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STUDIES ON THE ALKYLATION AND SILYLATION OF ALKENES CATALYZED BY EARLY TRANSITION METALS

（前周期遷移金属触媒を用いるアルケン類のアルキル化及びシリル化反応に関する研究）

JUN TERAO

OSAKA UNIVERSITY

1999

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General Introduction

The reactions which introduce functionalities to carbon-carbon unsaturated bonds have been widely used for organic syntheses as useful methods for the construction of organic molecules.[1] As one methodology for such transformations, there have been developed a number of reactions using a transition metal catalyst, but in many cases the late transition metal catalysts have been employed.[2] The main object of the present studies is to develop new catalytic reactions using the characteristics of early transition metals.[3]

This thesis consists of four chapters. Chapter 1 deals with zirconocene-catalyzed silylation of alkenes with chlorosilanes. Terminal alkenes undergo silylation by the reaction with chlorosilanes in the presence of a Grignard reagent employing a catalytic amount of zirconocene dichloride to give alkenyl and/or allylsilanes as the products. The reaction also proceeds under mild conditions when silyl sulfides, silyl selenides, and silyl tellurides are used in place of chlorosilanes. As an extension of chapter 1, Chapter 2 refers to a new transformation of aryl alkenes via regioselective alkylation using alkyl tosylates, sulfates and bromides having a β-hydrogen catalyzed by a zirconocene complex. Chapter 3 deals with titanocene-catalyzed alkylation of aryl alkenes with alkyl bromides in the presence of ^{n}BuMgCl. Double alkylation of aryl alkenes proceeds in THF to give 1,2-dialkylated products. Combined use of primary and secondary, primary and tertiary, or secondary and tertiary alkyl bromides affords double alkylated products with high regioselectivities in a manner that more branched alkyl groups were introduced at the terminal carbon of alkenes and less branched ones at the benzylic carbons. On the other hand, Heck type transformation of aryl alkenes with alkyl bromides proceeds in ether under similar conditions as the double alkylation. Chapter 4 describes carbosilylation and double silylation of 1,3-butadienes with chlorosilanes and/or alkyl bromides. This reaction proceeds under mild conditions by the use of titanocene catalyst in the presence of ^{n}BuMgCl and gives rise to 1,4-carbosilylated or 1,4-double silylated 2-butenes.

Aryl substituted alkenes also afford 1,2-carbosilylated or 1,2-double silylated products under similar conditions.

References

[1] (a) *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; WILEY-VCH, Weinheim, 1998. (b) *Comprehensive Organic Functional Group Transformations Vol. 1*; Stanley, M. R., Ed.; Pergamon Press: Oxford, 1995

[2] (a) *Metal-catalyzed Cross-coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; WILEY-VCH: Weinheim, 1997. (b) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons, Inc.: Chichester, 1995.

[3] Tatumi, K. In *Kikan Kagaku Sousetu No. 17, Organic Chemistry of the early transition Metals*; Gattkai syuppan center: Tokyo, 1993, pp.1-20.

Chapter 1. Zirconocene-Catalyzed Silylation of Alkenes

1.1. Introduction

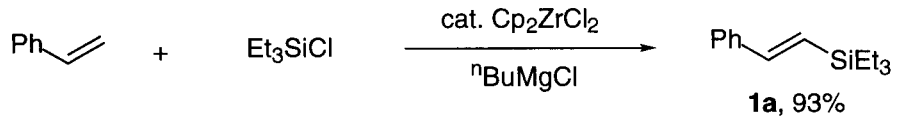
Organosilanes play important roles in organic synthesis as useful intermediates in a number of synthetic transformations.[1] To date, a variety of procedures have been developed for the introduction of silyl functionalities into organic molecules. The most straightforward and practical methodology which is employed for C-Si bond formation involves the electrophilic trapping of the corresponding organometallic reagents of non-transition metals with chlorosilanes. An attractive alternative to this conventional methodology is the transition metal catalyzed silylation of unsaturated compounds,[1,2] as exemplified by the hydrosilylation of alkenes and alkynes.[2a,3]

The reactions in this category proceed, not only with silanes having a hydrogen(s), but also with various silylating reagents such as disilanes,[2c,d] silacyclobutanes or -propanes,[4] silyl cyanides,[5] silylgermanes,[6] silylstannanes,[7] silylselenides,[6] and iodosilanes.[8] Although chlorosilanes are the most readily available silylating reagents, their use in catalytic silylation has not yet been achieved. This is probably due to the difficulty of the oxidative addition of the Si-Cl bonds to transition metals.[9] We wish to report herein the first example of the transition metal catalyzed silylation of alkenes with chlorosilanes, as well as with silylsulfides, -selenides, and -tellurides. This reaction proceeds under mild conditions using a catalytic amount of a zirconocene complex[10] in the presence of a Grignard reagent to give alkenyl and/or allylsilanes as the products.

1.2. Results and Discussion

For example, styrene reacted with chlorotriethylsilane in refluxing THF in the presence of

^{n}BuMgCl and a catalytic amount of zirconocene dichloride (conditions A) to give the *E*-isomer of alkenylsilane **1a** in 93% yield with >99% regio- and stereoselectivities (eq 1). In this reaction, only a trace amount of Et_3Si^nBu (<5%) was formed as a by-product probably via the direct reaction of Et_3SiCl with ^{n}BuMgCl.



1a, 93% (1)

Table 1 summarizes the results of the silylation of styrene using different reagents and catalysts. When Cp_2TiCl_2 was used in stead of Cp_2ZrCl_2, only a 21% yield of **1a** was obtained (run 2). Under the same conditions employed, Cp_2HfCl_2 was ineffective (run 3). The use of ^{n}BuMgCl and EtMgBr in place of ^{n}BuMgCl afforded 78% and 57% yields of **1a**, respectively (runs 4,5), but no reaction took place with MeMgCl and ^{n}BuMgCl. When Me_3SiCl was used as the silylating reagent, only a moderate yield of (*E*)-2-phenyl-1-(trimethylsilyl)ethylene (**1b**) was obtained, along with unreacted styrene, probably due to the low boiling point of Me_3SiCl (run 6). This problem was solved by employing Me_3SiSPh which afforded **1b** in an excellent yield (run 7). The reaction also proceeds when $Me_3SiSePh$ and $Me_3SiTePh$ are used as the silylating reagents (runs 8,9).

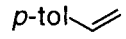
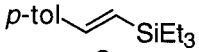
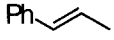
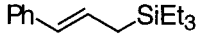
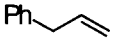
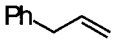
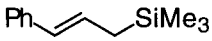
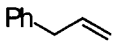
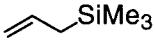
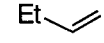
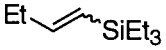
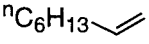
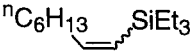
Table 1. Silylation of Styrene with R_3SiX

run	R_3SiX	R'MgX'	M	product	yield (%) [a]
1	Et_3SiCl	^{n}BuMgCl	Zr	**1a**	93(84)
2	Et_3SiCl	^{n}BuMgCl	Ti	**1a**	21
3	Et_3SiCl	^{n}BuMgCl	Hf	**1a**	0
4	Et_3SiCl	^{s}BuMgCl	Zr	**1a**	78
5	Et_3SiCl	EtMgBr	Zr	**1a**	57
6	Me_3SiCl	^{n}BuMgCl	Zr	**1b**	48
7	Me_3SiSPh	^{n}BuMgCl	Zr	**1b**	92(86)
8	$Me_3SiSePh$	^{n}BuMgCl	Zr	**1b**	89
9	$Me_3SiTePh$	^{n}BuMgCl	Zr	**1b**	48

Conditions: styrene (1.0 mmol), R_3SiX (2.0 mmol), R'MgX' (1.5 mmol), Cp_2ZrCl_2 (0.05 mmol), THF (1.7 mL), reflux, 40 min. [a]NMR yield. Isolated yield is in parentheses.

Results with some other representative alkenes are shown in Table 2.

Table 2. Zirconocene-Catalyzed Silylation of Alkenes with R_3SiX

run	alkene	R_3SiX	conditions[a]	temp (°C)	product	yield (%)[b]
1		Et_3SiCl	A	66	 **2**	91(90)
2	$CH_2=CH_2$	$^nPr_3SiCl$	B	80	**3**	75[c]
3		Et_3SiCl	A	66	 **4a**	22[d]
4		Et_3SiCl	A C	66 20	**4a**	46 87(82)
5		Me_3SiCl	C	20	 **4b**	82(73)
6		Me_3SiSPh	C	20	**4b**	69
7		Me_3SiCl	C	20	**5**(*E*/*Z*=52/48)	73(69)
8		Et_3SiCl	D	20	 **6**(*E*/*Z*=74/26)	74
9		Et_3SiCl	C	20	 **7**(*E*/*Z*=27/73)	70

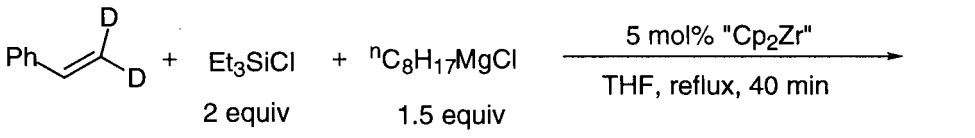
[a] For detailes of Conditions A–D, see Experimental Section. [b] NMR yield. Isolated yield is in parentheses. [c] Based on $^nPr_3SiCl$ used. [d] Unreacted alkene was recovered (67%).

4–Methylstyrene yielded the corresponding alkenylsilane **2** in 91% yield (run 1). A reaction at 80 °C using ethylene, charged at 1 atm at 20 °C in an autoclave, gave **3** in 75% yield based on the $^nPr_3SiCl$ used (conditions B, run 2). Interestingly, when β-methylstyrene was employed as an internal alkene, allylsilane **4a** was obtained in 22% yield as the sole product rather than the corresponding alkenylsilane (run 3). This result can be explained by assuming that β-methylstyrene isomerized to allylbenzene in the reaction medium which then underwent silylation to give **4a**. Indeed, when allylbenzene was employed **4a** was obtained in 46% yield

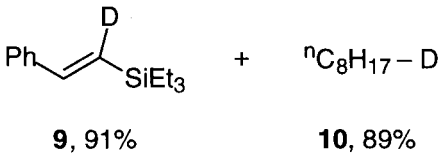
under the same conditions (run 4 under conditions A). It is noteworthy that the reaction proceeded smoothly at room temperature to yield **4a** in 87% yield (run 4 under conditions C). Trimethylsilyl group could be introduced efficiently by the use of either Me_3SiCl or Me_3SiSPh (runs 5 and 6). A similar reaction of allyltrimethylsilane with Me_3SiCl afforded 1,3-bis (trimethylsilyl)propene (**5**) in 73% yield as a 1:1 mixture of stereoisomers (run 7). Alkenes having a simple alkyl substituent also afforded the corresponding alkenylsilane **6** and **7** in 74% and 70% yields, respectively, along with by-products which may involve stereoisomers of the corresponding allylsilanes (runs 8 and 9). The product selectivities, i.e., alkenylsilanes vs allylsilanes, can be rationalized by assuming the common intermediate **8**, which affords alkenylsilanes and/or allylsilanes via β-elimination by the abstraction of H_a or H_b, respectively, along with the concomitant formation of butane and "Cp_2Zr". This mechanism accounts for the selective formation of allylsilanes **4** from allylbenzene, i.e., the β-elimination from **8** proceeds exclusively at the benzylic side when R=Ph in favor of conjugated double bond formation via H_b abstraction. In the cases of 1-butene and 1-octene (R=Et, $^nC_5H_{11}$), H_a was abstracted predominantly giving rise to **6** and **7**.

1.3. Mechanism

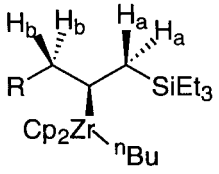
In order to prove the β-elimination mechanism the following labeling experiment was performed. A reaction of $PhCH{=}CD_2$ with Et_3SiCl (2 equiv) and ^{n}OctMgCl (1.5 equiv) in the presence of 5 mol% "Cp_2Zr", prepared in situ from Cp_2ZrCl_2 and 2 equiv of ^{n}BuMgCl,[11] was conducted under reflux for 40 min. The addition of benzaldehyde in order to trap the remaining ^{n}OctMgCl followed by quenching with 0.1 N HClaq gave nearly equal amounts of monodeuterated products **9** (deuterium content >98%) and **10** (deuterium content >95%) (eq 2). This result supports that one of the deuterium atoms of $PhCH{=}CD_2$ was transferred to the terminal carbon of the octyl group via β-elimination from **11**.



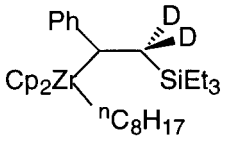
(2)



9, 91% **10**, 89%

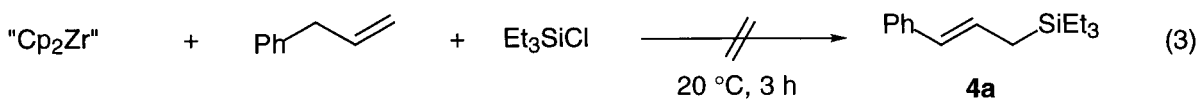


8

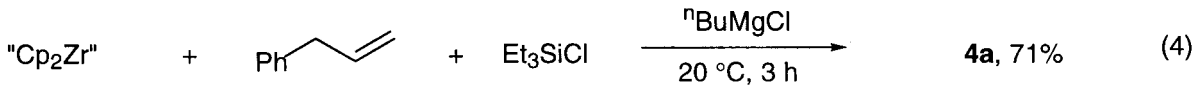


11

We also carried out several control experiments in order to elucidate the reaction pathway leading to the dialkyl zirconocene intermediates such as **8** or **11**. Since a small amount of the corresponding R_3SiH is formed as a by-product (<5%) in the present silylation reaction and since it is known that zirconocene complexes catalyze the addition of R_3SiH to alkenes,[12] we first examined whether the hydrosilylation process is involved in the present reaction. When a similar reaction of run 5 in table 2 was carried out in the presence of Et_3SiH, only **4b** was obtained as the silylated product in 86% yield and unreacted Et_3SiH was recovered. This result rules out the intermediacy of R_3SiH. We then examined the role of Grignard reagents. A reaction of a stoichiometric amount of "Cp_2Zr", generated in situ as described above, with allylbenzene (1 equiv) and Et_3SiCl (1 equiv) failed to give **4a** or saturated silylation product, $PhCH_2CH_2CH_2SiEt_3$, even after quenching the resulting mixture with Hclaq (eq 3). However, a similar reaction in the presence of one equiv of ^{n}BuMgCl afforded **4a** in 72% yield. These results indicate that ^{n}BuMgCl does, in fact, promote the C-Si bond forming step (eq 4).

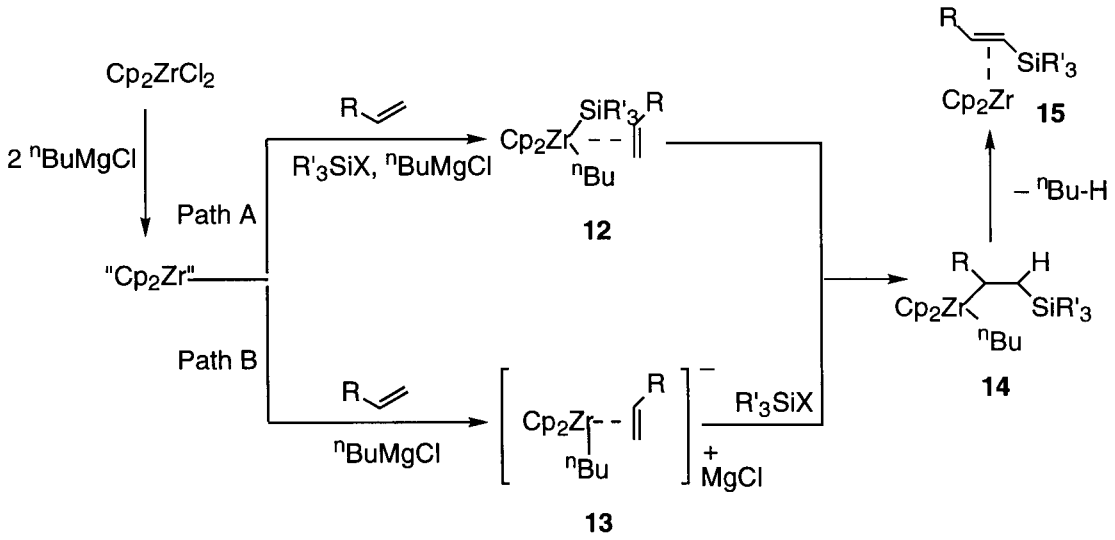


(3)



(4)

Although the detailed mechanism of this silylation reaction has not been clarified yet, it is possible that **12** or **13** serves as the key intermediate leading to the dialkyl zirconocene complex **14**. The former has a Zr-Si bond which undergoes alkene insertion (path A in Scheme 1).[13] In path B a zirconate complex **13** directly reacts with chlorosilanes at the olefinic terminal carbon to give **14**.[15] The resulting dialkyl complex **14** undergoes β-elimination to afford **15** which acts as a "Cp_2Zr" to complete the catalytic cycle.



Scheme 1. Plausible Pathways of Zirconocene-Catalyzed Silylation Reaction

1.4. Conclusion

In conclusion, a novel silylation reaction of alkenes with chlorosilanes and related silylating reagents has been developed by the use of a zirconocene catalyst. This reaction is promoted by Grignard reagents giving rise to alkenyl- and/or allylsilanes under mild conditions. Although chlorosilanes are the most easily available and widely used silylating reagents, their use are only limited to the reactions with nucleophiles such as organometallic compounds of non-transition metals. The catalytic reaction applicable to the introduction of silyl functionalities into organic molecules is of great importance in both synthetic chemistry and transition metal chemistry, but

it has never been achieved with halosilanes due to the difficulty of oxidative addition except the case of iodosilanes which are very reactive but much less available than chlorosilanes.

1.5. 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 SATURN GCMS-2000 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 Fuji-Davison silica gel WB-300 (100-250 mesh). Elemental analyses were performed on a Perkin Elmer 240C apparatus. Grignard reagents were used as purchased. Starting materials were used after purification by distillation. NMR yields were determined using trioxane as an internal standard.

A Typical Procedure

Conditions A. ***(E)*-1-Phenyl-2-(triethylsilyl)ethylene (1a)**: To a mixture of styrene (145 mg, 1.39 mmol), Et_3SiCl (420 mg, 2.79 mmol) and a catalytic amount of Cp_2ZrCl_2 (20.0 mg, 0.07 mmol), was added ^{n}BuMgCl (0.90 M in THF, 2.30 mL, 2.07 mmol) at 20 °C under nitrogen. After refluxing for 40 min, 1 N HClaq was added to the solution at 0 °C, and the mixture was again warmed to 20 °C. A saturated aqueous NH_4Cl solution (50 mL) was added,

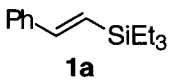
and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow crude product (93% NMR yield). Purification by silica gel column chromatography with hexane as the eluent afforded 255 mg (84%) of **1**.

Conditions B. **Ethenyltripropylsilane** (**3**): A magnetic stirring bar, $^nPr_3SiCl$ (257 mg, 1.33 mmol) and a catalytic amount of Cp_2ZrCl_2 (15.0 mg, 0.05 mmol) were placed in a 50 mL stainless steel autoclave equipped with a pyrex glass insert. To the mixture was added ^{n}BuMgCl (0.90 M in THF, 3.00 mL, 2.70 mmol) at 20 °C under nitrogen, and the autoclave was purged with ethylene several times and then charged at 1 atm at 20 °C in which about 2 mmol of ethylene was contained. After heating at 80 °C for 40 min, the autoclave was opened and 1 N HClaq was added to the resulting mixture at 0 °C. A similar work up to that mentioned above afforded **3** in 75% NMR yield based on $^nPr_3SiCl$.

Conditions C. **(*E*)-1-Phenyl-3-(triethylsilyl)prop-1-ene** (**4a**): To a mixture of allylbenzene (137.5 mg, 1.16 mmol), Et_3SiCl (438 mg, 2.91 mmol) and a catalytic amount of Cp_2ZrCl_2 (34.0 mg, 0.12 mmol) was added ^{n}BuMgCl (0.90 M in THF, 3.90 mL, 3.51 mmol) at 20 °C under nitrogen. Stirring the solution for 4 h at 20 °C, followed by the same workup as in Conditions **A** gave a yellow crude product (87% NMR yield). Purification by silica gel column chromatography with hexane as the eluent afforded 226 mg (82%) of **4a**.

Conditions D. **1-(Triethylsilyl)-1-butene** (**6**): A 50 mL pyrex glass vessel containing a magnetic stirring bar, Et_3SiCl (750 mg, 4.98 mmol) and a catalytic amount of Cp_2ZrCl_2 (58.0 mg, 0.20 mmol) was cooled at –78 °C and the gas was evaculated under reduced pressure. Into this was introduced 2.01 mmol of 1-butene (45 mL at 20 °C under 1 atm). After ^{n}BuMgCl (0.9 M in THF, 6.60 mL, 5.94 mmol) at the same temperature, the vessel was sealed and the solution was stirred for 24 h at 20 °C. The same workup as in Conditions A gave a pale yellow crude product **6** (*E*/*Z* = 74/26) in 74% NMR yield based on 1-butene.

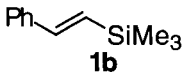
(*E*)-1-Phenyl-2-(triethylsilyl)etylene (1a) 21209-32-5



1a

IR (NaCl) 2953, 2909, 2874, 989, 786, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.23 (m, 5H), 6.88 (d, *J* = 19.3 Hz, 1H), 6.42 (d, *J* = 19.3 Hz, 1H), 0.98 (t, *J* = 7.8 Hz, 9H), 0.65 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 138.3, 128.4, 127.7, 126.2, 125.8, 7.6, 3.7; MS (EI) *m/e* (relative intensity, %) 210 (M^+, 33), 195 (100), 175 (11), 159 (15), 117 (12), 73 (30). HRMS calcd for $C_{14}H_{22}Si$ 218.1491, found 218.1503. Anal. Calcd: C, 76.99; H, 10.15. Found: C, 76.91; H, 10.04.

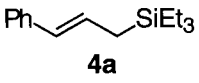
(*E*)-1-Phenyl-2-(trimethylsilyl)etylene (1b) 19372-00-0



1b

IR (NaCl) 2955, 1247, 988, 867, 843, 756, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.25 (m, 5H), 6.87 (d, *J* = 19.0 Hz, 1H), 6.47 (d, *J* = 19.0 Hz, 1H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 138.2, 129.4, 128.4, 127.8, 126.2, -1.0; MS (EI) *m/e* (relative intensity, %) 176 (M^+, 28), 161 (100), 145 (61), 135 (33), 73 (14), 59 (54). HRMS calcd for $C_{11}H_{16}Si$ 176.1021, found 176.1026. Anal. Calcd: C, 74.93; H, 9.14. Found: C, 75.17; H, 9.16.

(*E*)-1-Phenyl-3-(triethylsilyl)prop-1-ene (4a) 63522-98-5

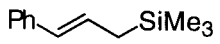


4a

IR (NaCl) 2952, 2910, 2874, 2360, 960, 728, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.30 (m, 4H), 7.11-7.16 (m, 1H), 6.24 (m, 2H), 1.69 (m, 2H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.56 (q, *J* = 8.0, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.3, 128.0, 127.9, 126.0, 125.3, 19.0, 7.6, 3.5; MS (EI) *m/e* (relative intensity, %) 232 ($M^{+\cdot}$ 32), 115 (100), 87 (91), 59 (28). HRMS calcd for $C_{15}H_{24}Si$ 232.1647, found 232.1634. Anal. Calcd: C, 77.51;

H, 10.41. Found: C, 77.36; H, 10.61.

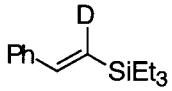
(*E*)-1-Phenyl-3-(trimethylsilyl)prop-1-ene (4b) 40595-34-4



4b

IR (NaCl) 3023, 2954, 1248, 1148, 961, 862, 740, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.31 (m, 4H), 7.11-7.17 (m, 1H), 6.21-6.26 (m, 2H), 1.65 (m, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 128.3, 128.1, 127.7, 126.1, 125.4, 24.1, -1.6; HRMS calcd for $C_{12}H_{18}Si$ 190.1178, found 190.1174. Anal. Calcd: C, 75.72; H, 9.53. Found: C, 75.59; H, 9.60.

(*E*)-Triethyl(2-phenylethenyl-1-*d*)silane (9)



9

Ethenyl-2,2-d_2-benzene was prepared in 87% yield from PhCHO and CD_3I following a reported procedure. (Fischetti, W.; Heck, R. F. *J. Organomet. Chem.* **1985**, *293*, 391-405.) A THF solution of "Cp_2Zr" was prepared by the addition of 2 equiv of ^{n}BuMgCl (0.9 M in THF, 0.22 ml, 0.20 mmol) to Cp_2ZrCl_2 (29 mg, 0.10 mmol) at -78 °C followed by stirring for 1 h at the temperature. Into this solution were added Ethenyl-2,2-d_2-benzene (212 mg, 2.0 mmol), Et_3SiCl (603 mg, 4.0 mmol) and ^{n}OctMgCl (1.0 M in THF, 3.0 ml, 3.0 mmol) and the mixture was refluxed for 40 min. The addition of benzaldehyde in order to trap the remaining ^{n}OctMgCl and subsequent quenching with 0.1 N HClaq afforded monodeuterated products **9** (91% NMR yield) and **10** (89% GC yield).

9 (deuterium content >98%), purified by HPLC.

IR (NaCl) 2953, 2909, 2874, 1494, 1015, 722, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.1 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 5.4 Hz, 1H), 6.88 (s, J = 2.4 Hz, 1H), 0.98 (t, J = 7.8 Hz, 9H), 0.65 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

144.5, 138.2, 128.3, 127.6, 126.1, 125.3 (t, J = 20.7) , 7.5, 3.6; MS (EI) *m/e* (relative intensity, %) 219 (M^+, 19), 191 (24), 190 (100), 162 (64), 134 (31), 132 (25). HRMS calcd for $C_{14}H_{21}DSi$ 219.1570, found 219.1547. Anal. Calcd: C, 76.63; H and D, 10.57. Found: C, 76.38; H and D, 10.02. The deuterium content was determined by a comparison of its mass spectrum with that of **1a**.

$DCH_2(CH_2)_6CH_3$ **10**

10 (deuterium content >95%)

The deuterium content of octane-1-*d* (**10**) was determined similarly by mass spectoscopy. The evidence that only a terminal carbon shows a triplet peak at δ 13.9 (t, J = 1.9 Hz) in the ^{13}C NMR spectrum (100 MHz, $CDCl_3$) indicates that a deuterium is incorporated at the terminal carbon.

Registry Nos of other products and their references

The following compounds are known and their spectral data (^1H-NMR, ^{13}C-NMR, Mass spectra) were consistent with those previously reported.

(*E*)-1-Phenyl-3-(triethylsilyl)prop-1-ene (**4a**) 63522-98-5

(*E*)-1-(Triethylsilyl)oct-1-ene (**6**) 31930-43-5

(*Z*)-1-(Triethylsilyl)oct-1-ene (**6**) 86539-21-1

Takeuchi, R.; Nitta, S.; Watanabe, D. *J. Org. Chem.* **1995**, *60*, 3045-3051.

(*E*)-1-Phenyl-2-(trimethylsilyl)etylene (**1b**) 19372-00-0

(*E*)-1-(*p*-Methylphenyl)-2-(triethylsilyl)etylene (**2**) 75476-54-9

Ethenyltripropylsilane (**3**) 1185-75-7

Chu, Y.; Colclough, D.; Hotchkin, D.; Tuazon, M.; White, J. B. *Tetrehedron*, **1997**, *53*,

14235-14246.

(*E*)-1-Phenyl-3-(triethylsilyl)prop-1-ene (**4a**) 63522-98-5

Seki, Y.; Takeshita, K.; Kawamoto, K.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1986**, *51*, 3890-3895.

(*E*)-1-Phenyl-3-(trimethylsilyl)prop-1-ene (**4b**) 40595-34-4

Slutsky, J.; Kwart, H. *J. Am. Chem. Soc.* **1973**, *95*, 8678-8685.

(*E*)-1,3-bis(Trimethylsilyl)propene (**5**) 52152-48-4

(*Z*)-1,3-bis(Trimethylsilyl)propene (**5**) 141291-16-9

Theuring, M.; Weber, W. P. *Polymer Bulletin* **1992**, *28*, 17-21.

Ethenyl-2,2-d_2-benzene 934-85-0

Fischetti, W.; Heck, R. F. *J. Organomet. Chem.* **1985**, *293*, 391-405.

(*E*)-Triethyl(2-phenylethenyl-1-*d*)silane (**9**) 129896-82-8

Tanke, R. S.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 7984-7989.

1.6. References and Notes

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1995, pp. 1-44. (e) Reichel, J. A.; Berry, D. H. In *Advances in Organometallic Chemistry*; Stone, F. G. A.; West, R., Eds.; Academic Press: New York, 1998; pp.197-265.

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[5] N. Chatani, T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, **1985**, 838-839.

[6] Ogawa, A.; Kuniyasu, H.; Takeba, M.; Ikeda, T.; Sonoda, N.; Hirao, T. *J. Organomet. Chem.* in press.

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[8] (a) Yamashita, H.; Kobayashi, T.; Hayashi, T.; Tanaka, M. *Chem. Lett.* **1991**, 761-762. (b) Chatani, N.; Amishiro, N.; Murai, S. *J. Am. Chem. Soc.* **1991**, *113*, 7778-7780. (c) Chatani, N.; Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834-1840.

[9] Yamashita, H.; Tanaka, M.; Goto, M. *Organometallics* **1997**, *16*, 4696-4704 and references therein.

[10] Recent reviews for synthetic application of zirconocene complexes: (a) Jordan, R. F. *Adv. Organomet. Chem.* **1991**, *32*, 325-387. (b) Negishi, E. In *Comprehensive Organic Synthesis Vol.5*, Paquette, L. A. Ed.; Pergamon Press: Oxford, 1991, pp. 1163-1184.

(c) Negishi, E.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124-130.

[11] It has been proposed that Cp_2ZrCl_2 reacts with 2 equiv of ^nBuMgCl to yield Cp_2Zr(butene) Complex which serves as a Cp_2Zr equivalent represented by "Cp_2Zr"; (a) Negishi, E.; Cederbaum, F. E.; Takahashi, T.*Tetrahedron Lett.* **1986**, *27,* 2829-2832. See also refs. 10b,c. For recent studies on the mechanism of Cp_2Zr(butene) formation, see (b) V. K. Dioumaev, J. F. Harrod, *Organometallics* **1997**, *16,* 1452-1464. (c) Soleil, F.; Choukroun, R. *J. Am. Chem. Soc.* **1997**, *119*, 2938-2939.

[12] (a) Takahashi, T.; Hasegawa, M.; Suzuki, N.; Saburi, M.; Rousset, C. J.; Fanwick, P. E.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 8564-8566. (b) Kesti, M. R.; Abdulrahman, M.; Waymouth, R. M. *J. Organomet. Chem.* **1991**, *417*, C12-15. (c) Corey, J. Y.; Zhu, X.-H. *Organometallics* **1992**, *11*, 672-683. (d) Kesti, M. R.; Waymouth, R. M. *Organometallics* **1992**, *11*, 1095-1103.

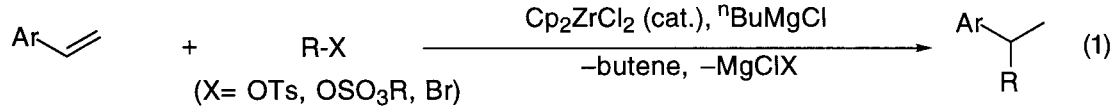
[13] $Cp_2Zr(SiMe_3)Cl$ does not react with ethylene (90 psi, Et_2O, 2 days); (a) Tilley, T. D. *J. Am. Chem. Soc.* **1985**, *107*, 4084-4085. But ethylene insertion to Zr–Si bonds of $Cp^*ZrCl_2Si(SiMe_3)_3$ and $CpCp^*ZrClSi(SiMe_3)_3$ has been reported; (b) Arnold, J.; Engeler, M. P.; Elsner, F. H.; Heyn, R. H.; Tilley, T. D. *Organometallics* **1989**, *8*, 2284-2286.

[14] As the similar pathways leading to **13**, it has been proposed that zirconate complexes, $Cp_2ZrEt(CH_2{=}CH_2)MgBr$ and $Cp_2ZrPh(CH_2{=}CH_2)MgBr$, are formed by the reaction of Cp_2ZrCl_2 with 3 equiv of EtMgBr or of Cp_2ZrPh_2 with one equiv of EtMgBr, respectively; Takahashi, T.; Suzuki, N.; Kageyama, M.; Nitto, Y.; Saburi, M.; Negishi, E.*Chem. Lett.* **1991**, 1579-1582.

Chapter 2. Zirconocene-Catalyzed Alkylation of Alkenes

2.1. Introduction

In recent organic chemistry, organozirconium compounds have emerged as synthetically useful reagents and intermediates providing a variety of possibilities for the efficient preparation of a multitude of organic molecules.[1] In particular, since a highly reactive zirconocene equivalent ("Cp_2Zr") was conveniently prepared from Cp_2ZrCl_2 and ^nBuLi via dibutylzirconocene,[2] zirconocene catalyzed reactions, as well as stoichiometric reactions, have widely been investigated. Zirconocene complexes catalyze the addition of organometallic reagents,[3] such as organoaluminum,[4] -zinc,[5] and -magnesium[6] compounds, to alkenes and alkynes. These reactions are synthetically useful for preparation of organometallic reagents with concomitant formation of carbon-carbon bonds, wherein anionic alkyl, allyl or benzyl groups are introduced into a carbon atom of the unsaturated bonds. We report herein zirconocene catalyzed alkylation of aryl alkenes with alkyl tosylates, sulfates and bromides. This reaction proceeds under mild conditions using a catalytic amount of a zirconocene complex in the presence of a Grignard reagent to give saturated alkylation products in which an alkyl moiety is introduced in an electrophilic manner at the benzylic carbons regioselectively (eq 1).



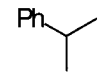
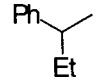
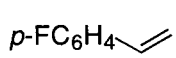
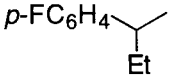
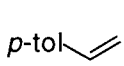
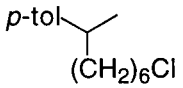
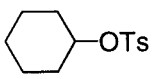
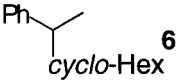
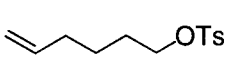
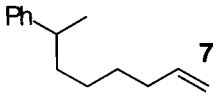
(1)

2.2. Results and Discussion

For example, into a mixture of styrene (3.00 mmol), octyl tosylate (2 equiv) and a catalytic amount of zirconocene dichloride (0.05 equiv) was added a THF solution of ^nBuMgCl (2

equiv, 6.6 mL) at 20 °C. The solution was stirred at 50 °C for 2 h and the products were extracted with ether. NMR analysis of the crude mixture indicated the formation of 2-phenyldecane (**1**) in 62% yield (Table 1, run 1). The product was obtained in pure form in 42% yield by HPLC. In this reaction octane was formed by the reduction of octyl tosylate as a by-product in a trace amount (<3% based on octyl tosylate) along with dodecane (<1%) which was formed probably via the direct reaction of octyl tosylate with ^{n}BuMgCl. Table 1 summarizes representative results obtained using various alkenes and the alkylating reagents.

Table 1 Zirconocene-Catalyzed Alkylation of Aryl Alkenes

run	alkene	R-X	product	yield (%)[a]
1		^{n}Oct-OTs	**1**	62
2		Me-OTs	 **2**	56
3		Et-OTs	 **3**	65
4		Et_2SO_4[b]	**3**	76
5		^{n}Oct-Br	**1**	65[c]
6		Et-OTs	 **4**	59
7		$Cl(CH_2)_6OTs$	 **5**	70
8			 **6**	44
9			 **7**	70

[a]GC yield for runs 1–5 and NMR yield for runs 6–9 based on alkenes unless otherwise stated. All products are known compounds except **5**.[5] [b]A stoichiometric amount of ethyl sulfate (3 mmol) was used. [c]Based on 1–bromooctane used. Styrene (1.5 equiv) and ^{n}BuMgCl (3 equiv) were used.

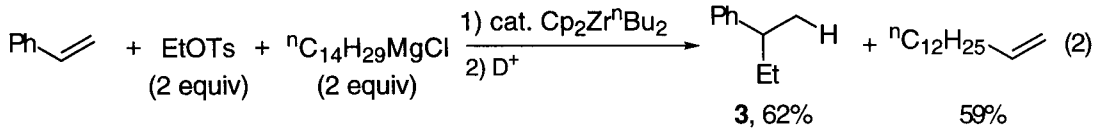
Under the same conditions, methyl and ethyl tosylates afforded cumene (**2**) and *se*c–buthylbenzene (**3**) in 56% and 65% yield, respectively (runs 2 and 3). Reactions of styrene

with ethyl tosylate using ^{i}PrMgBr and EtMgBr in place of ^{n}BuMgCl afforded **2** in poor yields (6% and 17%, respectively) but no reaction took place with MeMgCl and PhMgCl under the same conditions. The reaction also failed when ethyl triflate is used as the alkylating reagents due to the rapid reaction with Grignard reagents, whereas ethyl sulfate afforded **3** in 76% yield (run 4). Under the same conditions, 1–bromooctane gave 2–phenyldecane (**1**) only in 34% yield, **1** was formed in 65% based on 1–bromooctane when excess amounts of styrene and ^{n}BuMgCl were used (run 5). *p*–Fluorostyrene and *p*–methyl styrene yielded the corresponding products **4** and **5** in 59% and 70% yields, respectively (runs 6,7). The result of run 7 shows that chloro substituents are not affected in this reaction system. When cyclohexyl tosylate was employed as an alkylating reagent the corresponding product **6** was formed in 44% yield (run 8), indicating that secondary alkyl groups can be introduced. Since alkenes having no aromatic substituent are sluggish for this alkylation reaction, carbon–chains having a carbon–carbon double bond can also be introduced successfully (run 9). Under the same conditions, Cp_2TiCl_2 and Cp_2HfCl_2 were ineffective.

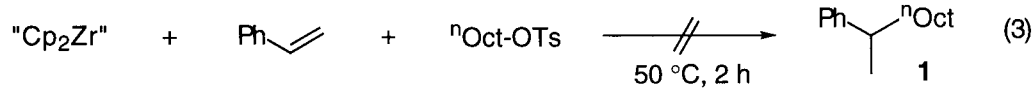
2.3. Mechanism

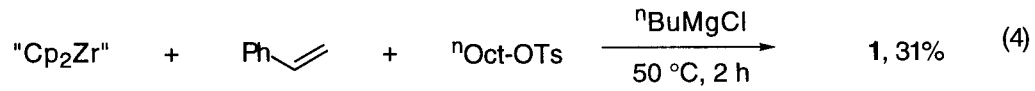
We carried out several control experiments in order to prove the reaction pathway. Since it is known that a titanocene complex catalyzes hydromagnesiation of styrene to give benzylmagnesium chloride.[7] We first examined whether a similar hydromagnesiation process is involved in the present reaction. A mixture of styrene, ^{n}BuMgCl (2 equiv), and a catalytic amount of Cp_2ZrCl_2 in THF was stirred at 50 °C for 2 h. Subsequent addition of D_2O did not afford deuterated ethylbenzene. This result ruled out the hydromagnesiation mechanism. We then carried out a reaction of styrene with ethyl tosylate in the presence of $^{n}C_{14}H_{29}MgCl$ using a catalytic amount of "Cp_2Zr", prepared from Cp_2ZrCl_2 and 2 equiv of ^{n}BuMgCl at –78 °C.[8]

Quenching the reaction with D_2O afforded nearly equal amounts of non-deuterated products **3** and 1–tetradecene (eq 2). This result suggests that β–hydrogen of the tetradecyl group was removed and transferred into the terminal carbon of styrene leading to **3**.



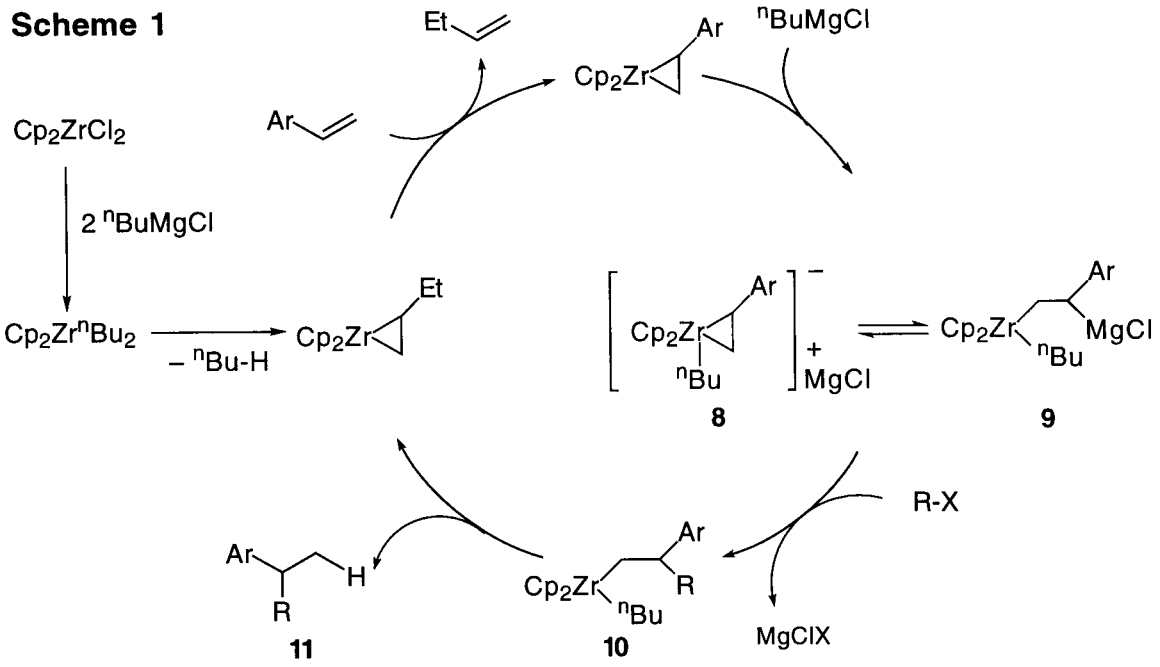
It should also be noted that a stoichiometric reaction of "Cp_2Zr" with styrene and octyl tosylate gave neither **1**, octane nor octene (eq 3). On the other hand, a similar reaction in the presence of ^{n}BuMgCl (1 equiv) afforded **1** in 31% yield (eq 4). These results indicate that ^{n}BuMgCl promotes the present alkylation reaction.





Although the mechanistic details of this reaction is still under investigation, a plausible reaction pathway is shown in Scheme 1. It is possible that a zirconate complex[9] **8** or a benzylmagnesium compound **9** serves as the key intermediate which reacts with alkylating reagents at the benzylic carbon leading to the dialkyl zirconocene complex **10**. The successive hydrogen abstraction proceeds exclusively at the less hindered butyl group[10] to afford corresponding alkylated product **11** along with Cp_2Zr(butene) complex which acts as a "Cp_2Zr" to complete the catalytic cycle.

Scheme 1



2.4. Conclusion

The present reaction provides a new and unique transformation of aryl alkenes via regioselective alkylation with alkyl tosylates, sulfates and bromides catalyzed by a zirconocene complex. This study will open up a new field of synthetic chemistry and also transition metal chemistry by way of providing a new methodology for carbon-carbon bond formation.

2.5. Experimental Section

General Comments

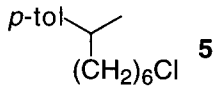
Grignard reagents were used as purchased. Starting materials were used after purification by distillation. Methyl- and ethyltosylates were obtained from commercial sources and other tosylates were prepared by tosylation of the corresponding alcohols. NMR yields were determined using trioxane as an internal standard. GC yields were determined using decane as

an internal standard.

A Typical Procedure

To a mixture of styrene (312 mg, 3.00 mmol), $^{n}C_8H_{15}OTs$ (1713 mg, 6.07 mmol) and a catalytic amount of Cp_2ZrCl_2 (45 mg, 0.15 mmol), was added *n*BuMgCl (0.90 M in THF, 6.6 mL, 6.00 mmol) at 50 °C under nitrogen. After stirring for 2 h at 50 °C, 1 N HClaq was added to the solution at 0 °C, and the mixture was again warmed to 20 °C. A saturated aqueous NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow crude product (62% NMR yield). Purification by HPLC with $CHCl_3$ as the eluent afforded 275 mg (42%) of **1**.

1-Chloro-7-(4-methylphenyl)octane (5)



5

IR (neat) 2956, 2928, 2856, 1514, 1456, 816 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 135.0, 128.8, 126.7, 45.2, 39.6, 38.4, 32.7, 29.1, 27.7, 26.9, 22.6, 21.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.05 (m, 4H), 3.50 (t, J = 6.7 Hz, 2H), 2.63 (sextet, J = 7.1 Hz, 1H), 2.32 (s, 3 H), 1.72 (quint-like tt, J = 6.7, 7.4 Hz, 2H), 1.56-1.23 (m, 8H), 1.21 (d, J = 7.1 Hz, 3H); MS (EI) *m/z* (relative intensity, %, ^{35}Cl) 238 (M^+, 14), 120 (10), 119 (100), 117 (16), 91 (14). Anal. Calcd for $C_{15}H_{23}Cl$: C, 75.44; H, 9.71. Found: C, 75.40; H, 9.59.

Registry Nos of other products and their references

The following compounds are known and their spectral data (^{1}H-NMR, ^{13}C-NMR, Mass spectra) were consistent with those previously reported.

1-*sec*-Butyl-4-fluoro-benzene (4) 329-76-0

1-Cyclohexyl-ethylbenzene (**6**) 4413-16-5

1-Methyl-2-heptenyl-benzene (**7**) 92776-46-0

2.6. References and Notes

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N. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115,* 6614-6624. (m) Hoveyda, A. H.; Morken, J. P. *J. Org. Chem.* **1993**, *58,* 4237-4244. (n) Knight, K. S.; Wang, D.; Waymouth, R. M. *Organometallics* **1994**, *13,* 2575-2577. (o) Takahashi, T.; Kondakov, D. Y.;Suzuki, N. *Organometallics* **1994**, *13,* 3411-3412. (p) Knight, K. S.; Wang, D.; Waymouth, R. M.; Ziller, J. *J. Am. Chem. Soc.* **1994**, *116,* 1845-1854. (q) Morken, J. P. ;Didiuk, M. T.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 3123-3124. (r) Morken, J. P.; Didiuk, M. T.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115,* 6997-6998. (s) Houri, A. F.; Xu, Z-M.; Cogan, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 2943-2944. (t) Didiuk, M. T.; Johannes, C. W.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117,* 7097-7104. (u) Lewis, D. P.; Whitby, R. J.; Jones, R. V. H. *Tetrahedron* **1995**, *51*, 4541. (v) Bell, L.; Whitby, R. J.; Jones, R. V. H.; Standen, M. C. H. *Tetrahedron Lett.* **1996**, *37*, 7139-7142. (w) Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118,* 3779-3780.

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[10] The reactivities of the alkyl ligands on Zr as β-hydrogen donors decrease in the order: β-methyl > β-methylene > β-methine, see: Negishi, E.; Nguyen, T.; Maye, J. P.; Choueiri,

D.; Suzuki, N.; Takahashi, T. *Chem. Lett.* **1992**, 2367-2370.

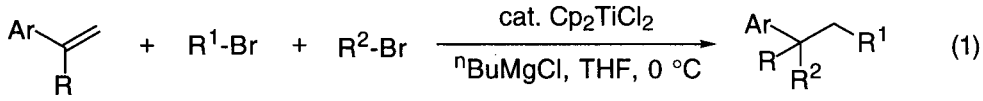
Chapter 3. Titanocene-Catalyzed Alkylation of Alkenes

3-1. Regioselective Double Alkylation of Styrenes with Alkyl Halides Using a Titanocene Catalyst

3-1.1. Introduction

Soon after their introduction in the early 1950's organotitanium compounds have attracted considerable and growing interest in several areas of chemistry. The ability of titanium to form δ- or π-bonds with large variety of ligands has led to the synthesis and characterization of numerous organotitanium derivatives. Some of these have attracted early attention for their application in the Zigler-Natta polimerization of olefins. More recently, several types of organotitanium compounds have been explored as reagents for organic synthesis and catalysis. The high abundance, low cost and low intrinsic toxicity of titanium have made possible a variety of catalytic as well as stoichiometric applications.

We wish to describe an unprecedented metal catalyzed double alkylation of alkenes with alkyl halides using a titanocene complex (eq 1). This reaction proceeds via the use of Cp_2TiCl_2 in the presence of ^{n}BuMgCl and gives rise to *vic*-dialkylated products regioselectively in high yields under mild conditions.[1] This reaction is of synthetic interst because a regioselective introduction of two different alkyl groups to a carbon-carbon unsaturated bond in one step is very difficult.

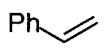
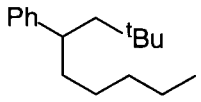
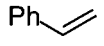
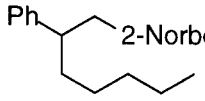
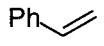
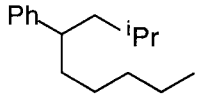
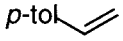
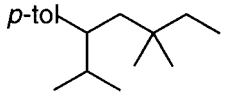
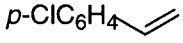
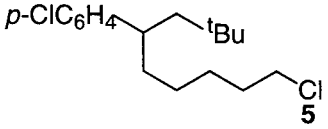
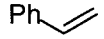
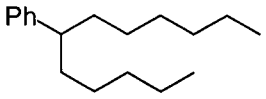
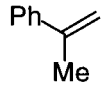
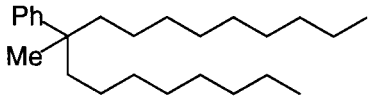
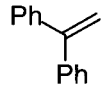
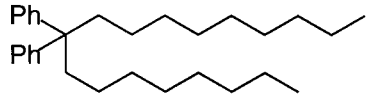
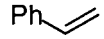
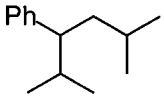
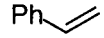
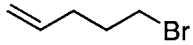
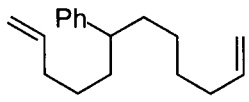
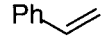
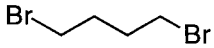
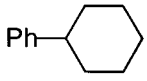


(1)

3-1.2. Results and Discussion

A typical example is as follows. To a mixture of styrene (1.03 mmol), 1-bromopenta ne (1.1 equiv), *tert*-butyl bromide (1.1 equiv) and titanocene dichloride (0.05 equiv) was added a THF solution of ^{n}BuMgCl (2.2 equiv, 2.5 mL) at 0 °C, and the solution was stirred for 1 h. The NMR analysis of the crude mixture indicated the formation of the double alkylation product **1** in 94% yield in which pentyl and *tert*-butyl groups are regioselectively incorporated at the adjacent carbons (Table 1, run 1). The product was obtained in pure form in 88% yield by a recycling preparative HPLC using $CHCl_3$ as the eluent. No evidence for the presence of the regioisomer of **1** nor dialkylated products which contained the same alkyl moiety was detected. The combined use of secondary and primary bromides (runs 2,3) or tertiary and secondary bromides (run 4) afforded the corresponding dialkylated products **2–4** in good yields with high regioselectivities. In run 2, only the *exo*-isomers were obtained in a diastereomer ratio of ca. 1:1. Chloro substituents were not affected in this reaction system and the desired product **5** was obtained in good yield (run 5). The same primary alkyl groups can be introduced at both vicinal carbons by the use of 2.2 equiv of the corresponding alkyl bromide (runs 6-8). Under the same conditions 1-iodooctane gave 9-phenyloctadecane in 54% yield, whereas no dialkylated product was obtained when 1-chlorooctane was used. Double alkylation also occurred when *sec*-alkyl bromides were used as shown in run 9, but *tert*-butyl bromide failed to give the corresponding dialkylated product under the same conditions. α-Substituted styrenes also efficiently underwent double alkylation (runs 7,8). The reaction was sluggish with respect to internal alkenes, such as β-methyl styrene or stilbene, and to 1-alkenes which contain no aryl group, such as 1-octene or 3-ethyl-1-butene. This chemoselectivity allows the successful synthesis of diene **10** in 82% yield, using 5-bromo-1-pentene (run 10). Interestingly, when 1,4-dibromobutane was used as the alkylating reagent, cyclohexylbenzene was obtained in moderate yield (run 11).

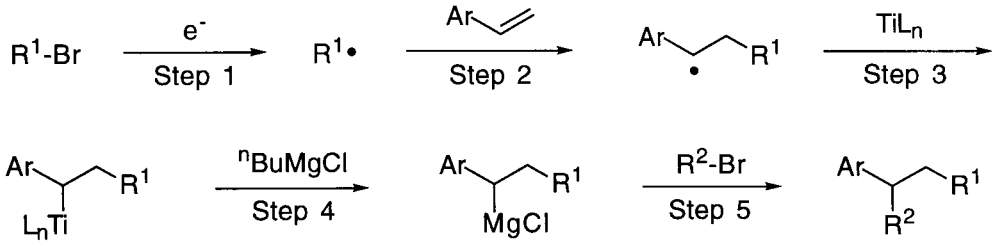
Table 1. Titanocene-Catalyzed Double Alkylation of Olefins with Alkyl Bromides

run	olefin	R^1-Br, R^2-Br	product	yield (%)[a]
1		^tBu-Br $^nC_5H_{11}$-Br	 **1**	94 (88)
2		2-Norbornyl-Br $^nC_5H_{11}$-Br	 **2**	91 (79)[b]
3		^iPr-Br $^nC_5H_{11}$-Br	 **3**	63 (54)[c]
4		^tAmyl-Br ^iPr-Br	 **4**	65 (52)[d]
5		^tBu-Br $Cl(CH_2)_5$-Br	 **5**	76 (71)
6		$^nC_5H_{11}$-Br	 **6**	76 (72)
7		^nOct-Br	 **7**	74 (62)
8		^nOct-Br	 **8**	84 (75)
9		^iPr-Br	 **9**	75 (73)
10			 **10**	82 (80)
11			 **11**	46[e]

[a]NMR yield. Isolated yield is in parentheses. [b]*exo*-2-Norbornyl bromide was used in 1.5 equiv. As a by-product, **6** was formed in 7% yield. [c]Besides, **6** and **9** were formed in 22% and 5% yields, respectively. [d]A trace amount of the by-product having two ^iPr groups was formed in <1% which was identified by GC-MS. [e]GC yield. 1,4-Dibromobutane (5 equiv), ^nBuMgCl (5 equiv), and Cp_2TiCl_2 (10 mol%) were used.

3-1.3. Mechanism

A plausible reaction pathway is shown in Scheme 1.[2] Alkyl radicals, formed by the electron transfer to alkyl bromides from some reduced titanocene complex[3] (step 1) add to the terminal carbon of styrene yielding benzyl radical intermediates (step 2). Recombination of the benzyl radicals with a titanocene complex gives rise to benzyl-Ti intermediates (step 3) which then undergo transmetallation with ^{n}BuMgCl to afford benzylmagnesium chlorides (step 4). The dialkylated products are formed by the reaction of benzylmagnesium chlorides with the alkyl halides (step 5).

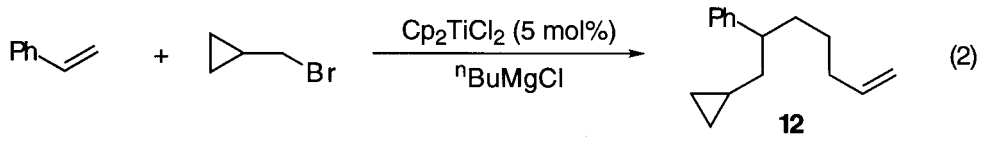


Scheme 1

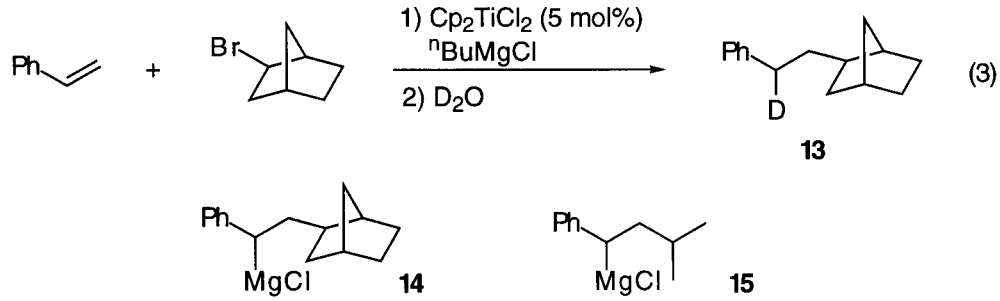
This pathway clearly explains the observed regioselectivity by taking into account the features of the following reactions. The rates of alkyl radical formation increase in the order of primary < secondary < tertiary reflecting the stabilities of alkyl radicals. The radical addition to carbon-carbon unsaturated bonds takes place at the terminal carbons exclusively. The alkylation at the benzylic carbon, probably via an S_N2 mechanism, would be favorable for less hindered alkyl halides in the order of primary > secondary > tertiary.

In order to confirm the validity of the proposed pathway, we employed (bromomethyl)cyclopropane as the alkylating reagent. As might be expected, cyclopropylmethyl and 3-butenyl units were introduced regioselectively giving rise to **12** as the sole dialkylation product in 50% yield (eq 2). This result along with the evidence that ring opening of cyclopropylmethyl radical to 3-butenyl radical is a rapid process which is much faster than the addition of primary radicals to styrene[4] strongly supports the proposal that the

first alkylation step is a radical process but that the second step is not.



The intermediacy of benzylmagnesium chlorides in the second alkylation step is supported by the following results. The reaction of styrene with 1.5 equiv of 2-norbornyl bromide was conducted at 0 °C for 1 h using 2.2 equiv of ^{n}BuMgCl in the presence of 5 mol% of Cp_2TiCl_2. Quenching the reaction with D_2O afforded the monoalkylated compound **13** which contained a deuterium at the benzylic position (*d*-content > 95%) in 59% yield (eq 3). This result suggests that a benzylmagnesium chloride **14** was formed in this reaction. While **14** could not be trapped efficiently with 2-norbornyl bromide probably due to steric reasons, sterically non-encumbered primary and secondary alkyl bromides react smoothly with α-substituted benzylmagnesium chlorides under the reaction conditions employed. For example, the reaction of **15**[5] (0.36 M) with isopropyl bromide (1.5 equiv) in THF at 0 °C afforded **9** in 62% yield after only 10 min.[6]



Interestingly, when ^{i}PrMgCl was used instead of ^{n}BuMgCl, the reduction of the alkyl bromides[3,7] predominated and only a trace amounts of dialkylated products (<2%) were obtained. It should also be noted that the Ti-catalyzed hydromagnesiation of olefins, which can proceed under similar conditions,[8] is completely suppressed in this reaction system. The fact that Cp_2TiCl_2 reacts with Grignard reagents (RMgX) to form anionic Ti (III) ate complexes $Cp_2TiR_2^-$ and that $Cp_2Ti^{i}Pr_2^-$ is unstable at temperatures above –50 °C yielding hydride

complexes whereas $Cp_2TiEt_2^-$ is stable at room temperature,[8b,9] leads us to propose that an ate complex $Cp_2Ti^nBu_2^-$ may play an important role as the active species for the electron transfer to alkyl halides. A detailed study of the mechanism of this titanocene catalyzed double alkylation is currently under investigation.

3-1.4. Conclusion

In conclusion, we report that a titanocene complex catalyzes the double alkylation of aryl alkenes with various alkyl halides in the presence of ^{n}BuMgCl.[10] Transition metal catalysts provide powerful tools for addition reactions to carbon-carbon double bonds, which enable versatile and useful transformations of alkenes by means of introducing a variety of carbon functionalities at the olefinic carbons. Although aryl, vinyl and allyl halides have widely been used for a number of transformations catalyzed by transition metals, the use of alkyl halides in transition metal chemistry is very limited mainly due to the facile β-elimination from the alkylmetal intermediates.[11] The present study outlines a novel methodology for overcoming this drawback by the use of a titanocene catalyst and will provide a useful synthetic method, especially for the construction of carbon skeletons with the concomitant formation of two carbon-carbon bonds at the adjacent carbons.

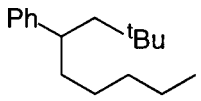
3-1.5. Experimental Section

General Comments

^{1}H NMR and ^{13}C NMR spectra were recorded with a JEOL JNM-Alice 400 spectrometer (400 MHz and 100 MHz, respectively). Chemical shifts are given in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were obtained 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 analyses (EI) were run using a SATURN

GCMS-2000 operating in the electron impact mode (70 eV) equipped with a RTX-5 30MX.25MMX.25U column. The HPLC separation was 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 the eluent. Elemental analyses were performed on a Perkin Elmer 240C apparatus. Grignard reagents except **15** were used as purchased. NMR yields were determined using trioxane as an internal standard.

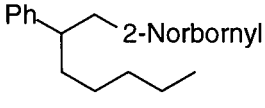
2,3-Dimethyl-4-phenyl-nonane (1)



1

To a mixture of styrene (107 mg, 1.03 mmol), 1-bromopentane (170 mg, 1.13 mmol) *tert*-butyl bromide (158 mg, 1.15 mmol) and 5 mol% of Cp_2TiCl_2 (12.4 mg, 0.05 mmol) was added ^{n}BuMgCl (0.9 M in THF, 2.5 mL, 2.25 mmol) at 0 °C under nitrogen. After stirring for 1 h at 0 °C, 1 N HClaq was added to the solution. The mixture was warmed to 20 °C and a saturated aqueous NH_4Cl solution (50 mL) was added. The product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a pale yellow crude product (94% NMR yield). Purification by HPLC with $CHCl_3$ as the eluent afforded 211 mg (88%) of **1**. IR (neat) 3026, 2955, 2927, 2859, 1494, 1475, 1467, 1453, 1364, 760, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.22 (m, 2H), 7.16-7.11 (m, 3H), 2.58 (ddt, J = 3.5, 5.3, 8.5 Hz, 1H), 1.68 (dd, J = 8.5, 13.9 Hz, 1 H), 1.57-1.45 (m, 3H), 1.22-1.14 (m, 5H), 1.07-0.99 (m, 1H), 0.82 (t, J = 6.8 Hz, 3H), 0.77 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 127.9, 127.7, 125.3, 50.8, 42.7, 40.0, 32.0, 31.4, 30.3, 27.5, 22.7, 14.2; MS (EI) *m/z* (relative intensity, %) 232 (M^+, 31), 161 (48), 105 (100), 91 (39); HRMS calcd for $C_{17}H_{28}$ 232.2191, found 232.2206; Anal. Calcd for $C_{17}H_{28}$: C, 87.86; H, 12.14. Found: C, 87.79; H, 12.00.

***exo*-2-(2-phenylheptyl)norbornane (2)**



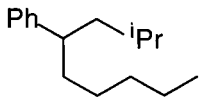
2

Although GC analysis using a SPB-5 30MX.25MMX.25U column showed only a single

peak, ^1H and ^{13}C NMR indicated a mixture of diastereomers with ca. 1:1 ratio. The ^1H NMR (see Fig. 1) showed four broad singlet peaks of bridgehead protons at δ 2.16, 2.11, 2.01 and 1.76 ppm and two septet-like peakes of benzyl protons at δ 2.53 and 2.46 ppm, ascribable to a triplet-triplet coupling (J = 5.6, 9.1 Hz and J = 5.2, 9.1 Hz respectively) due to the restricted free rotation, with the same ratio. These peaks are more reasonably assined to a pair of the diastereomers having different stereochemistries at the benzylic carbons rather than to the mixture of *exo*, *endo* isomers with the same stereochemistry at the benzylic carbons.

A 1:1 mixture of diastereomeres; RI (neat) 3026, 2949, 2869, 1493, 1453, 760, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.22 (m, 2H), 7.18-7.11 (m, 3H), 2.53 and 2.46 (septet-like tt, J = 5.6, 9.1 Hz and J = 5.2, 9.1 Hz, total 1H), 2.16, 2.11, 2.01 and 1.76 (br s, total 2H), 1.62-0.92 (m, 19H), 0.82 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 146.0, 127.8, 127.43, 172.36, 125.3, 44.6, 44.3, 44.2, 43.3, 41.9, 41.8, 40.3, 39.5, 38.51, 38.50, 37.7, 37.3, 36.8, 36.7, 36.4, 35.6, 35.5, 35.2, 31.9, 30.0, 28.68, 28.67, 27.3, 22.5 14.08, 14.07; MS (EI) *m/z* (relative intensity, %) 270 (M^+, 11), 199 (41), 162 (100), 161 (33), 105 (35), 91 (40); HRMS calcd for $C_{20}H_{30}$ 270.2382, found 270.2357. Anal. Calcd for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 88.90; H, 11.13.

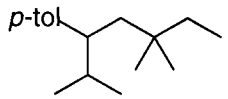
2-Methyl-4-phenylnonane (3)



3

RI (neat) 3027, 2955, 2925, 2868, 1494, 1452, 1366, 758, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.18-7.12 (m, 3H), 2.57 (septet-like tt, J = 5.4, 9.0 Hz, 1H), 1.59-1.49 (m, 3H), 1,42-1.29 (m, 2H), 1.23-1.08 (m, 6H), 1.84-0.76 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 128.0, 127.5, 125.5, 46.4, 43.7, 37.6, 32.1, 27.4, 25.5, 23.7, 22.7, 22.0, 14.2; MS (EI) *m/z* (relative intensity, %) 218 (M^+, 3), 162 (63), 161 (23), 147 (21), 105 (85), 91 (100). HRMS calcd for $C_{16}H_{26}$ 218.2035, found 218.2034; Anal. Calcd for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 87.88; H, 11.84.

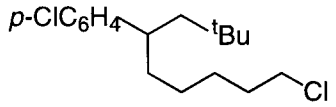
2,5,5-trimethyl-3-(4-methylphenyl)heptane (4)



4

IR (neat) 2959, 2871, 1514, 1463, 1385, 1366, 1114, 1020, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 2.39 (ddd, J = 1.9, 6.6, 9.8 Hz, 1H), 2.31 (s, 3H), 1.70 (dd, J = 9.8, 14.0 Hz, 1H), 1.67 (octet-like dqq, J = 6.6, 6.3, 6.8 Hz, 1H), 1.55 (dd, J = 1.9, 14.0 Hz, 1H), 1.19-1.06 (m, 2H), 0.85 (d, J = 6.8 Hz, 3H), 0.71 (t, J = 7.1 Hz, 3H), 0.70 (d, J = 6.3 Hz, 3H), 0.68 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 134.5, 128.7, 128.2, 48.0, 44.2, 35.3, 35.0, 33.8, 27.4, 27.3, 21.14, 21.08, 20.2, 8.6; MS (EI) *m/z* (relative intensity, %) 232 (M^+, 6), 189 (58), 147 (25), 133 (23), 119 (68), 105 (54), 85 (33), 71 (100); HRMS calcd for $C_{17}H_{28}$ 232.2191, found 232.2175. Anal. Calcd for $C_{17}H_{28}$: C, 87.90; H, 12.10. Found: C, 87.68; H, 12.25.

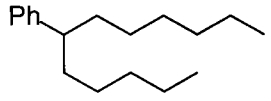
9-Chloro-4-(4-chlorophenyl)-2,2-dimethylnonane (5)



5

IR (neat) 2936, 2860, 1490, 1475, 1466, 1364, 1093, 1014, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.21 (m, 2H), 7.10-7.07 (m, 2H), 3.46 (t, J = 6.6 Hz, 2H), 2.58 (ddt, J = 3.5, 5.3, 8.8 Hz, 1H), 1.71-0.98 (m, 10H), 0.76 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 131.0, 129.0, 128.2, 50.8, 45.1, 42.1, 39.7, 32.6, 31.4, 30.26, 30.22, 26.9; MS (EI) *m/z* (relative intensity, %, (^{35}Cl) 300 (M^+, 39), 195 (63), 151 (42), 139 (72), 127 (29), 125 (86), 57 (100); HRMS calcd for $C_{17}H_{26}Cl_2$ (^{35}Cl) 300.1411, found 300.1409; Anal. Calcd for $C_{17}H_{26}Cl_2$: C, 67.80; H, 8.70. Found: C, 67.95; H, 8.83.

6-Phenyldodecane (6)

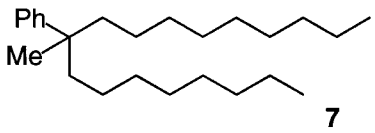


6

IR (neat) 3027, 2956, 2925, 2855, 1494, 1466, 1453, 760, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.24 (m, 2H), 7.17-7.11 (m, 3H), 2.46 (septet-like tt, J = 5.4, 9.0 Hz, 1H), 1.65-1.47 (m, 4H), 1.23-1.05 (m, 14H), 0.84 (t, J = 6.6 Hz, 3H), 0.82 (t, J = 6.6 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 128.0, 127.5, 125.5, 46.2, 37.14, 37.09, 32.1, 31.9, 29.6, 27.8, 27.5, 22.8, 22.7, 14.3; MS (EI) *m/z* (relative intensity, %) 246 (M^+, 28), 175 (31), 161 (36), 119 (55), 105 (64), 91 (100); HRMS calcd for $C_{18}H_{30}$ 246.2347, found 246.2348; Anal. Calcd for $C_{18}H_{30}$: C, 87.73; H, 12.27. Found: C, 87.56; H, 12.00.

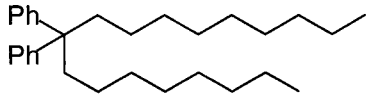
9-Methyl-9-phenyloctadecane (7)



7

IR (neat) 2927, 2853, 1466, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 4H), 7.17-7.13 (m, 1H), 1.70-1.62 (m, 2H), 1.53-1.46 (m, 2H), 1.26 (s, 3H), 1.23-1.16 (m, 22H), 1.13-1.08 (m, 2H), 0.97-0.93 (m, 2H), 0.864 (t, J = 6.9 Hz, 3H), 0.856 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 127.7, 126.2, 124.9, 43.4, 40.8, 32.0, 30.6, 29.8, 29.7, 29.6, 29.5, 24.3, 22.8, 14.3; MS (EI) *m/z* (relative intensity, %) 344 (M^+, 8), 217 (25), 133 (26), 119 (34), 105 (100), 91 (28); HRMS calcd for $C_{25}H_{44}$ 344.3443, found 344.3443; Anal. Calcd for $C_{25}H_{44}$: C, 87.13; H, 12.87. Found: C, 86.91; H, 12.75.

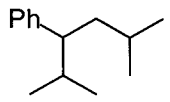
9,9-Diphenyloctadecane (8)



8

IR (neat) 2926, 2854, 1495, 1466, 1444, 753, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 4H), 7.17-7.13 (m, 6H), 2.07-2.03 (m, 4H), 1.25-1.18 (m, 22H), 0.97-0.91 (m, 4H), 0.86 (t, J = 6.8 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 127.8, 127.5, 125.1, 49.3, 37.7, 32.01, 31.99, 30.5, 29.7, 29.61, 29.57, 29.4, 24.0, 22.82, 22.81, 14.3; MS (EI) *m/z* (relative intensity, %) 406 (M^+, 2), 294 (26), 293 (100), 280 (24), 279 (99), 167 (34), 131 (22), 91 (21); HRMS calcd for $C_{30}H_{46}$ 406.3599, found 406.3584; Anal. Calcd for $C_{30}H_{46}$: C, 88.60; H, 11.40. Found: C, 88.31; H, 11.17.

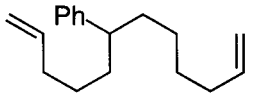
2,5-Dimethyl-3-phenylhexane (9)



9

IR (neat) 3027, 2955, 2926, 2867, 1494, 1468, 1452, 1384, 1367, 772, 747, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.24 (m, 2H), 7.18-7.09 (m, 3H), 2.35 (ddd, *J* = 4.1, 7.3, 11.2 Hz, 1H), 1.73 (octet-like dqq, *J* = 7.3, 6.4, 6.8 Hz, 1H), 1.60 (ddd, *J* = 3.9, 11.2, 13.4 Hz, 1H), 1.46 (ddd, *J* = 4.1, 10.1, 13.4 Hz, 1H), 1.26-1.18 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.4 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.70 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 128.2, 127.5, 125.3, 50.5, 42.1, 33.8, 25.4, 24.1, 21.2, 21.0, 20.7; MS (EI) *m/z* (relative intensity, %) 190 (M^+, 11), 147 (42), 105 (100), 91 (74); HRMS calcd for $C_{14}H_{22}$ 190.1721, found 190.1715; Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.29; H, 11.62.

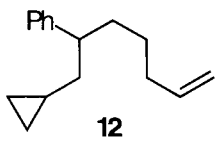
6-Phenyl-1,11-dodecadiene (10)



10

IR (neat) 3076, 3026, 2976, 2927, 2855, 1640, 1494, 1452, 992, 910, 761, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.24 (m, 2H), 7.18-7.09 (m, 3H), 5.74 (ddt, *J* = 10.2, 17.1, 6.7 Hz, 1H), 5.72 (ddt, *J* = 10.2, 17.1, 6.7 Hz, 1H), 4.94 (d, *J* = 17.1 Hz, 1H), 4.93 (d, *J* = 17.1 Hz, 1H), 4.89 (d, *J* = 10.2 Hz, 1H), 4.88 (d, *J* = 10.2 Hz, 1H), 2.46 (septet-like tt, *J* = 5.4, 9.0 Hz, 1H), 2.04-1.89 (m, 4H), 1.68-1.50 (m, 4H), 1.40-1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 138.8, 138.7, 128.0, 127.5, 125.6, 114.2, 114.0, 46.0, 36.9, 36.5, 34.0, 33.8, 29.2, 27.2, 27.0; MS (EI) *m/z* (relative intensity, %) 242 (M^+, 1), 159 (100), 158 (42), 131 (25), 117 (49), 91 (29), 81 (24); HRMS calcd for $C_{18}H_{26}$ 242.2035, found 242.2046; Anal. Calcd for $C_{18}H_{26}$: C, 89.19; H, 10.81. Found: C, 88.97; H, 10.86.

7-Cyclopropyl-6-phenyl-1-heptene (12)

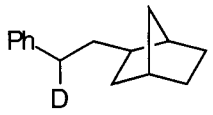


12

IR (neat) 2924, 1453, 1015, 910, 755, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, $HCCl_3$ as

the internal standered) δ 7.30-7.25 (m, 2H), 7.19-7.15 (m, 3H), 5.74 (ddt, J = 10.2, 17.1, 6.7 Hz, 1H), 4.94 (d, J = 17.1 Hz, 1H), 4.89 (d, J = 10.2 Hz, 1H), 2.63 (sept-like, tt, J = 5.6, 9.0 Hz, 1H), 2.03-1.96 (m, 2H), 1.72-1.53 (m, 3H), 1.35-1.19 (m, 3H), 0.55-0.45 (m, 1H), 0.39-0.26 (m, 2H), 0.01- -0.11(m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 135.8, 127.7, 127.3, 125.4, 113.9, 46.2, 42.2, 35.6, 33.7, 26.8, 9.3, 4.6, 4.5; MS (EI) *m/z* (relative intensity, %) 214 (M^+, 6), 159 (47), 143(29), 117 (58), 115 (36), 91 (100); HRMS calcd for $C_{16}H_{22}$ 214.1721, found 214.1719; Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.24; H, 10.25.

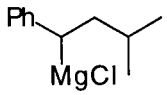
1-(2-Norbornyl)-2-phenylethane (13)



13

IR (neat) 3084, 3061, 3025, 2948, 2868, 1496, 1451, 739, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.18-7.14 (m, 3H), 2.60-2.53 (m, 1H), 2.20 (br s, 1H), 2.00 (br s, 1H), 1.64-1.55 (m, 1H), 1.53-1.31 (m, 6H), 1.17-1.04 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 128.0, 127.9, 125.1, 41.7, 41.0, 38.7, 38.1, 36.5, 35.3, 33.8 (t, $^1J_{C\text{-}D}$ = 19.4 Hz), 30.0, 28.7; MS (EI) *m/z* (relative intensity, %) 201 (M^+, 100), 172 (19), 109 (57), 93 (26), 92 (46), 67 (35); HRMS calcd for $C_{15}H_{19}D$ 201.1628, found 201.1636; Anal. Calcd for $C_{15}H_{19}D$: C, 89.49; H(D), 10.51. Found: C, 89.11; H(D), 10.56.

Preparation of **15** by the reaction of 1-chloro-3-methyl-1-phenylbutane (**16**) with Mg-anthracene complex and its alkylation with iPrBr.

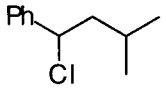


15

Magnesium turings (1224 mg, 50.35 mmol) and anthracene (9.99 g, 56.03 mmol) were placed in a three-necked 50 mL flask and heated at 110 °C for 15 min under nitrogen. Dry THF (47 mL) was added and then butylmagnesium chloride (2.7 mmol, 3 mL, 0.9 M in THF) was added in order to initiate the reaction. The mixture was stirred at 60 °C for 18 h. At this stage all the magnesium had reacted and an orange suspension was obtained. The mixture was stirred

at room temperature for 4 h. To a 2.5 mL aliquot of the suspension was slowly added dropwise a THF solution of **16** (0.97 M, 1.93 mL, 1.88 mmol) at 0 °C for 15 min, until a deep brown homogeneous solution was obtained. In order to determine the concentration of **15**, a 20 μL aliquot of the solution was treated with 0.1 N HClaq and analyzed by GC using decane as an internal standard. The formation of isoamylbenzene (84% yield based on **16** used, 63% based on Mg used) indicated that the concentration of **15** is 0.36 M. To a remaining solution of **15** was added 1.5 equiv of ^{i}PrBr (291 mg, 2.36 mmol) at 0 °C and the solution was stirred for 10 min. Quenching the reaction with 0.1 N HClaq at 0 °C followed by GC analysis showed the formation of **9** in 62% yield.

1-Chloro-3-methyl-1-phenylbutane (16)



16

Isobutylphenyl carbinol (935 mg, 5.7 mmol), prepared by the reaction of isovaleraldehyde with phenylmagnesium bromide, was added dropwise to thionyl chloride (1017 mg, 8.6 mmol) at room temperature. The mixture was stirred for 1 h and then at 80 °C for 5 min. The solution was poured onto crushed ice. The product was extracted with ether, washed with 5% $NaHCO_3$ solution, and dried over $MgSO_4$. Purification by HPLC with $CHCl_3$ as the eluent afforded 873 mg (84%) of **16**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 4.93 (dd, J = 6.3, 8.8 Hz, 1H), 2.06 (ddd, J = 6.3, 8.8, 14.0 Hz, 1H), 1.84 (ddd, J = 6.3, 7.5, 14.0 Hz, 1H), 1.74 (nonet-like ddqq, J = 6.3, 7.5, 6.3, 6.6 Hz, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 128.5, 128.0, 126.8, 62.1, 48.9, 25.8, 22.6, 22.0; MS (EI) *m/z* (relative intensity, %, ^{35}Cl) 182 (M^+, 1), 147 (100), 125 (30), 105 (77), 91 (32).

Reference: Kwart, H.; Hoster, D. P. *J. Org. Chem.* **1967**, *32*, 1867-1870.

3-1.6. References and Notes

[1] For recent reviews on synthetic application of titanium complexes, see: (a) Bochmann, M. In *Comprehensive Organiometallic Chemistry II*; Abel, E. W., Ed. in chief; Pergamon Press: Oxford, U.K., 1995; vol. 4, Chapters 4 and 5. (b) Houri, A. F.; Hoveyda, A. H. In *Reagents for Organic Synthesis*; Paquette, L. A., Ed. in chief; John Wiley & Sons: Chichester, 1995; vol. 3, pp 1663-1667.

[2] A similar pathway has been proposed for three-component coupling reactions of alkyl iodides, electron-deficient olefins, and carbonyl compounds using excess amounts of manganese or chromium salts. (a) Takai, K.; Ueda, T.; Ikeda, N.; Moriwake, T. *J. Org. Chem.* **1996**, *61*, 7990-7991. (b) Takai, K.; Matsukawa, N.; Takahashi, A.; Fujii, T. *Angew. Chem. Int. Ed.* **1998**, *37*, 152-155.

[3] It is known that alkyl radicals are formed in the titanocene catalyzed reduction of alkyl bromides with ^{i}PrMgBr. Rilatt, J. A.; Kitching, W. *Organometallics* **1982**, *1*, 1089-1093.

[4] The rate constant $k = 1.3 \times 10^{8}$ s^{-1} (at 25 °C) for the isomerization of cyclopropylmethyl radical to butenyl radical has been reported: (a) Maillard, B.; Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7024-7026. The rate constant $k = 5.4 \times 10^{4}$ $M^{-1}s^{-1}$ (at 25 °C) for the addition of 5-hexenyl radical to styrene has been reported: (b) Citterio, A.; Minisci, F. *J. Org. Chem.* **1979**, *44*, 2674-82. Although cyclopropylmethylmagnesium bromide is known to rearrange to CH_2=$CHCH_2CH_2MgBr$, it is not likely that these species are the intermediates, since the rearrangement is too slow ($t_{1/2}$ = 30 h in THF at 27 °C): (c) Silver, M. S.; Shafer, P. R.; Nordlander, J. E.; Ruchardt, C.; Roberts, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 2646-2647.

[5] Prepared following a literature description: Harvey, S.; Junk, P. C.; Raston, C. L.; Salem, G. *J. Org. Chem.* **1988**, *53*, 3134-3140.

[6] Reactivities of Grignard reagents toward alkyl bromides largely depend on the structures of the Grignard reagents. For example, $PhCH_2MgCl$ (1.09 M) reacted with $^{i}PrBr$ (1.5 equiv) much slower giving isobutylbenzene in only 8% at 0 °C for 1 h, and $^{n}BuMgCl$ was not alkylated by $^{i}PrBr$ under the same conditions.

[7] Colomer, E.; Corriu, R. *J. Organomet. Chem.* **1974**, *82*, 367-373.

[8] (a) Sato, F.; Ishikawa, H.; Sato, M. *Tetrahedron Lett.* **1980**, *21*, 365-368. (b) Ashby, E. C.; Ainsle, R. D. *J. Organomet. Chem.* **1983**, *250*, 1-12. (c) Gao, Y.; Sato, F. *J. Chem. Soc., Chem. Commun.*, **1995**, 659-660. See for a review of hydromagnesiation: (d) Sato, F. *J. Organomet. Chem.* **1985**, *285*, 53-64.

[9] (a) Brintzinger, H. H. *J. Am. Chem. Soc.* **1967**, *89*, 6871-6877. (b) Troyanov, S. I.; Varga, V.; Mach, K. *J. Organomet. Chem.* **1993**, *461*, 85-90.

[10] The dialkylation of alkenes with alkyl halides proceeds by the use of Li metal or by an electrochemical procedure, but these reactions are inefficient and regioselectivedialkylation has never been reported, see: (a) Davis, A.; Morgan, M. H.; Richards, D. H.; Scilly, N. F. *J. Chem. Soc., Perkin I* **1972**, *52*, 286-288. (b) Satoh, S.; Taguchi, T.; Itoh, M.; Tokuda, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 951-952.

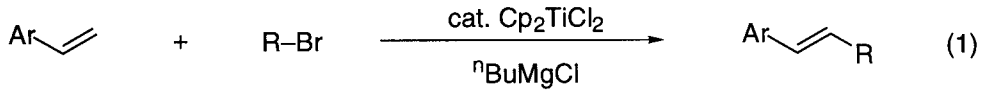
[11] See for example, Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons, Inc.; Chichester, 1995.

3-2. Heck Type Transformation of Aryl Alkenes with Alkyl Bromides Catalyzed by a Titanocene Complex

3-2.1. Introduction

Transition metal-catalyzed coupling reaction of alkyl halides with unsaturated compounds are practically unknown, whereas the corresponding aryl and alkenyl halide couplings, known as the Heck reaction, are well documented.[1] The first step in such a reaction involves formation of an δ-organopalladium halide to an active Pd(0) species.[2] In contrast, the alkylpalladium complex formed from an alkyl halide is prone to undergo rapid β-hydride elimination to yield an alkene, thus rendering a coupling with an added alkene impossible. Aryl- and alkenylpalladium halides are persistent, because β-elimination would yield an aryne or alkyne.[3] Consequently they react regio- and stereoselectively with added alkenes to yield coupling products.

We wish to describe the first example of transition metal catalyzed Heck-type reaction of arylalkenes with alkyl halides.[4] This reaction proceeds via the use of Cp_2TiCl_2 in ether solution of ^nBuMgCl and gives rise to terminal-alkylated alkenes stereoselectively in good yields under mild conditions (eq 1).



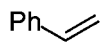
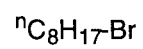
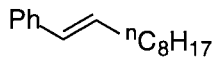
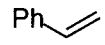
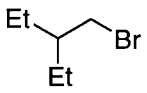
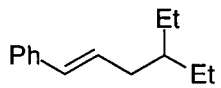
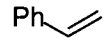
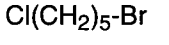
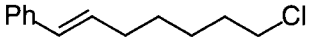
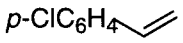
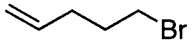
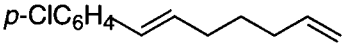
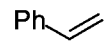
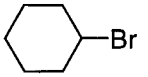
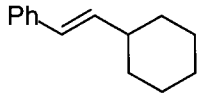
(1)

3-2.2. Results and Discussion

A typical example is as follows. To a mixture of styrene (14.83 mmol), decyl bromide (2.72 mmol), and ^nBuMgCl (2.0 M in ether, 1.65 mL, 3.30 mmol) was added a catalytic amount of Cp_2TiCl_2 (0.09 mmol) at 0 °C under nitrogen. After stirring for 4 h, 3 N HClaq was

added to the solution at 0 °C, and the mixture was again warmed to 20 °C. The product was obtained in pure form in 70% yield by a recycling preparative HPLC using $CHCl_3$ as the eluent. No evidence for the presence of the stereoisomer of **1** nor dialkylated products[4] which contained the same alkyl moiety was detected.

Table 1. Titanocene-Catalyzed Alkylation of Aryl Alkenes

run	aryl alkene	R-Br	product	yield (%)[a]
1			 **2**	81
2			 **3**	66
3			 **4**	77
4			 **5**	78
5			 **6**	67[b]

[a]NMR yield. [b]styrene (2.0 mmol), bromide (3.0 mmol), BuMgCl (5.0 mmol), Cp_2TiCl_2 (1.0 mmol), ether (2.5 mL), 0 °C, 90 min.

Results with some other representative examples are shown in Table 1. The use of primary bromides (runs 1-4) afforded the corresponding monoalkylated products **2–5** in good yields with high regio- and stereoselectivities. When cyclohexyl bromide was employed as an alkylating reagent with excess amount of titanocene catalyst the corresponding product **6** was formed in 67% yield (run 5), indicating that secondary alkyl groups can be introduced. Chloro substituents were not affected in this reaction system and the desired product **4** was obtained in good yield (run 3). Since alkenes having no aromatic substituent are sluggish for this alkylation reaction, carbon–chains having a carbon–carbon double bond can also be introduced successfully to give **5** in 78% yield (run 4).

3-2.3. Conclusion

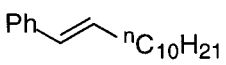
Although a wide variety of R-X, such as aryl, 1-alkenyl, benzyl, allyl, and 1-alkynyl halides, have been efficiently utilized for the transition metal catalyzed cross-coupling reactions. It has been considered that such reactions can not be extended to alkyl halides having β-hydrogens due to the slow rate of oxidative addition of alkyl halides to metal complexes and the fast β-hydride elimination from δ-alkylmetal intermediates in the catalytic cycle. Thus, the use of alkyl halides as coupling partners is a challenging problem in several recent publications. The present reaction provides a new transformation of aryl alkenes via regio- and stereoselective mono alkylation using alkyl bromides catalyzed by a titanocene complex under mild conditions.

3-2.4. Experimental Section

A Typical Procedure

To a mixture of styrene (1544 mg, 14.8 mmol), decyl bromide (601 mg, 2.717 mmol), and ^{n}BuMgCl (2.0 M in ether, 1.65 mL, 3.30 mmol) was added a catalytic amount of Cp_2TiCl_2 (22.8 mg, 0.09 mmol) at 0 °C under nitrogen. After stirring for 3 h, 3 N HClaq was added to the solution at 0 °C, and the mixture was again warmed to 20 °C. A saturated aqueous NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give an orange crude product (82% NMR yield). The product was obtained in pure form by a recycling preparative HPLC using $CHCl_3$ as the eluent afforded 465 mg (70%) of **1**.

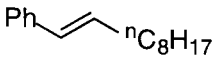
Dec-1-enylbenzene (1)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (br s, 5H), 6.37 (d, J = 15.9 Hz, 1H), 6.23 (dt, J = 6.6, 15.9 Hz, 1H), 2.20 (dt, J = 6.6, 6.9 Hz, 2H), 1.46 (quint, J = 6.9 Hz, 2H), 1.31-1.28

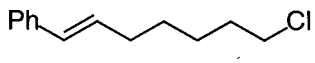
(m, 10H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 131.1, 129.5, 128.3, 126.6, 125.7, 33.2, 32.0, 29.6, 29.5, 29.43, 29.39, 22.8, 14.3. MS (EI) (^{35}Cl) *m/z* (relative intensity, %) 216 (M^+, 100), 215 (37), 214 (26), 213 (16), 117 (37).

Dodec-1-enylbenzene (2)



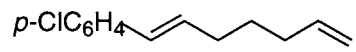
IR (neat) 3025, 2956, 2924, 2853, 1466, 962, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.15 (m, 5H), 6.37 (d, J = 15.9 Hz, 1H), 6.22 (dt, J = 6.9, 15.9 Hz, 1H), 2.19 (q-like, J = 6.9 Hz, 2H), 1.48-1.42 (m, 2H), 1.31-1.26 (m, 14H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 131.1, 129.5, 128.3, 126.6, 125.7, 33.2, 32.1, 29.8, 29.7, 29.53, 29.49, 29.39, 22.9, 14.3; MS (EI) *m/z* (relative intensity, %) (^{35}Cl) 244 (M^+, 100), 243 (30), 242 (27), 241 (11), 117 (28); HRMS calcd for $C_{18}H_{28}$ 244.2191, found 244.2192; Anal. Calcd for $C_{18}H_{28}$: C, 11.55; H, 88.45. Found: C, 11.71; H, 89.07.

1-Chloro-4-hepta-1,6-dienylbenzene (4)



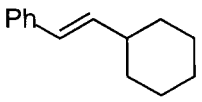
IR (neat) 2928, 1490, 1092, 965, 912 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (br s, 4H), 6.31 (d, J = 15.9 Hz, 1H), 6.17 (dt, J = 6.8, 15.9 Hz, 1H), 5.82 (ddt, J = 6.6, 7.1, 14.2 Hz, 1H), 5.02-4.96 (m, 2H), 2.20 (dt, J = 6.7, 7.1 Hz, 2H), 2.10 (dt, J = 7.1, 7.1 Hz, 2H), 1.55 (tt, J = 7.1, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 136.1, 132.1, 131.2, 128.7, 128.4, 127.1, 114.6, 33.3, 32.5, 28.6; MS (EI) *m/z* (relative intensity, %) (^{35}Cl) 206 (M^+, 35), 171 (100), 138 (63), 129 (69), 115 (76), 91 (40); HRMS calcd for $C_{13}H_{15}Cl$ (^{35}Cl) 206.0862, found 206.0863; Anal. Calcd for $C_{13}H_{15}Cl$: C, 75.54; H, 7.31. Found: C, 75.35; H, 7.51.

6-(Chlorohex-1-enyl)benzene (5)



IR (neat) 3025, 2934, 1494, 1448, 965, 745, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.17 (m, 5H), 6.38 (d, *J* = 15.9 Hz, 1H), 6.21 (dt, *J* = 6.8, 15.9 Hz, 1H), 3.53 (t, *J* = 6.8, 3H), 2.24-2.21 (m, 2H), 1.83-1.78 (m, 2H), 1.54-1.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 130.4, 129.9, 128.3, 126.7, 125.8, 45.1, 32.9, 32.6, 28.7, 26.6; MS (EI) *m/z* (relative intensity, %) 208 (M^+, 78), 117 (100), 115 (56), 104 (62), 91 (37); HRMS calcd for $C_{13}H_{17}Cl$ 208.1019, found 208.1017; Anal. Calcd for $C_{13}H_{17}Cl$: C, 74.81; H, 8.21. Found: C, 74.77; H, 8.29.

(2-Cyclohexylvinyl)benzene (6)



IR (neat) 2924, 2851, 1448, 964, 745, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.15 (m, 5H), 6.34 (d, *J* = 15.9 Hz, 1H), 6.70 (dd, *J* = 6.8, 15.9 Hz, 1H), 2.16-2.08 (m, 1H), 1.82-1.74 (m, 4H), 1.70-1.50 (m, 1H), 1.38-1.12 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 136.6, 128.3, 127.1, 126.6, 125.8, 41.2, 33.1, 26.3, 26.2; MS (EI) *m/z* (relative intensity, %) 186 (M^+, 66), 129 (21), 128 (19), 115 (21), 104 (100), 91 (16); HRMS calcd for $C_{14}H_{18}$ 186.1421, found 186.1409; Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.12; H, 9.71.

3-2.5. References and Notes

[1] Heck, R. F. *Org. React.* **1982**, *27*, 345.

[2] Heck, R. F. In *Comprehensive Organic Synthesis*; Torst, B. M.; Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol.4, p 833. Brase, S.; de Meijere, A. In *Metal-Catalized Cross-Coupling Reactions*; Stang, P. J.; Diederich, F., Eds.; Wiley-VCH: Weinheim, 1997.

[3] Successful Suzuki-type cross-coupling reactions between iodo-cyclopropanes and cyclopropylboronates, which must involve cyclopropylpalladium iodide intermediates not undergoing β-hydride elimination, have recently been reported: Charette, A. B.; Pereira De Freitas-Gil, R. *Tetrahedron Lett.* **1997**, *38*, 2809.

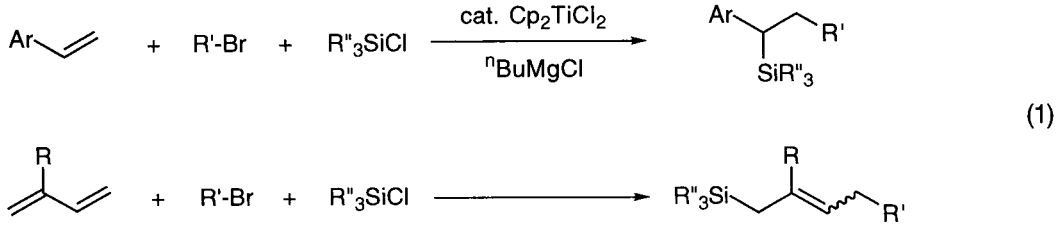
[4] (a) Terao, J.; Saito, K.; Nii, S.; Kambe, N.; Sonoda, N.*J. Am. Chem. Soc.* **1998**, *120*, 11822. (b) Terao, J.; Watanabe, T.; Saito, K.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1998**, *39*, 9201.

Chapter 4. Titanocene-Catalyzed Silylation of Alkenes

New C-C and C-Si Bonds Forming Reaction Using a Titanocene Catalyst

4-1.1. Introduction

Addition of organosilanes to unsaturated compounds is a most useful reaction for synthesis of a wide variety of organosilicon compounds.[1] On the other hand, if a carbon and a silicon unit, instead of a hydrogen and a silicon, are introduced simultaneously into unsaturates, the reaction might be far more beneficial as synthetic method. However, while some carbon-metal bonds[2] are reactive enough to undergo so-called carbometalation reaction, most C-Si bonds are inert under usual reaction conditions. Therefore, it seems extremely difficult to activate C-Si bonds directly toward insertion of unsaturates into these bonds.[3] In order to resolve this problem, a variety of three-component coupling procedures, in which a carbon and a silicon substituents are introduced from different sources into unsaturated substrates have been developed for the formation of C-C and/or C-Si bonds.[4] Although alkyl halides and chlorosilanes are the most readily available reagents, their use in catalytic addition to unsaturated bonds has not yet been achieved. Herein, we describe a new method for carbosilylation by titanocene-catalyzed three-component coupling of alkyl halides, chlorosilane and aryl alkenes or dienes (eq 1).

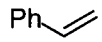
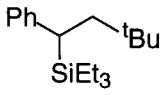
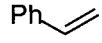
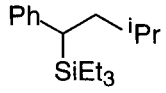
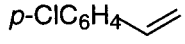
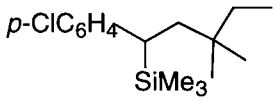
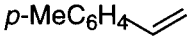
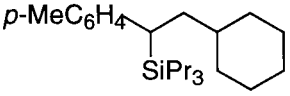
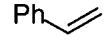
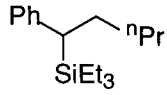
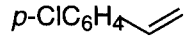
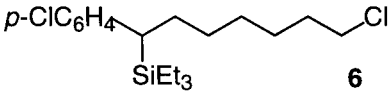
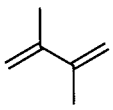
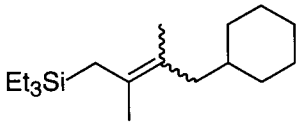
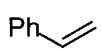
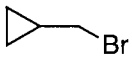
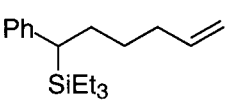


(1)

4-1.2. Results and Discussion

For example, into a mixture of styrene, *tert*-butyl bromide, chlorotriethylsilane, and a catalitic amount of titanocene dichloride was added a THF solution of ^{n}BuMgCl at 0 °C for 1 h to give carbosilylated product (**1**) in high yield (run 1). No evidence for the presence of the regioisomer of **1** nor dialkylated products which contained the same alkyl moiety was detected. The combined use of tertary or secondary bromides and chlorotriethylsilane (runs 1-4) afforded the corresponding carbosilylated products **1-4** in high yields and regioselectivities. When

Table 1. Titanocene-Catalyzed Carbosilylation of Alkenes

run	arylalkene	R'-Br, R"$_3$Si-Cl	product	yield (%)[a]
1		^{t}Bu-Br Et$_3$Si-Cl	 **1**	96 (94)
2		^{i}Pr-Br Et$_3$Si-Cl	 **2**	85 (83)
3		^{t}Amyl-Br Me$_3$Si-Cl	 **3**	85
4		*cyclo*-Hex-Br ^{n}Pr$_3$Si-Cl	 **4**	89
5		^{n}Pr-Br Et$_3$Si-Cl	 **5**	51 (41)
6		Cl-C$_5$H$_{10}$-Br Et$_3$Si-Cl	 **6**	54
7		*cyclo*-Hex-Br Et$_3$Si-Cl	 **7**	66[b] [*E*/*Z* = 96/4][c]
6		 Et$_3$Si-Cl	 **8**	50

[a]NMR yield. Isolated yield is in parentheses. [b]BuMgCl (3 equiv) was used.
[c]Determined by GC.

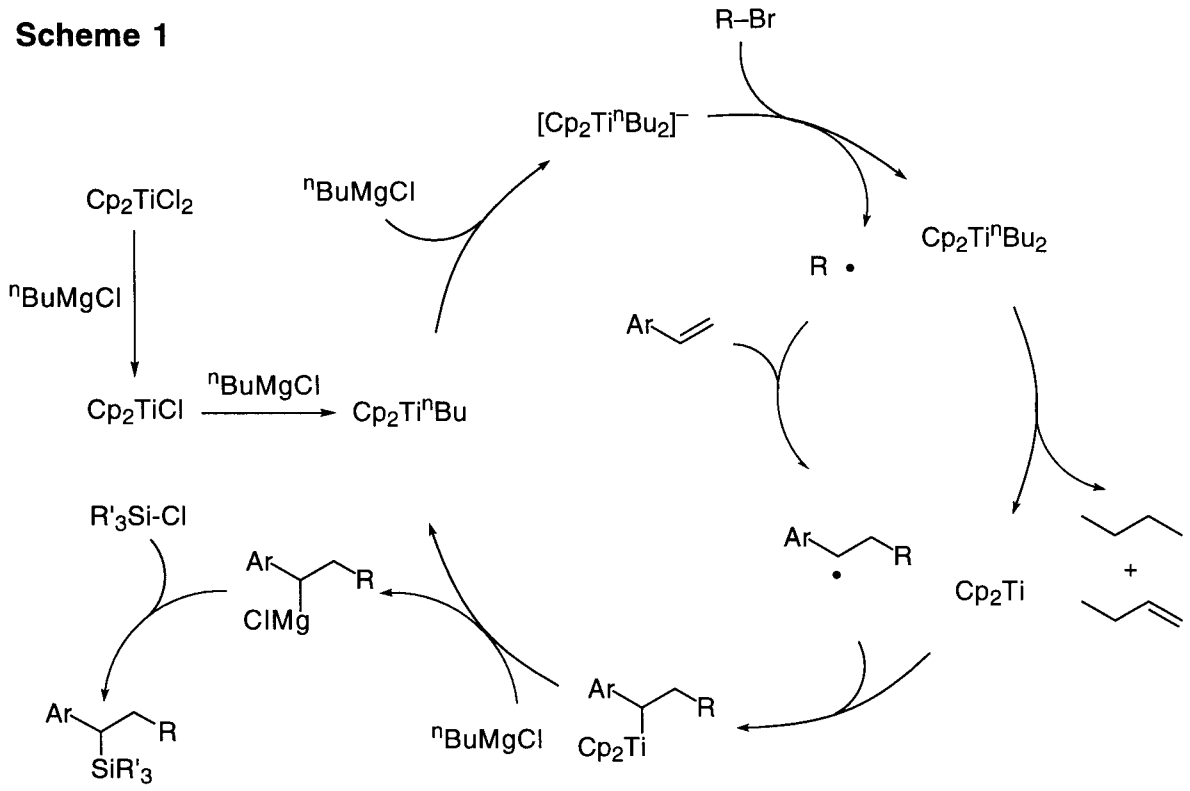
primary bromides were used as the alkylating reagent, the corresponding carbosilylated products were obtained in moderate yield (runs 5,6). Chloro substituents were not affected in this reaction system and the desired product **6** was obtained in 54% yield (run 5). The reaction was sluggish with respect to internal alkenes, such as β-methyl styrene or stilbene, and to 1-alkenes which contain no aryl group, such as 1-octene. Under similar conditions, 2,3-dimetylbutadiene afforded **7** in 75% yield (run 7).

When we employed (bromomethyl)cyclopropane and chlorotriethylsilane, 3-butenyl and triethylsilyl units were introduced regioselectively giving rise to **8** as the sole carbosilylation product in 50% yield (run 8). This result along with the evidence that ring opening of cyclopropylmethyl radical to 3-butenyl radical is a rapid process which is much faster than the addition of primary radicals to styrene[5] strongly supports the proposal that the terminal alkylation step is a radical process.

4-1.3. Mechanism

Although the mechanistic details of this reaction is still under investigation, a plausible catalitic cycle for the present reaction is shown in Scheme 1. The reaction of titanocene dichloride with excess amount of ^{n}BuMgCl afforeds dibutyltitanate(III) complex via butyltitanium(III). It is possible that this complex serves as one electron transferring reagent which reacts with alkyl halide leading to alkyl radical. The successive addition of alkyl radical proceeds to styrene at terminal olefinic carbon to afford corresponding benzyl radical spices along with $Cp_2Ti^{n}Bu_2$ complex which acts as a "Cp_2Ti". The benzyl radical spices recombinds with "Cp_2Ti" to give benzyl titanium complex, which reacts with ^{n}BuMgCl to regenerate $Cp_2Ti^{n}Bu$ along with benzyl Grignard reagent by transmetallation of the benzyl group from titanium to magnesium. The benzyl Grignard reagent reacts with chlorosilane to give carbosilylated compound.

Scheme 1



4-1.3. Conclusion

The transition metal catalyzed alkylation and silylation of unsaturated compounds provides a useful method for the constraction of organic molecules. These reactions have been studied extensively using late transition metal catalysts. Although alkyl halides and chlorosilanes are the most readily available alkylating and silylating reagents, their use in catalytic reaction have limited. The present study will open up a new field of methodology for the transition metal catalyzed formation of carbon-carbon and/or carbon-silicon bonds.

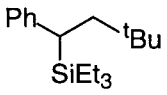
4-1.4 Experimental Section

A Typical Procedure

To a mixture of styrene (114 mg, 1.10 mmol), *tert*-butyl bromide (169 mg, 1.23 mmol),

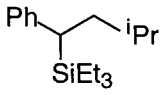
Et_3SiCl (181 mg, 1.20 mmol) and ^nBuMgCl (0.90 M in THF, 2.70 mL, 2.43 mmol) was added a catalytic amount of Cp_2TiCl_2 (13.1 mg, 0.53 mmol) at 0 °C under nitrogen. After stirring for 40 min, 0.1 N HClaq was added to the solution at 0 °C, and the mixture was again warmed to 20 °C. A saturated aqueous NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give an orange crude product (96% NMR yield). Purification by silica gel column chromatography with hexane as the eluent afforded 286 mg (95%) of **1**.

(3,3-Dimethyl-1-triethylsilylbutyl)benzene (1)



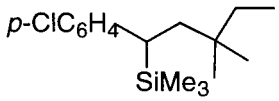
IR (neat) 2953, 2909, 2876, 1466, 1006, 789, 750, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.02 (m, 5H), 2.28 (d, J = 11.2 Hz, 1H), 1.89 (dd, J = 10.4, 11.2 Hz, 1H), 1.57 (d, J = 10.4, 3H), 0.87 (t, J = 7.6 Hz, 9H), 0.74 (s, 9H), 0.48 (q, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 127.8, 127.7, 123.6, 43.6, 33.1, 30.6, 30.2, 30.1, 7.7, 2.4; MS (EI) *m/z* (relative intensity, %) 276 (M^+, 12), 248 (21), 247 (100), 115 (31); HRMS calcd for $C_{18}H_{32}Si$ 276.2273, found 276.2281; Anal. Calcd for $C_{18}H_{32}Si$: C, 78.18; H, 11.66. Found: C, 78.2; H, 11.58.

(3-Methyl-1-triethylsilylbutyl)benzene (2)



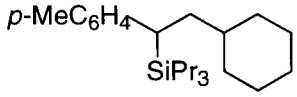
IR (neat) 2953, 2911, 2875, 766, 727, 713, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.03 (m, 5H), 2.28 (dd, J = 2.8, 12.8 Hz, 1H), 1.90 (ddd, J = 2.8, 12.8, 13.2 Hz, 1H), 1.48-1.34 (m, 1H), 1.36-1.30 (m, 1H), 0.87 (t, J = 7.6 Hz, 9H), 0.82 (d, J = 6.2 Hz, 2H), 0.78 (d, J = 6.2 Hz, 2H), 0.49 (q, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 127.82, 127.80, 123.9, 38.9, 31.6, 26.2, 24.2, 20.8, 7.7, 2.5; MS (EI) *m/z* (relative intensity, %) 262 (M^+, 12), 234 (18), 233 (100), 232 (10), 115 (8); HRMS calcd for $C_{17}H_{20}Si$ 262.2117, found 262.2108. Anal. Calcd for $C_{17}H_{20}Si$: C, 77.78; H, 11.52. Found: C, 77.64;

H, 11.56.

4-(2-Cyclohexyl-1-tripropylsilylethyl)-1-methylbenzene (3) 

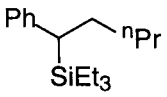
IR (neat) 2953, 2922, 2866, 1510, 1067, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 7.8 Hz, 2H), 2.30 (s, 3H), 2.25 (dd, *J* = 1.3, 12.8 Hz, 1H), 1.84-1.1.76 (m, 2H), 1.63-1.50 (m, 4H), 1.40-1.33 (m, 1H), 1.31-1.17 (dt, *J* = 7.8, 7.9 Hz, 6H), 0.98-091 (m, 1H), 0.96-0.89 (t, *J* = 7.8 Hz, 9H), 0.54-0.41 (t, *J* = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.63, 133.1, 128.5, 127.6, 37.6, 35.4, 35.0, 31.8, 30.5, 26.9, 26.4, 26.2, 21.1, 18.9, 17.7, 14.4; MS (EI) *m/z* (relative intensity, %) 358 (M^+, 5), 315 (12), 200 (100), 157 (86), 115 (55), 73 (49); HRMS calcd for $C_{24}H_{42}Si$ 358.3056, found 358.3066; Anal. Calcd for $C_{24}H_{42}Si$: C, 80.37; H, 11.80. Found: C, 80.07; H, 11.83.

1-Chloro-4-(3,3-dimethyl-4-trimethylsilylpentyl)benzene (4)



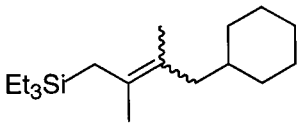
IR (neat) 2959, 1489, 1464, 1260, 1249, 1012, 855, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.4 Hz, 2H), 7.6.97 (d, *J* = 8.4 Hz, 2H), 2.08 (d, *J* = 10.4 Hz, 1H), 1.76 (dd, *J* = 10.4, 14.4 Hz, 1H), 1.56 (d, *J* = 10.4, 1H), 1.16-1.10 (m, 2H), 0.73-0.66 (m, 9H), -0.1 (m, 9H), 0.83-0.76 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 129.2, 128.7, 127.9, 41.0, 35.3, 34.4, 32.3, 27.2, 8.5, -2.9; MS (EI) *m/z* (relative intensity, %) (^{35}Cl) 282 (M^+, 7), 159 (27), 145 (100), 104 (57), 73 (72), 71 (53); HRMS calcd for $C_{16}H_{27}SiCl$ (^{35}Cl) 282.1570, found 282.1573; Anal. Calcd for $C_{16}H_{27}SiCl$: C, 67.92; H, 9.62. Found: C, 68.16 H, 9.61.

(1-Triethylsilylbutyl)benzene (5)



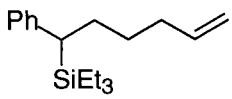
IR (neat) 2955, 2875, 1458, 1016, 782, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.03 (m, 5H), 2.13 (dd, *J* = 3.2, 12.4 Hz, 1H), 1.83-1.77 (m, 1H), 1.72-1.68 (m, 1H), 1.40-1.02 (m, 4H), 0.87 (t, *J* = 8.0 Hz, 9H), 0.82 (t, *J* = 6.8 Hz, 3H), 0.49 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 127.8, 127.8, 124.0, 34.2, 31.7, 29.6, 22.6, 14.1, 7.7, 2.6; MS (EI) *m/z* (relative intensity, %) 262 (M^+, 17), 235 (6), 234 (20), 233 (100), 117 (6), 115 (24); HRMS calcd for $C_{17}H_{30}Si$ 262.2116, found 262.2137; Anal. Calcd for $C_{17}H_{30}Si$: C, 77.78; H, 11.52. Found: C, 77.65; H, 11.49.

(*E*)-1-Cyclohexyl-2,3-dimethyl-4-triethylsilylbut-2-ene (7)



IR (neat) 2921, 2875, 2852, 774, 752, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.90 (d, *J* = 7.8 Hz, 2H), 1.72-1.62 (m, 3H), 1.62 (s, 3H), 1.58 (s, 3H), 1.53 (s, 2H), 1.45-1.30 (m, 1H), 1.27-1.05 (m, 4H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.93-0.81 (m, 3H), 0.53 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.4, 123.8, 42.5, 37.4, 33.7, 26.9, 26.7, 21.3, 20.8, 19.8, 7.6, 4.4; MS (EI) *m/z* (relative intensity, %) 280 (M^+, 94), 251 (100), 115 (43); HRMS calcd for $C_{18}H_{36}Si$ 280.2586, found 280.2567; Anal. Calcd for $C_{18}H_{36}Si$: C, 77.06; H, 12.93. Found: C, 76.78; H, 12.74.

(1-Triethylsilylhex-5-enyl)benzene (8)



IR (neat) 3023, 2952, 2934, 2875, 1450, 769, 714, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24-7.03 (m, 5H), 5.73 (tdd, *J* = 6.6, 10.3, 18.5 Hz, 1H), 4.94 (d, *J* = 18.5 Hz, 1H), 4.89 (d, *J* = 10.3 Hz, 1H), 2.14 (dd, *J* = 3.2, 12.4 Hz, 1H), 2.08-1.91 (m, 2H), 1.89-1.79 (m, 1H), 1.77-1.66 (m, 1H), 1.45-1.34 (m, 1H), 1.29-1.14 (m, 1H), 0.87 (t, *J* = 7.8

Hz, 9H), 0.49 (q, J = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 138.7, 127.9, 127.8, 124.1, 124.1, 114.1, 33.7, 29.3, 28.7, 7.7, 2.5; MS (EI) *m/z* (relative intensity, %) 274 (M^+, 0.5), 246 (21), 245 (100), 217 (6), 115 (15); HRMS calcd for $C_{18}H_{30}Si$ 274.2117, found 274.2110; Anal. Calcd for $C_{18}H_{30}Si$: C, 78.75; H, 11.02. Found: C, 78.45; H, 11.03.

4-1.5. References and Notes

[1] (a) *The Chemistry of Organic Silicon Compounds* Patai. S.; Rappoport. Z., Eds., John Wiley & Sons, Chichester, **1989**. (b) *The Chemistry of Organic Silicon Compounds Vol. 2*; Patai. S.; Rappoport. Z., Eds.; John Wiley & Sons; Chichester, **1998**. (c) Collman, J. P.; Heggedus, L. S.; Norton, J. R.; Finke, R. G. Principles and Applications of Organotransition Metal Chemistry; University Science Books: Mill Valley, CA, 1987; pp 564-568. (d) Reichel, J. A.; Berry, D. H. In *Advances in Organometallic Chemistry*; Stone, F. G. A.; West, R., Eds.; Academic Press: New York, 1998; pp.197-265.

[2] (a) Negishi, E.-I. *Pure Appl. Chem.* **1981**, *53*, 2333. (b) Negishi, E.-I,; King, A. O.; Klima, W. L.; Patterson, W.; Silveria, A., Jr. *J. Org. Chem.* **1980**, *45*, 2526. (c) Millar, R. B.; Al-Hassan, M. I. *J. Org. Chem.* **1985**, *50*, 2121. (d) Akaki, S.; Imai, A.; Shimizu, K.; Butsugan, Y. *Tetrahedron Lett.* **1992**, *33*, 2581. (e) Germon, C.; Alexakis, A.; Normat, J. F. *Synthesis* **1984**, 40 and 43.

[3] (a) Lin, W.; Wilson, S. R.; Girolami, G. S. *J. Am. Chem. Soc.* **1993**, *115*, 3022. (b) Horton, A. D.; Orpen, A. G. *Organometallis* **1992**, *11*, 1193. (c) Chang, L. S.; Johnson, M. P.; Fink, M. J. *Organometallics* **1991**, *10*, 1219. Lewis acid-catalyzed carbosilylation, see: Asano, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4874-4875.

[4] Paladium-catalized three-component carbosilylation were reported: (a) Chatani, N.; Amishiro, N.; Murai, S. *J. Am. Chem. Soc.* **1991**, *113*, 7778-7780. (b) Obora, Y.; Tsuji, Y.; Kawamura, T. *J. Am. Chem. Soc.* **1995**, *117*, 9814-9821. (c) Chatani, N.;

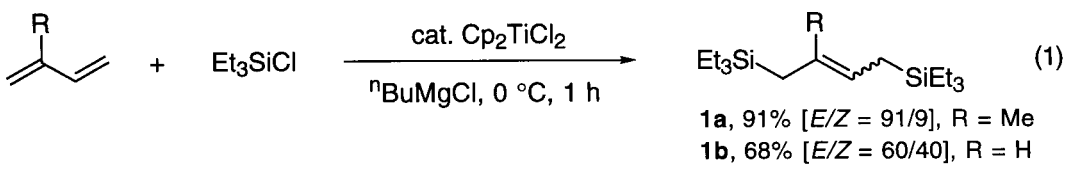
Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834-1840.

[5] The rate constant $k = 1.3 \times 10^8$ s^{-1} (at 25 °C) for the isomerization of cyclopropylmethyl radical to butenyl radical has been reported: (a) Maillard, B.; Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7024-7026. The rate constant $k = 5.4 \times 10^4$ $M^{-1}s^{-1}$ (at 25 °C) for the addition of 5-hexenyl radical to styrene has been reported: (b) Citterio, A.; Minisci, F. *J. Org. Chem.* **1979**, *44*, 2674-82. Although cyclopropylmethylmagnesium bromide is known to rearrange to CH_2=$CHCH_2CH_2MgBr$, it is not likely that these species are the intermediates, since the rearrangement is too slow ($t_{1/2}$ = 30 h in THF at 27 °C): (c) Silver, M. S.; Shafer, P. R.; Nordlander, J. E.; Ruchardt, C.; Roberts, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 2646-2647.

Titanocene-Catalyzed Double Silylation of Dienes and Ary Alkenes with Chlorosilanes

4-2.1. Introduction

The reactivity of compounds containing silicon-hydrogen bonds is known to be more analogous of that of dihydrogen than to that of similar compounds with carbon-hydrogen than to that of similar compounds with carbon-hydrogen bonds. Ample precedent exists to support the casual statement that "silicon acts like a fat hydrogen", including similar catalytic additions of Si-H and H-H bonds to olefins and general trends in migratory aptitudes for organic and organometallic process. Further extension of this analogy leads one to consider the addition of a Si-Si bond across an olefin, resulting in silicon-carbon bond formation. Indeed, the transition metal-catalyzed "double addition" of disilanes to unsaturated organic substrates is a highly efficient method of functionalization.[1] The first example of this double silylation reaction was reported by Kumada and co-workers in 1972, involving the nickel-catalyzed addition of a disilane to dienes.[2] Several groups have screened a variety of transition metal complexes for activity in the double silylation system, but only compounds of nickel, palladium, and platinum appear to be viable catalysts. The best substrates for double additions are unsaturated organic compounds such as dienes[3] and alkynes.[4] Alkenes are less reactive. In fact, only a few successful instances of double silylation have been demonstrated for alkenes not tethred to a disilane.[5] We report herein the first example of a metal-catalyzed double silylation of dienes and alkenes with chlorosilanes,[6] which proceeds under mild conditions by the use of Cp_2TiCl_2 in the presence of ^{n}BuMgCl (eq 1).

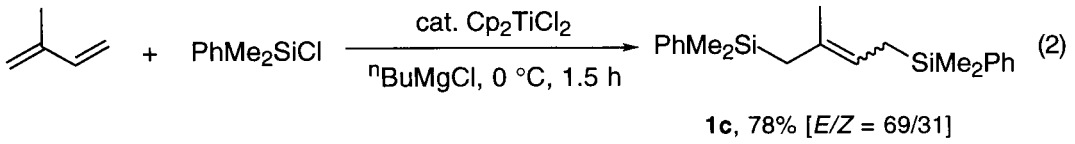


(1)

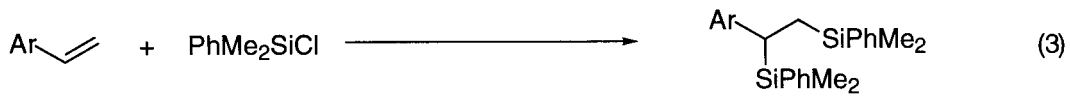
1a, 91% [*E*/*Z* = 91/9], R = Me
1b, 68% [*E*/*Z* = 60/40], R = H

4-2.2. Results and Discussion

For example, into a mixture of isoprene (3.12 mmol), chlorotriethylsilane (2.2 equiv, 6.86 mmol) and titanocene dichloride (0.05 equiv) was added a THF solution of ^{n}BuMgCl (2.2 equiv, 0.9 M, 7.6 mL) at 0 °C. The solution was stirred for 1 h and the product was extracted with ether. The NMR analysis of the crude product indicated the formation of 1,4-bis (triethylsilyl)-2-butene **1a** in 91% yield (*E*/*Z* = 91/9) (eq 2). Under similar conditions, 1,3-butadiene afforded **1b** in 68% yield,[7] whereas 2,3-dimethylbutadiene failed to give the corresponding disilylated product. When chlorodimethylphenylsilane (3 equiv) and ^{n}BuMgCl (3 equiv) were used, **1c** was obtained in 78% yield (eq 3).



1c, 78% [*E*/*Z* = 69/31]



2a, 72%, Ar = *p*-ClC$_6$H$_4$
2b, 64%, Ar = Ph

We then applied this procedure to the double silylation of alkenes. Under the same conditions as those of eq 2, *p*-chlorostyrene afforded **2a** in only 29% yield along with a substantial amount of Me$_2$PhSi^{n}Bu. This result suggests that silylation of *p*-chlorostyrene is slow and competes with the direct reaction of Me$_2$PhSiCl with ^{n}BuMgCl.[8] This problem was practically overcome by using a large amount of the catalyst and by adopting a dropwise addition procedure as follows. Into a mixture of *p*-chlorostyrene (2.02 mmol) and ^{n}BuMgCl (3.0 equiv) in THF (6.7 mL) was added a THF solution (10 mL) containing Me$_2$PhSiCl (3.0 equiv) and Cp$_2$TiCl$_2$ (0.15 equiv) over a period of 30 min at 0 °C. After stirring the solution for another 1 h, **2a** was formed in 72% yield (eq 4). In a similar manner **2b** was formed in 64% yield from styrene, whereas double silylation did not proceed with alkenes having no aromatic

substituent such as 1-octene.

4-2.3. Conclusion

The present titanocene-catalyzed reaction provides a new and synthetically useful method for double silylation of dienes and aryl alkenes with chlorosilanes. The transition metal catalyzed double silylation of unsaturated compounds provides a useful method for the formation of carbon-silicon bonds. These reactions have been studied extensively using late transition metal catalysts and employing disilanes as the silylating reagents. Although chlorosilanes are the most readily available silylating reagents, their use in catalytic double silylation has not yet been achieved. The present reaction is the first example of transition metal catalyzed double silylation with chlorosilanes.

4-2.4. Experimental Section

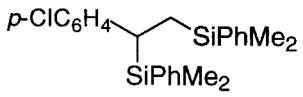
General Procedure for Double Silylation of Dienes

Into a mixture of isoprene (212.5 mg, 3.12 mmol), chlorotriethylsilane (1034 mg, 6.86 mmol) and titanocene dichloride (45.6 mg, 0.16 equiv) was added a THF solution of ^{n}BuMgCl (7.6 ml, 0.9 M) at 0 °C. The solution was stirred for 1 h, 1 N HClaq was added to the solution at 0 °C, and the mixture was again warmed to 20 °C. An saturated aqueous NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give an orange crude product. The NMR analysis of the crude product indicated the formation of 1,4-bis(triethylsilyl)-2-butene **1a** in 91%, 846 mg yield (*E*/*Z* = 91/9). The product **1a** (as a mixture of stereoisomers) was obtained in pure form by HPLC with $CHCl_3$ as the eluent in 86% (801 mg) yield.

General Procedure for Double Silylation of Styrenes

Into a mixture of *p*-chlorostyrene (280mg, 2.02 mmol) and ^{n}BuMgCl (3.0 equiv) in THF (6.7 mL) was added a THF solution (10 mL) containing $Me_2PhSiCl$ (1034 mg, 3.0 equiv) and Cp_2TiCl_2 (76 mg, 0.15 equiv) over a period of 30 min at 0 °C. After stirring the solution for another 1 h, followed by the same workup as in conditions of **1a** gave an ogange crude product (72% NMR yield). Purification by HPLC afforded 545 mg (66%) of **2a**.

1,2-Bis(phenyldimethylsilyl)-1-(4-Chlorophenyl)etane (2a)



IR (neat) 3068, 2955, 1489, 1427, 1114, 1096, 863, 836, 811, 775, 729, 700 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 138.8, 136.7, 133.9, 133.2, 129.7, 129.0, 128.8, 128.5, 127.6, 127.4, 127.3, 30.7, 15.4, -1.9, -2.9, -4.2, -5.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 10H), 7.11 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 2.30 (dd, J = 3.4, 11.8 Hz, 1H), 1.23 (dd, J = 11.8, 15.1 Hz, 1H), 1.17 (dd, J = 3.4, 15.1 Hz, 1H), 0.26 (s, 3 H), 0.17 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); MS (EI) *m/z* (relative intensity, %, (^{35}Cl) 408 (M^+, 1), 238 (24), 223 (65), 135 (100), 107 (16), 105 (14). HRMS calcd for $C_{24}H_{29}Si_2Cl$ (^{35}Cl) 408.1496,found 408.1506; Anal. Calcd for $C_{24}H_{29}Si_2Cl$: C, 70.46; H, 7.15. Found: C, 70.41; H, 7.22.

The products **1a-c** and **2b** are known compounds and their yields and *E/Z* ratios were determined by NMR except the case of **1b**. The stereochemistry of **1b** was deduced by comparison of its ^{1}H and ^{13}C NMR spectra with those of a related compound $Me_3SiCH_2CH=CHCH_2SiMe_3$ (Marciniec, B.; Pietraszuk, C.; Foltynowicz, Z. *J. Organomet. Chem.* **1994**, *474*, 83-87), since sufficient spectral data are not available for **1b**. The products **1b,c** (as a mixture of stereoisomers) and **2b** were obtained in pure form by HPLC in 62%, 76%, 54% yields, respectively.

Registry Nos of other products and their references

1,4-Bis(triethylsilyl)-2-methyl-2-butene (1a) 84812-47-5

1,4-Bis(triethylsilyl)-2-butene (1b) 84812-44-2

(*E*)-1,4-Bis(dimethylphenylsilyl)-2-butene (1c) 84812-54-4

(*Z*)-1,4-Bis(dimethylphenylsilyl)-2-butene (1c) 84812-55-5

Hiyama, T.; Obayashi, M.; Mori, I.; Nozaki, H. *J. Org. Chem.* **1983**, *48*, 912-914.

1,2-Bis(phenyldimethylsilyl)ethylbenzene (2b)

Hayashi, T.; Kawamoto, A. M.; Kobayashi, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.*, **1990**, 563.

4-2.5. References and Notes

[1] For reviews, see: Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317-1350. Reichel, J. A.; Berry, D. H. In *Advances in Organometallic Chemistry*; Stone, F. G. A.; West, R., Eds.; Academic Press: New York, 1998; pp.197-265. See, also: Sakaki, S.; Ogawa, M.; Musashi, Y. *J. Organomet. Chem.* **1997**, *535*, 25-28 and references therein.

[2] Okinoshima, H.; Yamamoto, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 9263-9665.

[3] Obora, Y.; Tsuji, Y.; Kawamura, T. *Organometalics 12*, **1993**, 2853.

[4] (a) Okinoshima, H.; Yamamoto, K.; Kumada, M. *J. Orgnomet. Chem.* **1975**, *96*, C27. (b) Kusukawa, T.; Kabe, Y.; Nestler, B.; Ando, W. *Organometalics 14*, **1995**, 2556.

[5] (a) Hayashi, T.; Kawamoto, A. M.; Kobayashi, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1990**, 563. (b) Hayashi, T.; Kobayashi, T.; Kawamoto, A. M.; Yamashita, H.; Tanaka, M. *Organometalics 9*, **1990**, 280. (c) Murakami, M.; Yoshida, T.; Ito, Y. *Organometalics 13*, **1994**, 2900.

[6] For a unique reaction of $Cl(SiMe_2)_2Cl$ with acetylenes catalyzed by Pd complexes, see:

Tanaka, Y.; Yamashita, H.; Tanaka, M. *Organometallics* **1995**, *14*, 530-541.

[7] The reaction was performed by adding Cp_2TiCl_2 into a THF solution of Et_3SiCl, ^nBuMgCl, and butadiene, which was condensed at 0 °C under slightly reduced pressure, in a glass vessel equipped with a dry ice condenser.

[8] The direct reaction of Et_3SiCl with ^nBuMgCl is negligibly slow under the conditions employed; however, Et_3SiCl afforded only poor yields of the desired products (<10%) when styrenes were used as the substrates.

Conclusion

The aim of this research is to develop new methodologies for catalytic introduction of functionalities to alkenes using early transition metals. In this study, the author have investigated new alkylation and silylation of alkenes using the ate-complex of zirconocene and titanocene as an active species. It is usually difficult to use alkyl halides and chlorosilanes as the alkylating and silylating reagents in late transition metal catalyzed reactions. This study is attractive from both mechanistic and synthetic view points and provides one methodology which overcomes this problem by an unprecedented catalytic system based on the characteristics of early transition metals. The results obtained from this thesis are summarized as follows.

Chapter 1 disclosed that a zirconocene complex efficiently catalyze the silylation of alkenes with chlorosilanes and related compounds such as thio-, seleno-, and tellurosilanes. This reaction is the first example of transition metal catalyzed silylation with chlorosilanes. The reaction proceeds via dialkyl zirconocene complexes, and the subsequent β-elimination from the intermediates accounts for the product selectivities, i.e., alkenylsilanes vs. allylsilanes. It has been demonstrated that the C-Si bond forming step does be promoted by Grignard reagents. It was also shown that a known hydrosilylation process is not involved in the present reaction and that frequently referred neutral zirconocene-alkene complexes do not undergo silylation. With these results, two unique pathways were proposed for the C-Si bond forming step. The one involves oxidative addition of chlorosilanes to a zirconium complex, and the other involves direct "electrophilic" attack of chlorosilanes toward coordinated alkenes of zirconate complexes.

Based on the mechanistic information obtained in chapter 1, zirconocene-catalyzed alkylation of aryl alkenes with several alkylating reagents was examined in chapter 2. This reaction provides a new transformation of aryl alkenes via regioselective alkylation using alkyl tosylates, sulfates and bromides having β-hydrogens catalyzed by a zirconocene complex. It is possible that a zirconate complex or a benzylmagnesium compound serves as the key

intermediate which reacts with alkylating reagents at the benzylic carbon leading to a dialkyl zirconocene complex.

Chapter 3 described titanocene-catalyzed alkylation of aryl alkenes. The present reaction provides a novel method for alkylation of aryl alkenes using alkyl halides under mild conditions. A variety of alkyl bromides and iodides can be used as the suitable alkylating reagents but alkyl chlorides were sluggish. This reaction gave different products depending on the solvents used, that is, regioselective double alkylation proceeds in THF, whereas ether solvent facilitated Heck type monoalkylation. These results can be explained by that the transmetalation of benzyltitanium complexes to benzylmagnesium spices proceeds predominantly over the β-elimination from the titanocene complex in THF. This might be because the strongly coordinating THF enhances the nucleophilicity of Grignard reagents than in ether and because β-elimination from benzyltitanium complexes is suppressed in THF by occupying the coordinating sites on titanium.

Chapter 4 described titanocene-catalyzed silylation of alkenes. The present reaction enables regioselective carbosilylation and double silylation of aryl alkenes and dienes using alkyl halides and/or chlorosilanes in the presence of ^{n}BuMgCl. It is possible that a titanate complex $Cp_2Ti^{n}Bu_2^-$ plays an important role as the active species for the electron transfer to alkyl halides and/or to chlorosilanes providing alkyl and silyl radicals, which react with aryl alkenes to give benzyl or allyl radical spices.

Thus, several new synthetic reactions were developed by using zirconocene and titanocene as catalysts. The author believes that the present study will arrest much attention from many chemists especially in the fields of synthetic and organometallic chemistry and will open up a new methodology for the formation of carbon-carbon and/or carbon-silicon bonds.

List of Publications

(1) Zirconocene-Catalyzed Silylation of Alkenes with Chlorosilanes
Jun Terao, Kazushi Torii, Koyu Saito, Nobuaki Kambe, Akio Baba, and Noboru Sonoda
Angew. Chem., Int. Ed. Engl. **1998**, *37*, 2653.

(2) Zirconocene-Catalyzed Alkylation of Aryl Alkenes with Alkyl Tosylates, Sulfates and Bromides
Jun Terao, Tsunenori Watanabe, Koyu Saito, Nobuaki Kambe, and Noboru Sonoda
Tetrahedron Lett. **1998**, *39*, 9201.

(3) Regioselective Double Alkylation of Styrenes with Alkyl Halides Using a Titanocene Catalyst
Jun Terao, Koyu Saito, Shinsuke Nii, Nobuaki Kambe, and Noboru Sonoda
J. Am. Chem. Soc. **1998**, *120*, 11822.

(4) Titanocene-Catalyzed Double Silylation of Dienes and Aryl Alkenes with Chlorosilanes
Jun Terao, Nobuaki Kambe, and Noboru Sonoda
Tetrahedron Lett. **1998**, *39*, 9697.

(5) New C-C and C-Si Bonds Forming Reaction Using a Titanocene Catalyst
Jun Terao, Shinsuke Nii, Nobuaki Kambe, and Noboru Sonoda
in preparation.

(6) Heck Type Transformation of Aryl Alkenes with Alkyl Bromides Catalyzed by a Titanocene Complex
Jun Terao, Masako Miyamoto, Nobuaki Kambe, and Noboru Sonoda
in preparation.

List of a Supplementary Publications

(1) A New Preparative Method of Alkenylaluminum Reagents via Tellurium-Aluminum Exchange Reactions
Jun Terao, Nobuaki Kambe, and Noboru Sonoda
Synlett, **1996**, 779.

(2) Tellurium-Zinc Exchange Reaction. A New Preparative Method of Alkenylzinc Reagents
Jun Terao, Nobuaki Kambe, and Noboru Sonoda
Tetrahedron Lett. **1996**, *37*, 4741.

(3) Synthesis of Internal Acetylenes from Vinylic Tellurides
Jun Terao, Nobuaki Kambe, and Noboru Sonoda
Tetrahedron Lett. **1998**, *39*, 5511.

(4) Synthesis and Reaction of Vinylic Tellurides
Jun Terao, Nobuaki Kambe, and Noboru Sonoda
Phosphorus, Sulfur, and Silicon in press.

Preface

The study described in this thesis have been carried out (1993-1999) under the direction of Professor Noboru Sonoda and Professor Akio Baba at Department of Applied Chemistry, Faculty of Engineering, Osaka University. The objective of this thesis is concerned with Studies on the Alkylation and Silylation of Alkenes Catalyzed by Early Transition Metals.

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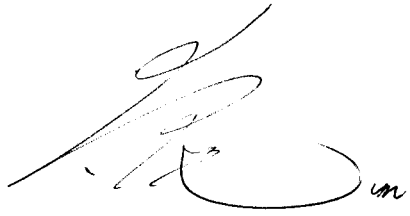

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