 1**. Titanocene-catalyzed coupling reaction of vinyl Grignard reagent with alkyl halides and quenching with 3-pentanone[a]



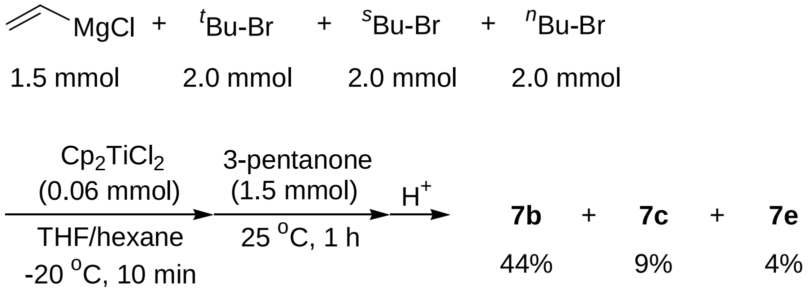
| Entry | Alkyl-X | Time (h) | Yield (%)[b] |
|---|---|---|---|
| 1 |  | 3 | **7a**; 87 |
| 2 | $^t$BuBr | 1 | **7b**; 77 |
| 3 | $^s$Bu-Br | 3 | **7c**; 64 |
| 4 | 2-Norbornyl-Br | 4 | **7d**; 63 |
| 5[c] | $^n$Bu-Br | 3 | **7e**; 50 |
| 6 | 1-Adamantyl-I | 1 | **7f**; 56 |
| 7[c] | $^n$Oct-I | 1 | **7g**; 48 |
| 8 | $^c$Hex-I | 3 | **7h**; 69 |

[a] $Cp_2TiCl_2$ (0.06 mmol), hexane (0.22 ml), alkyl halide (0.5 mmol) vinyl Grignard reagent (1.5 mmol), -20 °C, then 3-pentanone (0.75 mmol) 25 °C, 1 h. [b] Isolated yield. [c] Vinyl Grignard reagent (1.7 mmol) and $Cp_2TiCl_2$ (0.075 mmol) were used.

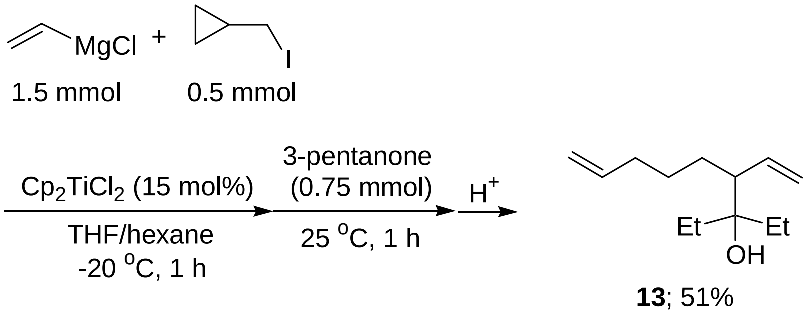


**Scheme 1**. A plausible reaction pathway

I performed two control experiments to confirm the radical mechanism of the alkylation step. I first carried out a competitive reaction by using equimolar amounts of *tert*-butyl, *sec*-butyl, and *n*-butyl bromides to obtain the relative reactivities of alkyl halides (Eq. 6). The quenching of the reaction with 3-pentanone afforded alcohols **7b**, **7c** and **7e** in 44%, 9% and 4% yields, respectively. The evidence that alkyl bromides having more branched chains reacted faster than those having less branched chains may suggest that alkyl groups are introduced to the coupling products as alkyl radicals intermediates. Next, I employed cyclopropylmethyl iodide as an alkylating reagent. As expected, an acyclic product **13** was obtained via the ring opening of the cyclopropylmethyl radical to 3-butenyl radical (Eq. 7).



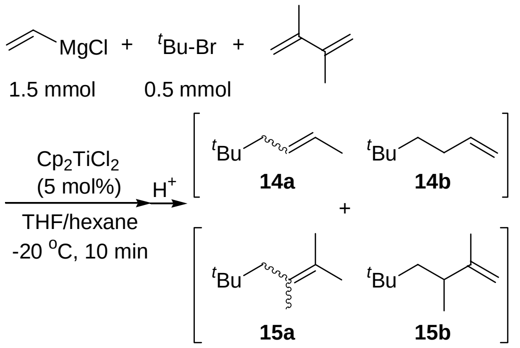
(6)



(7)

From a mechanistic viewpoint, it is interesting to examine whether the alkyl radical attacks butadiene coordinated on the Ti complex or that in the free state. In order to determine this behavior of alkyl radical, I reacted the vinyl Grignard reagent with *tert*-butyl bromide in the presence of 2,3-dimethylbutadiene at different concentrations, and the ratio of **15** to **14** was plotted against the amount of 2,3-dimethylbutadiene added (Eq. 8, Figure 1). Figure 1 shows that the addition of 2,3-dimethylbutadiene causes a increase in the ratio of **15** to **14**; however, this ratio does not obey the first-order kinetics equation on the concentration of 2,3-dimethylbutadiene, i.e., three times the concentration of the 2,3-dimethylbutadiene leads to 1.7 times increase in the ratio. This result may imply that the alkyl radical attacks coordinated form of

2,3-dimethylbutadiene and not free 2,3-dimethylbutadiene, where the former 2,3-dimethylbutadiene is formed by the ligand exchange in the titanocene complex **11**. Next, I carried out similar competitive reactions in the presence of a constant concentration of 2,3-dimethylbutadiene and varying amounts of 1,3-butadiene (Eq. 9, Figure 2). Figure 2 shows the ratio of **14** to **15** plotted against the amount of 1,3-butadiene used, revealing that the concentration of 1,3-butadiene did not significantly affect the ratio of two products (the addition of 20 times the amounts of butadiene increased the ratio of **14** to **15** ratio by only 1.5 times). This result clearly suggests that the alkyl radical does not attack free 1,3-butadiene, which, however, may inhibit the ligand exchange in the titanocene complex **11**.



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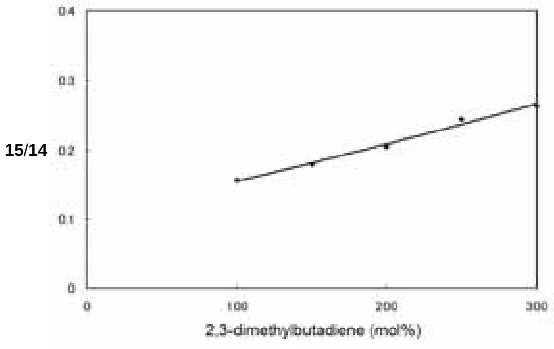
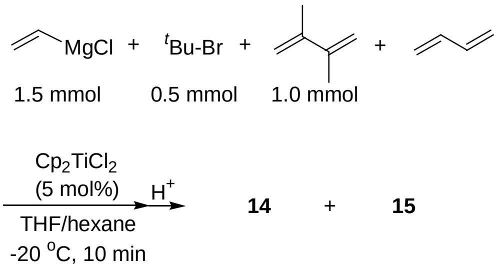


Figure 1



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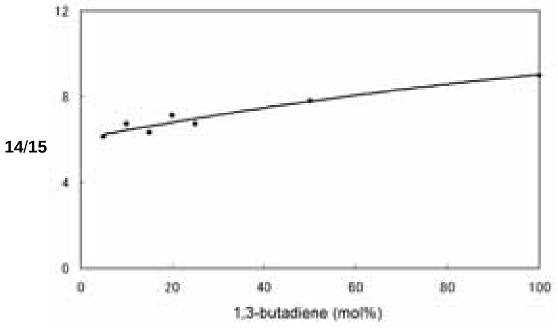

Figure 2

## 4-3. Conclusion

In conclusion, I have shown that titanocene catalyzes the alkylative dimerization of a vinyl Grignard reagent with alkyl halides to afford allyl Grignard reagents having a carbon chain at a terminal carbon. The Ti catalyst would play an important role in the generation of alkyl radicals from alkyl halides by electron transfer from Ti(III) ate complexes. It is also proposed that alkyl radicals would preferentially attack coordinated butadiene rather than free butadiene.

## 4-4. Experimental Section

### General Comments

$^1$H NMR and $^{13}$C NMR spectra were recorded with a JEOL JNM-Alice 400 (400 MHz and 100 MHz, respectively) spectrometer. Chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were recorded with a Perkin-Elmer FT-IR (Model 1600). Both conventional and high resolution mass spectra were recorded with a JEOL JMS-DX303HF spectrometer. GC Mass spectra (EI) were obtained using a JMS-mate operating in the electron impact mode (70 eV) equipped with a RTX-5 30MX.25MMX.25U column. HPLC separations were performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using $CHCl_3$ as an eluent. Column chromatography was conducted using Kanto Chemical Co., Inc. silica gel 60 (63-210 μm). Elemental analyses were performed on a Perkin Elmer 240C apparatus. GC yields were determined using octane as an internal standard. Vinyl Grignard reagent, $Cp_2TiCl_2$ (Kanto Chemical Company), *tert*-butyl Bromide, cyclohexyl bromide (Tokyo Chemical Industry Company), norbornyl bromide, adamanty iodide, 2,3-dimethylbutadiene, dimethylphenylchlorosilane, (Aldrich Chemical Company), *sec*-butyl Bromide, *n*-butyl bromide, *n*-octyl iodide, cyclohexyl iodide, cyclohexyl chloride, 3-pentanone, $D_2O$ (Wako Pure Chemical Industries) were purchased and used as received. 2-Bromo-2-methyloctane was prepared from 2-methyloctane-2-ol and phosphorus tribromide. Cyclopropylmethyl iodide were prepared according to the literature (R. S. Tipson, M. A. Clapp, L. H. Cretcher, *J. Org. Chem.* **1947**, *12*, 133.)

### Procedures and Characterization of Reaction Products

### 1-Deuterio-5,5-dimethyl-2-undecene (3-*d*$_1$) and 3-Deuterio-5,5-dimethyl-1-undecene (4-*d*$_1$)

To a mixture of 2-bromo-2-methyloctane (102.1 mg, 0.50 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, $D_2O$ was added to the solution at 25 °C. Aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane) gave 84 mg (92%) of **3-*d*$_1$** and **4-*d*$_1$**. IR(NaCl): 2958, 2928, 1640, 1469, 1364, 908 cm$^{-1}$; Anal. Calcd for $C_{13}H_{25}D$: C, 85.16; H and D, 14.84. found: C, 85.20; H and D, 14.80; **3-*d*$_1$**: (*E* isomer) δ 5.48-5.34 (m, 2H), 1.84 (d, $J$ = 6.1 Hz, 2H), 1.66-1.62 (m, 2H), 0.88 (t, $J$ = 6.8 Hz, 3H), 0.81 (s, 6H); $^{13}$C NMR (100

MHz, $CDCl_3$): δ 128.3, 126.7, 45.1, 41.9, 33.2, 32.0, 30.3, 27.0, 23.9, 22.7, 17.8 (t, *J* = 19.3 Hz), 14.0; MS (EI) *m*/*z* (relative intensity, %): 183 ($M^+$, 0.2), 127 (30), 126 (23), 98 (8), 86 (5), 85 (64), 84 (4), 72 (6), 71 (100), 70 (7), 69 (12), 57 (62), 56 (24), 55 (16), 43 (50), 41 (16); HRMS calcd for $C_{13}H_{25}D$: 183.2096, found 183.2088.; (*Z* isomer) $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.56-5.48 (m, 2H), 1.92 (d, *J* = 7.3 Hz, 2H), 1.60-1.56 (m, 2H), 1.32-1.10 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.84 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 127.6, 125.0, 42.0, 38.8, 33.7, 32.0, 30.3, 27.0, 24.1, 22.7, 14.0, 12.7 (t, *J* = 19.3 Hz); MS (EI) *m*/*z* (relative intensity, %): 183 ($M^+$, 1), 128 (3), 127 (31), 126 (14), 125 (24), 112 (6), 99 (13), 98 (100), 97 (13), 85 (46), 84 (12), 83 (10), 82 (23), 71 (69), 70 (18), 69 (24), 57 (46), 56 (70), 55 (62), 43 (45), 41 (22); HRMS calcd for $C_{13}H_{25}D$: 183.2096, found 183.2089.; **4-*d*$_1$**: $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.82 (ddd, *J* = 6.7, 10.2, 17.0 Hz, 1H), 5.02-4.90 (m, 2H), 2.01-1.91 (m, 1H), 1.34-1.12 (m, 12H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.84 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 140.0, 113.6, 42.0, 41.1, 32.6, 32.0, 30.3, 28.3 (t, *J* = 19.0 Hz), 27.2, 24.0, 22.7, 14.1; MS (EI) *m*/*z* (relative intensity, %): 183 ($M^+$, 0.2), 127 (32), 126 (18), 98 (6), 86 (4), 85 (60), 72 (6), 71 (100), 70 (7), 69 (10), 57 (59), 56 (20), 55 (15), 43 (50), 41 (13); HRMS calcd for $C_{13}H_{25}D$: 183.2096, found 183.2093.

**2-(2,2-dimethyl-octyl)-3-butenoic acid (5)**

To a mixture of 2-bromo-2-methyloctane (103.6 mg, 0.50 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, $CO_2$ was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 2/1) gave 82 mg (72%) of **5**. IR(NaCl): 3083, 2957, 2929, 2859, 1708, 1637, 1469, 1416, 1388, 1367, 1286, 1220, 991, 920 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.81 (ddd, *J* = 8.3, 10.0, 16.9 Hz, 1H), 5.21-5.09 (m, 2H), 3.13 (ddd, *J* = 8.3, 7.8, 4.4 Hz, 1H), 1.88 (dd, *J* = 7.8, 14.2 Hz, 1H), 1.42 (dd, *J* = 4.4, 14.2 Hz, 1H), 1.30-1.20 (m, 10H), 0.90-0.86 (m, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 137.4, 116.7, 46.6, 43.6, 42.3, 33.4, 31.9, 30.1, 27.2, 27.1, 23.8, 22.7, 14.1; MS (EI) *m*/*z* (relative intensity, %): 226 ($M^+$, 0.3), 211 (2), 171 (2), 165 (6), 143 (7), 142 (4), 141 (37), 128 (5), 127 (47), 126 (16), 125 (8), 123 (7), 109 (9), 100 (6), 99 (40), 98 (5), 97 (41), 96 (15), 95 (100), 94 (4), 86 (6), 85 (59), 83 (10), 81 (17), 79 (4), 73 (4), 72 (5), 71 (90), 70 (10), 69 (29), 67 (11), 59 (10), 57 (69), 56 (14), 55 (43), 53 (7), 43 (63), 41 (37); HRMS calcd for $C_{14}H_{26}O_2$ 226.1933, found 226.1928. Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. found: C, 74.18; H, 11.41.

### 5,5-Dimethyl-1-dimethylphenylsilyl-2-undecene (6)

To a mixture of 2-bromo-2-methyloctane (103.6 mg, 0.50 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, chlorodimethylphenylsilane (126 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane) gave 114 mg (72%, *E*/*Z* = 97/3) of **6**. (*E* isomer) IR(NaCl): 3050, 3018, 2955, 2927, 2858, 1654, 1467, 1427, 1383, 1364, 1248, 1156, 1113, 967, 837, 729, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.51-7.50 (m, 2H), 7.35-7.32 (m, 3H), 5.38-5.22 (m, 2H), 1.83 (d, *J* = 6.6 Hz, 2H), 1.68 (d, *J* = 7.3 Hz, 2H), 1.32-1.06 (m, 10H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.77 (s, 6H), 0.27 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 139.0, 133.6, 128.9, 127.7, 127.4, 126.5, 45.4, 41.9, 33.3, 32.0, 30.3, 27.0, 23.9, 22.7, 21.8, 14.2, -3.2. ; MS (EI) *m*/*z* (relative intensity, %): 316 ($M^+$, 2), 190 (1), 137 (4), 136 (13), 135 (100), 121 (2), 107 (2), 105 (2), 85 (2), 71 (3), 57 (2), 43 (3); HRMS calcd for $C_{21}H_{36}Si$ 316.2586, found 316.2593. Anal. Calcd for $C_{21}H_{36}Si$: C, 79.67; H, 11.46. found: C, 79.40; H, 11.50.

### 3-Ethyl-4- vinyl-6,6-dimethyl-3-dodecanol (7a)

To a mixture of 2-bromo-2-methyloctane (102 mg, 0.50 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 95/5) gave 116 mg (87%) of **7a**. IR(NaCl): 3491, 2930, 2858, 1636, 1466, 1385, 1365, 1254, 1159, 1006, 952, 910 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.72 (ddd, *J* = 10.0, 10.2, 17.3 Hz, 1H), 5.14-5.07 (m, 2H), 2.32-2.28 (m, 1H), 1.60-1.38 (m, 5H), 1.30-1.19 (m, 12H), 0.89-0.84 (m, 15H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 142.2, 117.3, 75.3, 47.3, 43.0, 40.5, 33.6, 32.0, 30.2, 28.6, 28.0, 27.9, 23.9, 22.7, 14.1, 7.6, 7.4; MS (CI) *m*/*z* (relative intensity, %): 269 (M+1, 0.2), 252 (5), 251 (26), 249 (3), 195 (3), 181 (7), 167 (10), 153 (5), 141 (4), 139 (6), 128 (10), 127 (100), 126 (5), 125 (32), 113 (3), 111 (6), 97 (4), 87 (28), 85 (9), 71 (7); HRMS (CI) calcd for $C_{18}H_{37}O$ 269.2844, found 268.2837. Anal. Calcd for $C_{18}H_{36}O$: C, 80.53; H, 13.52. found: C, 80.39; H, 13.36.

### 3-Ethyl-4- vinyl-6,6-dimethyl-3-heptanol (7b)

To a mixture of *t*-butyl bromide (66 mg, 0.48 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 1 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (pentane/ether = 95/5) gave 73 mg (77%) of **7b**. IR(NaCl): 3494, 2953, 1636, 1465, 1365, 1244, 1160, 953, 911 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.72 (ddd, *J* = 10.0, 10.0, 17.1 Hz, 1H), 5.16-5.07 (m, 2H), 2.33-2.29 (m, 1H), 1.63-1.41 (m, 5H), 1.28-1.22 (m, 2H), 0.90-0.85 (m, 15H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 142.2, 117.4, 75.2, 47.7, 42.6, 31.3, 30.4, 28.6, 27.9, 7.6, 7.4; MS (CI) *m*/*z* (relative intensity, %): 199 (M+1, 1), 182 (14), 181 (100), 126 (2), 125 (18), 111 (16), 109 (2), 97 (8), 87 (22), 85 (10), 71 (5); HRMS (CI) calcd for $C_{13}H_{27}O$ 199.2062, found 199.2080. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. found: C, 78.54; H, 12.92.

### 3-Ethyl-4- vinyl-6-methyl-3-octanol (7c)

To a mixture of *s*-butyl bromide (66 mg, 0.48 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (pentane/ether = 95/5) gave 61 mg (64%) of **7c** as a mixture of diastereomers with ca. 1:1 ratio indicated by $^1H$, $^{13}C$ NMR and GC. A 1:1 mixture of diastereomers; IR(NaCl): 3492, 2964, 1636, 1460, 1377, 1260, 911 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 5.70-5.58 (m, 1H), 5.17-5.03 (m, 2H), 2.25-2.20 (m, 1H), 1.58-1.42 (m, 5H), 1.39-1.17 (m, 5H), 0.88-0.81 (m, 12H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 139.5, 139.2, 117.7, 117.6, 75.3, 75.2, 48.9, 48.8, 35.5, 35.1, 31.9, 31.7, 31.1, 28.50, 28.47, 28.3 (2C), 27.1, 20.5, 18.1, 11.5, 10.8, 7.59, 7.57, 7.4, 7.3; MS (CI) *m*/*z* (relative intensity, %): 199 (M+1, 3), 182 (15), 181 (100), 139 (7), 126 (6), 125 (60), 112 (12), 111 (99), 109 (7), 99 (18), 97 (51), 87 (44), 85 (58), 83 (10), 75 (5), 71 (18); HRMS (CI) calcd for $C_{13}H_{27}O$ 199.2062, found 199.2065. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. found: C, 78.98; H, 13.15.

### 3-Ethyl-2-vinyl-1-norbornyl-3-pentanol (7d)

To a mixture of *exo*-2-norbornyl bromide (87 mg, 0.49 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 95/5) gave 74 mg (63%) of **7d** as a mixture of diastereomers with ca. 1:1 ratio indicated by $^1$H, $^{13}$C NMR and GC. A 1:1 mixture of diastereomers; IR(NaCl): 3483, 2949, 2869, 1636, 1456, 1379, 1314, 1258, 1167, 1143, 1125, 1005, 948, 910 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 5.71-5.60 (m, 1H), 5.17-5.01 (m, 2H), 2.22-1.85 (m, 4H), 1.60-1.02 (m, 15H), 0.88-0.83 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 139.3, 139.2, 117.8 (2C), 75.1 (2C), 50.5, 48.6, 42.5, 39.65, 39.57, 39.21, 39.17, 37.3, 36.8, 36.4, 35.8, 35.5, 35.2, 35.0, 30.2, 29.9, 28.8, 28.6, 28.5 (2C), 28.4, 28.3, 7.5 (2C), 7.38, 7.36; MS (CI) *m*/*z* (relative intensity, %): 237 (M+1, 0.8), 220 (17), 219 (100), 217 (6), 177 (5), 163 (12), 150 (5), 149 (26), 137 (12), 136 (4), 135 (31), 123 (13), 121 (5), 109 (11), 97 (3), 95 (11), 87 (21), 69 (2); HRMS (CI) calcd for $C_{16}H_{29}O$ 237.2218, found 237.2211. Anal. Calcd for $C_{16}H_{28}O$: C, 81.29; H, 11.94. found: C, 81.08; H, 11.65.

### 3-Ethyl-4- vinyl-3-nonanol (7e)

To a mixture of *n*-butyl bromide (66 mg, 0.48 mmol), $Cp_2TiCl_2$ (18.7 mg, 0.075 mmol) and hexane (0.24 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.2 mL, 1.65 mmol) at -20 °C. After stirring for 3 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (pentane/ether = 95/5) gave 47 mg (50%) of **7e**. IR(NaCl): 3485, 2963, 2858, 1636, 1463, 1378, 1259, 1005, 948, 911 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 5.64 (ddd, $J$ = 10.0, 10.0, 17.1 Hz, 1H), 5.16-5.03 (m, 2H), 2.12-2.06 (m, 1H), 1.57-1.43 (m, 5H), 1.31-1.14 (m, 8H), 0.89-0.84 (m, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 139.2, 117.7, 75.2, 51.5, 31.9, 28.6, 28.4, 28.1, 27.8, 22.6, 14.1, 7.5, 7.4; MS (CI) *m*/*z* (relative intensity, %): 199 (M+1, 1), 182 (14), 139 (4), 125 (11), 111 (16), 97 (13), 87 (16), 85 (3), 83 (4); HRMS (CI) calcd for $C_{13}H_{27}O$ 199.2062, found 199.2051. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. found: C, 78.52; H, 12.97.

### 1-(1-Adamantyl)-3-ethyl-2-vinyl-3-pentanol (7f)

To a mixture of 1-adamantyl iodide (130 mg, 0.50 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 1 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 95/5) gave 78 mg (56%) of **7f**. IR(NaCl): 3490, 2967, 2899, 2846, 1636, 1452, 1362, 1347, 1326, 1257, 1160, 1099, 1005, 951, 909 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 5.71 (ddd, $J$ = 9.8, 9.8, 17.0 Hz, 1H), 5.14-5.07 (m, 2H), 2.39-2.34 (m, 1H), 1.94-1.90 (m, 4H), 1.69-1.38 (m, 17H), 1.29-1.25 (m, 1H), 1.12 (dd, $J$ = 9.8, 13.6 Hz, 1H), 0.89-0.82 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 142.6, 117.1, 75.3, 45.5, 43.6, 43.3, 37.1, 33.2, 28.8, 28.6, 27.9, 7.6, 7.4; MS (CI) *m/z* (relative intensity, %): 277 (M+1, 0.3), 275 (5), 260 (11), 259 (52), 257 (9), 190 (3), 189 (6), 136 (11), 135 (100), 123 (6), 87 (22); HRMS (CI) calcd for $C_{19}H_{31}$ (M-$H_2O$) 259.2428, found 259.2426. Anal. Calcd for $C_{19}H_{32}O$: C, 82.55; H, 11.67. found: C, 82.28; H, 11.39.

### 3-Ethyl-4-vinyl-3-tridecanol (7g)

To a mixture of *n*-octyl iodide (120 mg, 0.50 mmol), $Cp_2TiCl_2$ (18.7 mg, 0.075 mmol) and hexane (0.24 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.2 mL, 1.65 mmol) at -20 °C. After stirring for 1 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 95/5) gave 61 mg (48%) of **7g**. IR(NaCl): 3481, 2926, 2854, 1636, 1459, 1378, 1257, 1160, 948, 911 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 5.64 (ddd, $J$ = 9.8, 9.8, 17.1 Hz, 1H), 5.16-5.03 (m, 2H), 2.11-2.05 (m, 1H), 1.61-1.42 (m, 5H), 1.31-1.23 (m, 16H), 0.90-0.84 (m, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 139.2, 117.7, 75.2, 51.5, 31.9, 29.7, 29.63, 28.61, 29.3, 28.6, 28.4, 28.14, 28.11, 22.7, 14.1, 7.5, 7.4; MS (CI) *m/z* (relative intensity, %): 255 (M+1, 1), 238 (19), 237 (100), 235 (4), 181 (4), 167 (7), 153 (8), 139 (9), 125 (11), 111 (13), 97 (14), 87 (31), 83 (4); HRMS (CI) calcd for $C_{17}H_{35}O$ 255.2688, found 255.2665. Anal. Calcd for $C_{17}H_{34}O$: C, 80.24; H, 13.47. found: C, 79.97; H, 13.49.

### 1-Cyclohexyl-3-ethyl-2-vinyl-3-pentanol (7h)

To a mixture of cyclohexyl iodide (102 mg, 0.49 mmol), $Cp_2TiCl_2$ (14.9 mg, 0.06 mmol) and hexane (0.22 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.1 mL, 1.5 mmol) at -20 °C. After stirring for 3 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (hexane/ether = 95/5) gave 75 mg (69%) of **7h**. IR(NaCl): 3484, 2967, 2924, 2852, 1636, 1449, 1379, 1167, 1126, 1005, 956, 944, 924, 910 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 5.64 (ddd, *J* = 9.8, 9.8, 17.1 Hz, 1H), 5.16-5.03 (m, 2H), 2.28-2.22 (m, 1H), 1.82-1.79 (m, 1H), 1.69-1.43 (m, 10H), 1.28-1.10 (m, 7H), 0.85 (d, *J* = 7.6 Hz, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 139.3, 117.7, 75.2, 48.1, 36.0, 35.1, 34.9, 31.8, 28.5, 28.3, 26.7, 26.5, 26.2, 7.6, 7.3; MS (CI) *m/z* (relative intensity, %): 225 (M+1, 0.8), 208 (15), 207 (100), 205 (7), 165 (6), 151 (18), 138 (7), 137 (24), 125 (22), 123 (27), 112 (6), 111 (58), 109 (12), 97 (33), 95 (5), 87 (34), 83 (6); HRMS (CI) calcd for $C_{15}H_{29}O$ 225.2218, found 225.2223. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. found: C, 80.01; H, 12.64.

### 3-Ethyl-4-vinyl-8-nonene-3-ol (13)

To a mixture of cyclopropylmetyl iodide (91 mg, 0.50 mmol), $Cp_2TiCl_2$ (18.7 mg, 0.075 mmol) and hexane (0.24 mL) was added vinyl magnesium chloride (1.42 M in THF, 1.2 mL, 1.65 mmol) at -20 °C. After stirring for 1 h, 3-pentanone (64.6 mg, 0.75 mmol) was added to the solution at 25 °C. After stirring for 1 h, aqueous 1N HCl was added and the product was extracted with ether, dried over $Na_2SO_4$, and evaporated to give an orange crude product. Purification by column chromatography on silica gel (pentane/ether = 95/5) gave 51 mg (51%) of **13**. IR(NaCl): 3483, 3074, 2967, 1639, 1459, 1377, 1159, 1002, 950, 910 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 5.80 (tdd, *J* = 6.8, 10.3, 17.1 Hz, 1H), 5.65 (ddd, *J* = 10.0, 10.0, 17.1 Hz, 1H), 5.17-4.92 (m, 4H), 2.12-1.98 (m, 3H), 1.59-1.41 (m, 6H), 1.27-1.19 (m, 3H), 0.88-0.84 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 139.0, 138.9, 117.9, 114.4, 75.3, 51.4, 33.8, 28.6, 28.4, 27.6, 27.4, 7.5, 7.4; MS (CI) *m/z* (relative intensity, %): 197 (M+1, 3), 180 (14), 179 (100), 138 (3), 137 (21), 124 (6), 123 (71), 111 (6), 110 (11), 109 (100), 98 (6), 97 (76), 96 (4), 95 (43), 87 (40), 83 (22), 81 (9), 69 (5); HRMS (CI) calcd for $C_{13}H_{25}O$ 197.1905, found 197.1906. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. found: C, 79.29; H, 12.03.

## 4-5. References

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# Conclusion

In this study, the author succeeded in developing synthetic methods of Grignard reagents involving C-C bond formation by using transition metal catalysts. The results obtained are summarized as follows.

Chapter 1 disclosed that palladium catalyzes regioselective carbomagnesiation of allenes giving rise to allyl Grignard reagents. In the presence of chlorosilanes and alkyl halides, silylation and alkylation of allenes proceeded efficiently via the formation of palladate complexes or allyl Grignard reagents.

Chapter 2 described that silver catalyzes regioselective carbomagnesiation of non-functionalized terminal alkynes and enynes using *n*-, *sec*-, and *tert*-alkyl Grignard reagents in the presence of 1,2-dibromoethane. This reaction provides a new method for preparation of various vinyl, allenyl and propargyl Grignard reagents which could be trapped with a variety of electrophiles to form functionalized alkenes, allenes and alkynes.

Chapter 3 revealed that nickel catalyzes alkyllative dimerizarion of vinyl Grignard reagents using cyclic ethers to afford 2-alkyl-3-butenyl Grignard reagents. This reaction proceeds via electrophilic introduction of alkyl group derived from cyclic ethers to butadiene formed by dimerization of vinyl Grignard reagents.

Chapter 4 revealed that titanocene catalyzes alkylative dimerizarion of vinyl Grignard reagents using *n*-, *sec*-, and *tert*-alkyl halides to afford allyl Grignard reagents. This reaction system differs from nickel catalyzed system (Chapter 3) in that alkyl group are introduced to butadiene formed in *situ* as alkyl radical.

# List of Publications

1. Silylation and Alkylation of Allenes Using Chlorosilanes and Alkyl Halides in the Presence of Palladium Catalyst and Grignard Reagents
   Yuuki Fujii, Jun Terao, Hitoshi Kuniyasu and Nobuaki Kambe
   *J. Organomet. Chem.* **2007**, *692*, 375-381.

2. Nickel-Catalyzed Dimerization Coupling Reactions of Vinyl Grignard Reagents with 3,4-Membered Cyclic Ethers and Chlorosilanes
   Yuuki Fujii, Jun Terao, Hiroyasu Watabe, Hiroyuki Watanabe and Nobuaki Kambe
   *Tetrahedron* **2007**, *63*, 6635-6641.

3. Titanocene-Catalyzed Alkylative Dimerization of Vinyl Grignard Reagent Using Alkyl Halides
   Yuuki Fujii, Jun Terao, Yuichiro Kato and Nobuaki Kambe
   *Chem. Commun.* **2008**, 5836-5838.

4. Silver-Catalyzed Carbomagnesiation of Terminal Aryl and Silyl Alkynes and Enynes in the Presence of 1,2-Dibromoethane
   Yuuki Fujii, Jun Terao and Nobuaki Kambe
   *Chem. Commun.* **2009**, *in press*.

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