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Titanocene-Catalyzed Regioselective Alkylation of Styrenes with Grignard Reagents Using β-Bromoethyl Ethers, Thioethers, or Amines

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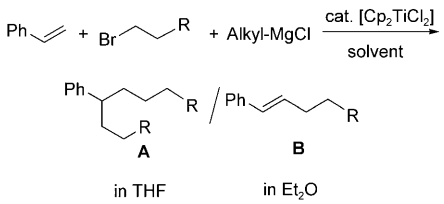
Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday

Abstract: Regioselective double alkylation of styrenes with alkyl Grignard reagents and alkyl bromides having a heteroatom functional group at the β-position has been achieved by the use of a titanocene catalyst in THF. When ether was used instead of THF as a solvent, monoalkylation by substitution of a vinylic hydrogen atom with an alkyl group proceeded under similar conditions. These reactions involve the addition of alkyl radicals to styrenes to form benzylic radical intermediates.

Keywords: alkylation · Grignard reaction · homogeneous catalysis · styrene · titanium

Introduction

Regioselective addition of carbon functional groups to carbon–carbon unsaturated bonds is a useful tool in the synthesis of organic compounds by constructing desired carbon skeletons. A number of catalytic reactions have been developed mainly by the use of late-transition-metal catalysts. During our study on the regioselective addition of alkyl groups to alkenes with the aid of early-transition-metal catalysts,[1] we found that anionic titanocene complexes have a high ability for electron transfer to alkyl halides, resulting in the formation of alkyl radical species as key intermediates. A successful example is the double alkylation of alkenes with alkyl halides.[2] This reaction is promoted by Grignard reagents in the presence of a catalytic amount of $[Cp_2TiCl_2]$. The combined use of primary and secondary, primary and tertiary, or secondary and tertiary alkyl bromides in THF affords the doubly alkylated products **A** in a manner such that more substituted alkyl groups are introduced at the terminal carbon atom of styrenes (Scheme 1). In ether, however, substitution of a styrene vinylic hydrogen atom with an alkyl group, rather than the addition reaction, proceeds to give **B** under similar conditions.[3]



Scheme 1. Titanocene-catalyzed double alkylation (**A**) or dehydrogenative monoalkylation (**B**) of styrenes.

Herein we report a similar but new type of regioselective alkylation of styrenes using alkyl Grignard reagents and β-functionalized ethyl bromides. In THF solution, the double-alkylation products **C**, possessing an alkyl group from a Grignard reagent at the terminal carbon atom and an alkyl group from the bromide at the benzylic carbon atom, were formed with high regioselectivities. Monoalkylation products **D** were obtained stereoselectively in ether solution (Scheme 2).

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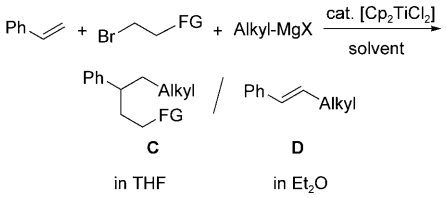
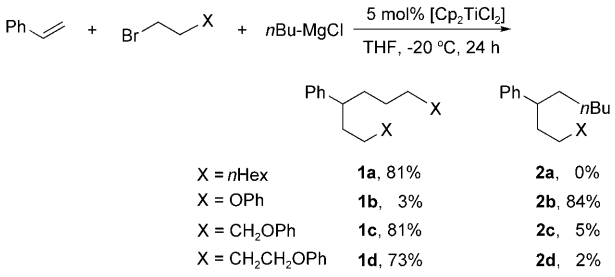


Scheme 2. Titanocene-catalyzed regioselective alkylation of styrenes with Grignard reagents and β-functionalized ethyl bromides.

Results and Discussion

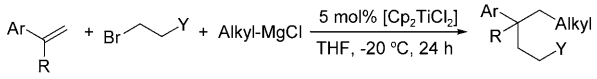
To a THF solution of styrene (1.0 mmol), *n*-octyl bromide (2.2 mmol), and the *n*-butyl Grignard reagent (4.5 mmol) was added [Cp_2TiCl_2] (0.05 mmol) and stirred at −20 °C for 24 h. The double-alkylation product **1a** was obtained in 81 % yield as the sole alkylation product.[2] When the reaction was performed using 3-bromopropyl or 4-bromobutyl phenyl ether as an alkyl bromide, the corresponding double-alkylation product **1c** or **1d** was obtained in 81 % or 73 % yield along with a small amount of the other double-alkylation product **2c** or **2d**, respectively, with the *n*-butyl group at the terminal carbon atom. Interestingly, however, use of the alkyl bromide bearing the phenoxy group at the β-position provided the double-alkylation product **2b** as the major product, in which *n*-butyl and phenoxyethyl groups were incorporated regioselectively at the terminal carbon atom of styrene in 84 % yield, along with a 3 % yield of **1b** (Scheme 3).



Scheme 3. Titanocene-catalyzed double alkylation of styrene.

The results obtained using various styrenes, alkyl bromides having an alkoxy, phenoxy, thiophenyl, or amino group at the β-position, and alkyl Grignard reagents are summarized in Table 1. 2-Bromoethyl ethyl ether also gave the corresponding product **2e** in high yield (Table 1, entry 1). The use of *n*-octyl Grignard reagent in place of the *n*-butyl Grignard reagent afforded **2f** in 70 % yield (Table 1, entry 2). No reaction took place with MeMgBr and PhMgBr under the same conditions. When 2-bromoethyl phenyl sulfide was employed, the corresponding product **2g** was obtained in 82 % yield (Table 1, entry 3). A 2-bromoethylamine also gave the corresponding double-alkylation product in a moderate yield (Table 1, entry 4). 2-Vinylnaphthalene and *p*-methyl-, *p*-fluoro-, and *o*-methoxystyrenes yielded the corresponding products in 66 % 72 %, 63 %, and 74 % yields, respectively (Table 1, entries 5–8). Although internal alkenes such as β-methyl styrene or stilbene, and 1-alkenes not having an aryl group (such as 1-octene) were sluggish under similar conditions, α-methyl- and α-phenylstyrenes also efficiently underwent the double alkylation (Table 1, entries 9 and 10).

Table 1. Titanocene-catalyzed double alkylation of styrenes.



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Entry	Ar	R	Alkyl	Y	Yield [%][a]
1	Ph	H	*n*Bu	OEt	**2e**, 85
2	Ph	H	*n*Oct	OEt	**2f**, 70
3	Ph	H	*n*Bu	SPh	**2g**, 82
4	Ph	H	*n*Bu	NMePh	**2h**, 47
5	2-Naphthyl	H	*n*Bu	OEt	**2i**, 66
6	*p*Tol	H	*n*Bu	OEt	**2j**, 72
7	*p*-FC_6H_4	H	*n*Bu	OEt	**2k**, 63
8	*o*-$MeOC_6H_4$	H	*n*Bu	OEt	**2l**, 74
9	Ph	Me	*n*Bu	OEt	**2m**, 73
10	Ph	Ph	*n*Bu	OEt	**2n**, 76

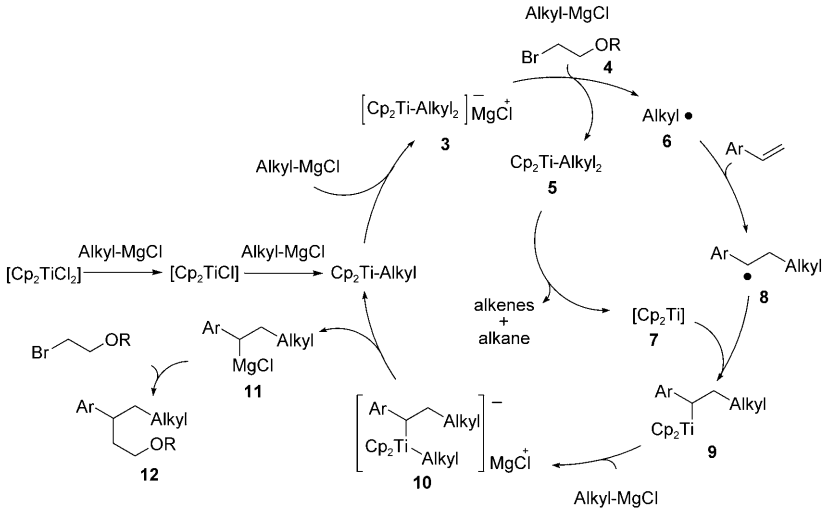
[a] Yield of isolated product based on the styrene used.

A plausible reaction pathway is shown in Scheme 4 involving a β-bromoethyl ether **4**. [Cp_2TiCl_2] reacts with three equivalents of alkyl Grignard reagent to generate the dialkyltitanate(III) complex **3**[4] through [Cp_2TiCl][5] and alkyltitanocene(III).[6] Electron transfer from **3** to the β-bromoethyl ether in the presence of an alkyl Grignard reagent leads to the formation of alkyl radical species **6** along with [Cp_2Ti^{III}] (**7**) via dialkyltitanocene(IV) **5**.[7] Addition of **6** to styrene at the terminal carbon atom affords the benzyl radical species **8**, which recombines with **7** to give the corresponding benzyl titanocene complex **9**. Subsequent transmetalation of **9** with the alkyl Grignard reagent via **10** gives the benzyl Grignard reagent **11**, along with regeneration of alkyltitanocene.[8] Finally, **11** reacts with β-bromoethyl ether to form the double-alkylation product **12**. The evidence provided below supports this reaction pathway.

Since it is known that [Cp_2TiCl_2] catalyzes the addition of allyl Grignard reagents to isoprene,[9] we first examined whether such an addition process of alkyl Grignard reagents to styrene is involved. When a reaction similar to entry 1 of Table 1 was carried out in the absence of 2-bromoethyl ethyl ether, no evidence for the formation of a butylation product of styrene was detected after quenching the reaction mixture

Abstract in Japanese:

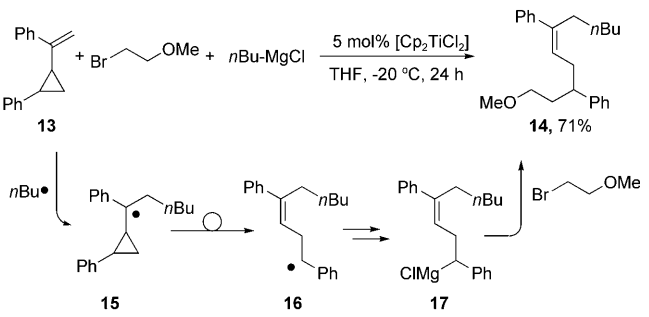
チタノセン触媒存在下、スチレン類とアルキルグリニヤール試薬とβ-ブロモエチルエーテル、チオエーテル、あるいはアミンとの反応をTHF溶媒中で行ったところ、スチレンの末端にグリニヤール試薬由来のアルキル基、内部にヘテロ原子官能基を有するブロミド由来のエチル基が位置選択的に導入されたダブルアルキル化生成物が位置選択的に得られた。また、THF溶媒の代わりにエーテル溶媒を用いた場合、スチレンの末端水素がグリニヤール試薬のアルキル基により置換された脱水素アルキル化物が立体選択的に生成した。



Scheme 4. Proposed reaction pathway of regioselective double alkylation of styrenes.

with 1 N HCl. This result suggests that carbomagnesiation products such as **11** are not formed in the absence of 2-bromoethyl ethyl ether.

We next tested for the presence of benzylic radical intermediates. In the reaction of α-cyclopropyl styrene derivatives **13** with 2-bromoethyl methyl ether, the product **14** was formed as the sole three-component coupling product by ring opening of the cyclopropyl group (Scheme 5).[10] This

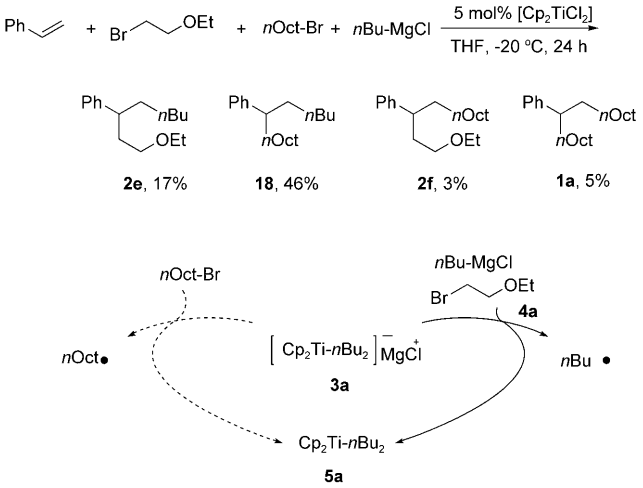


Scheme 5. Intermediate involvement of a benzyl radical **15**.

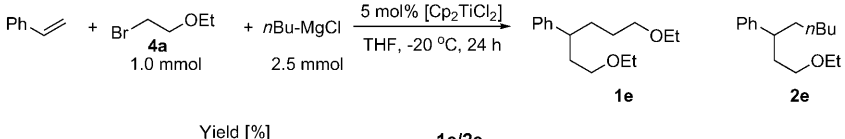
indicates that the terminal carbon–carbon bond-forming step proceeds by a radical mechanism to form the benzyl radical species **15**, which undergoes rapid ring opening, leading to **16**.[10] Following a similar pathway to that shown in Scheme 4, **16** gives **14** via **17**.

When a reaction similar to that of entry 1 in Table 1 was carried out in the presence of *n*-octyl bromide, double-alkylation products having an *n*-butyl group (**2e** and **18**) were preferentially formed compared with the corresponding *n*-octyl-substituted products (**2f** and **1a**; Scheme 6). This result indicates that the reaction in Scheme 1 via an octyl radical intermediate competes with that in Scheme 2 via a butyl radical intermediate, and that the latter proceeds preferentially.

To probe the mechanism of this new double-alkylation reaction, we performed exploratory kinetic studies as shown in Figure 1. The product ratio of **1e** to **2e** was plotted against the amount of styrene. Increasing the amount of styrene leads to the preferred formation of **1e** with concomitant suppression of **2e**, and the ratio obeys first-order kinetics on the concentration of styrene.



Scheme 6. Competitive reaction using two kinds of alkyl bromide.



Entry	Styrene mmol	Ratio 1e/2e	Yield [%] based on 4a 1e	2e
1	1.0	0.05	1.4	27.8
2	3.0	0.17	3.5	20.3
3	5.0	0.25	3.8	15.0
4	7.0	0.41	5.3	12.9

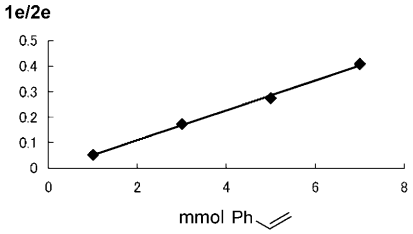


Figure 1. Plot of **1e**/**2e** ratio with different concentrations of styrene.

This result can be interpreted assuming that the ethoxyethyl radical **19a** is formed by electron transfer from the dibutyltitanate(III) complex **3a** to β-bromoethyl ether in situ and reacts in two competitive pathways: addition to styrene, and butyl radical formation. The mechanistic details of the latter process are still unknown, but a Ti complex may not be involved because the amount of $[Cp_2TiCl_2]$ used did not influence the **1e**/**2e** product ratio (Figure 2). Taking into account these results, possible reaction pathways are depicted in Scheme 7.

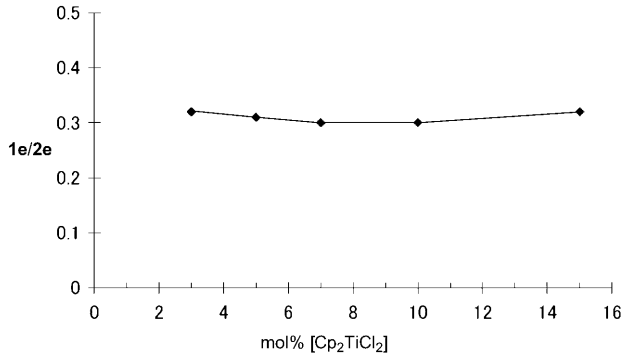
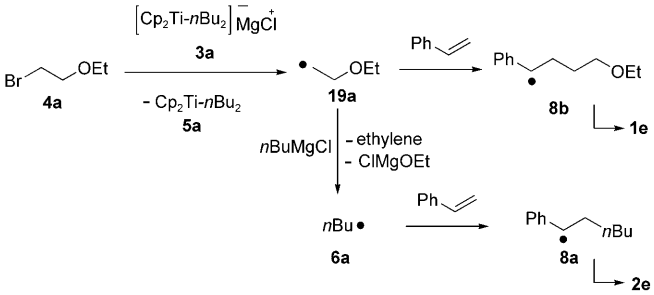
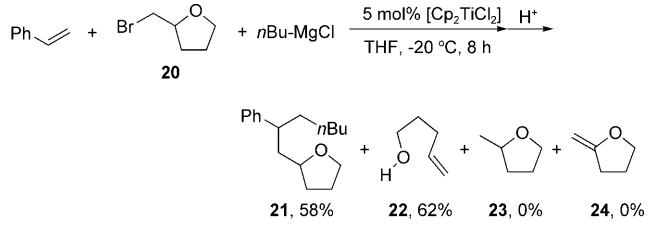


Figure 2. Plot of **1e**/**2e** ratio against the amount of $[Cp_2TiCl_2]$ used.

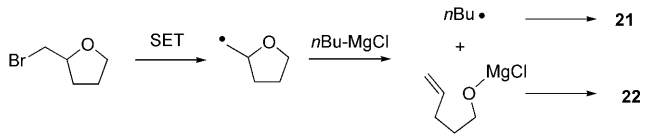


Scheme 7. Intermediate role of β-ethoxyethyl radical **19a** formed by electron transfer from the titanate complex **3a** to a β-bromoethyl alkyl ether.

To prove the degradation process of 2-alkoxyethyl radicals shown in Scheme 7, the reaction of styrene with 2-(bromomethyl)tetrahydrofuran **20** was conducted under similar conditions. After the usual workup, the corresponding product **21** was obtained in 58% yield along with a 62% yield of pentenol **22** (Scheme 8). No evidence was obtained for the formation of 2-methyl-tetrahydrofuran **23** or 2-methylene-tetrahydrofuran **24**. This result suggests that the reaction depicted in Scheme 9 proceeds efficiently.

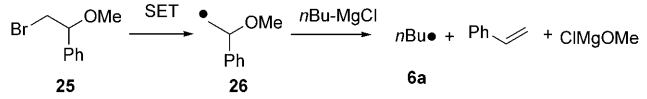


Scheme 8. Reaction using 2-(bromomethyl)tetrahydrofuran.



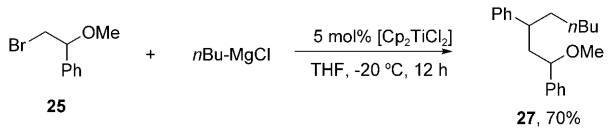
Scheme 9. β-Oxygen elimination of β-alkoxyethyl radical.

According to the reaction of Scheme 9, when (2-bromo-1-methoxyethyl)benzene **25** is used, styrene should be formed along with the concomitant formation of the butyl radical **6a** (Scheme 10).



Scheme 10. Generation of styrene from (2-bromo-1-methoxyethyl)benzene.

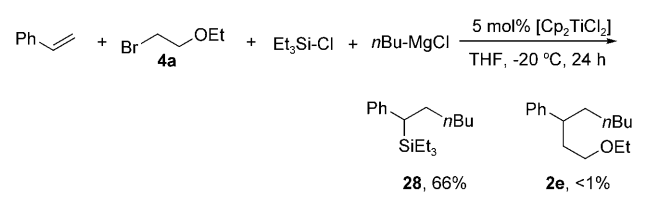
Reaction of **25** with the *n*-butyl Grignard reagent in the absence of styrene was carried out under conditions similar to those of entry 1 in Table 1. After general workup, the expected product **27** was obtained as a single product in 70% yield, indicating that styrene generated in situ was incorporated in this catalytic cycle (Scheme 11).



Scheme 11. Reaction of (2-bromo-1-methoxyethyl)benzene with *n*-butyl Grignard reagent.

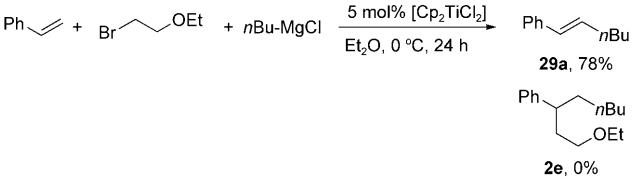
The intermediate role of the benzyl Grignard species **11** is supported by the observation that when the reaction of Scheme 2 was performed in the presence of a chlorosilane, the carbosilylation product **28** was obtained. This was proved by trapping **11** with chlorosilane, which resulted in suppression of the double alkylation (Scheme 12).

It should be noted that changing the solvent from THF to ether led to the formation of a different alkylation product in which a terminal vinylic hydrogen atom was replaced



Scheme 12. Titanocene-catalyzed carbosilylalkylation of styrenes with Grignard reagents and a chlorosilane.

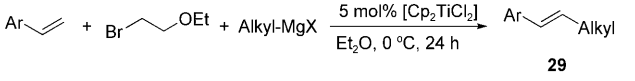
with an alkyl group of the Grignard reagent. When an ether solution of styrene (1.0 mmol), 2-bromoethyl ethyl ether (2.2 mmol), *n*-butyl Grignard reagent (4.5 mmol), and [Cp_2TiCl_2] (0.05 mmol) was stirred for 24 h at 0 °C, (*E*)-1-phenyl-1-hexene (**29a**) was obtained in 78% yield with greater than 98% regio- and stereoselectivities, without the formation of **2e** (Scheme 13).



Scheme 13. Titanocene-catalyzed dehydrogenative alkylation of styrene with a Grignard reagent.

Results obtained from reactions with other substrates are shown in Table 2. The use of an *n*-octyl Grignard reagent afforded the corresponding product **29b** in 63% yield (Table 2, entry 1). 2-Vinyl-naphthalene and *p*-chlorostyrene also gave the desired products in good yields (Table 2, entries 2 and 3).

Table 2. Titanocene-catalyzed dehydrogenative alkylation of styrenes with Grignard reagents.

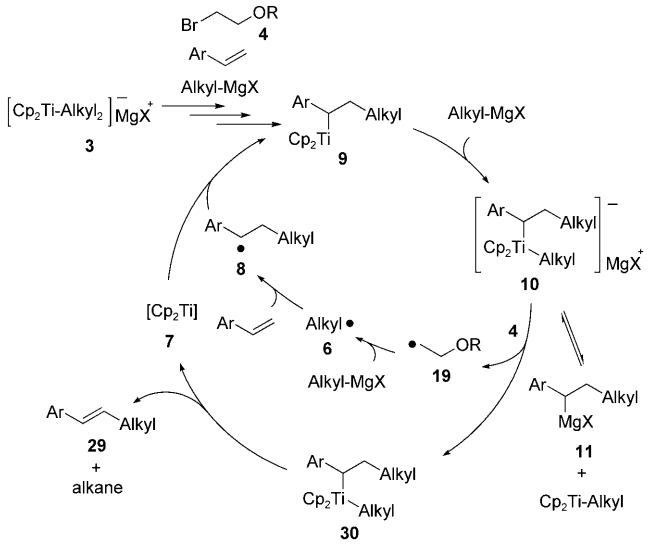


29

Entry	Ar	Alkyl-MgX	Yield [%][a]
1	Ph	*n*Oct-MgBr	**29b**, 63
2	2-Naphthyl	*n*Bu-MgCl	**29c**, 59
3	*p*-ClC_6H_4	*n*Bu-MgCl	**29d**, 75

[a] Yield of isolated product based on the styrene used.

A plausible pathway for this dehydrogenative alkylation is shown in Scheme 14. The titanate(III) complex **3** reacts with β-bromoethyl alkyl ether, styrene, and two equivalents of the Grignard reagent to form **10** by the same reaction pathway as that in Scheme 4. In ether solution, the electron transfer from the titanate(III) complex **10** to β-bromoalkyl ether took place predominantly to give **30**. Alternatively, **10** may undergo transmetalation leading to the benzylmagnesium **11**, as in the case of THF solvent; however, **11** may not react with alkyl halides in ether solvent.[11] The successive β-elimination of **30** by site-selective hydrogen abstraction at the benzylic side in favor of conjugated double-bond formation affords the corresponding product **29**, along with regeneration of **7**. The 2-alkoxyethyl radical **19** works in a similar way as in THF, giving rise to the benzyl radical **8**, which then regenerates the Ti^{III} complex **9**.



Scheme 14. Proposed reaction pathways of dehydrogenative alkylation of styrenes.

Conclusions

A new method for alkylation reactions of styrenes using alkyl Grignard reagents and β-bromoethyl ethers, thioethers, or amines has been developed with the aid of a titanocene catalyst. In these reactions, β-bromoethyl ethers play important roles as oxidizing reagents towards alkyl Grignard reagents to generate alkyl radicals and, in THF, as electrophiles. The reaction in THF involves two types of carbon–carbon bond-forming steps: 1) addition of alkyl radicals toward styrenes in the first step, and 2) electrophilic trapping of benzyl Grignard reagents with a β-bromoethyl ether in the second step. The titanocene catalyst plays important roles in generating active key species in promoting these crucial steps; alkyl radicals are formed by electron transfer from titanate complexes, and benzyl Grignard reagents are formed by transmetalation of the corresponding Ti^{III} complexes with Grignard reagents. In ether solution, the latter process is switched by β-hydrogen elimination, resulting in the formation of dehydrogenative alkylation products with high regio- and stereoselectivities.

Experimental Section

General

Infrared spectra were obtained with a Perkin–Elmer FTIR (Model 1600). ^{1}H NMR and 13C 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. Both conventional and high-resolution mass spectra were recorded with a JEOL JMS-DX303HF spectrometer. GC mass analyses (EI) were obtained using a JMS-mate operating in the electron-impact mode (70 eV) equipped with an RTX-5 30MX.25MMX.25U column. Elemental analyses were performed on a Perkin–Elmer 240C apparatus. Butylmagnesium chloride in THF, dicyclopentadienyltitanium dichloride (Kanto Chemical Company), butylmagnesium chloride in Et_2O, octylmagnesium halide solution, β-bromophenetole, 2-vinylnaphtalene, *p*-fluorostyrene, *o*-

methoxystyrene, 1,1-diphenylethylene (Aldrich Chemical Company), 4-bromobutylphenylether, styrene, *p*-methylstyrene, α-methylstyrene, 2-bromoethyl methyl ether (Wako Pure Chemical Company), octyl bromide, 3-bromopropyl phenyl ether, 2-bromoethyl ethyl ether, 2-bromoethyl phenyl sulfide, 2-(bromomethyl)tetrahydrofuran, *p*-chlorostyrene (Tokyo Chemical Industry Company) were purchased and used as received. α-Cyclopropylstyrene derivatives **13** were prepared according to the literature from *trans*-calcone via phenyl(2-phenylcyclopropyl)methanone.[12,13] 2-Bromoethyl methylphenyl amine and (2-bromo-1-methoxyethyl)benzene **25** were prepared from the corresponding alcohol according to the literature.[14]

Synthesis

Typical procedure of double alkylation of styrene (Table 1, entry 1): To a mixture of styrene (104.0 mg, 1.0 mmol), 2-bromoethyl ethyl ether (341.1 mg, 2.2 mmol), *n*-buthylmagnesium chloride (1.8 M, 2.5 mL, 4.5 mmol in THF) was added [Cp_2TiCl_2] (12.3 mg, 0.05 mmol) at −20 °C under nitrogen. After stirring for 24 h, the reaction mixture was quenched with a few drops of aqueous 1N HCl at −20 °C. H_2O (50 mL) was added, and the product was extracted with ether (50 mL). The organic layer was dried over Na_2SO_4 and evaporated. Purification by column chromatography on silica gel with 19:1 hexane/Et_2O afforded 198.6 mg (85 %) of **2e** as a colorless oil.

The spectra of compounds **29a**,[15] **29b**,[16] **29c**,[17] and **29d**[18] were identical to those reported in the literature.

2c: 1-Phenoxy-3-phenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.29–7.15 (m, 7H), 6.93–6.80 (m, 3H), 3.90–3.70 (m, 2H), 2.90–2.75 (m, 1H), 2.20–2.12 (m, 1H), 2.00–1.95 (m, 1H), 1.81–1.60 (m, 2H), 1.23–1.10 (m, 6H), 0.85–0.82 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 144.8, 129.2, 128.2, 127.5, 120.3, 114.41, 114.36, 66.0, 42.5, 37.0, 36.4, 32.0, 27.3, 22.7, 14.2; IR (NaCl): $\tilde{\nu}$ = 3062, 3029, 2954, 2928, 2857, 1600, 1586, 1496, 1469, 1453, 1245, 1171, 1078, 1035, 753, 701 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 282 ([*M*]$^+$, 0.1), 188 (9), 132 (15), 119 (16), 117 (43), 105 (31), 104 (8), 94 (8), 92 (8), 91 (100), 77 (13); HRMS calcd for $C_{20}H_{26}O$: 282.1984, found: 282.1988. Elemental analysis (%) calcd for $C_{20}H_{26}O$: C 85.06, H 9.28; found: C 84.79, H 9.27.

2e: 1-Ethoxy-3-phenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.29–7.25 (m, 2H), 7.19–7.13 (m, 3H), 3.42–3.30 (m, 2H), 3.27–3.14 (m, 2H, 2.65 (septet-like tt *J* = 4.8, 9.5 Hz, 1H), 2,00–1.92 (m, 1H), 1.82–1.73 (m, 1H), 1.66–1.52 (m, 2H), 1.21–1.09 (m, 9H), 0.84–0.80 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.2, 128.0, 127.5, 125.7, 68.7, 66.1, 42.6, 37.0, 36.9, 32.0, 27.3, 22.7, 15.4, 14.2 ppm; IR (NaCl): $\tilde{\nu}$ = 3029, 2956, 2928, 2859, 1602, 1494, 1453, 1380, 1353, 1123, 1028, 759, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 234 ([*M*]$^+$, 0.1), 188 (58), 132 (43), 119 (10), 118 (14), 117 (100), 105 (17), 104 (21), 92 (19), 91 (67), 79 (3), 78 (5), 77 (4), 59 (27); HRMS calcd for $C_{16}H_{26}O$: 234.1984, found: 234.1975. Elemental analysis (%) calcd for $C_{16}H_{26}O$: C 81.99, H 11.18; found: C 81.80, H 11.08.

2f: 1-Ethoxy-3-phenylundecane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.29–7.25 (m, 2H), 7.19–7.13 (m, 3H), 3.42–3.30 (m, 2H), 3.27–3.14 (m, 2H, 2.65 (septet-like tt, *J* = 4.9, 9.5 Hz, 1H), 2,00–1.91 (m, 1H), 1.81–1.73 (m, 1H), 1.66–1.55 (m, 2H), 1.27–1.09 (m, 17H), 0.84–0.80 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.5, 128.2, 127.7, 125.8, 68.7, 66.0, 42.6, 37.0, 36.8, 31.9, 29.7, 29.6, 29.5, 29.3, 27.5, 22.6, 15.2, 14.1 ppm; IR (NaCl): $\tilde{\nu}$ = 3062 3027, 2925, 2854, 2800, 1603, 1494, 1454, 1378, 1353, 1124, 1028, 760, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 290 ([*M*]$^+$, 0.1), 244 (82), 218 (7), 215 (2), 145 (4), 133 (10), 119 (11), 118 (16), 117 (100), 105 (14), 104 (23), 92 (17), 91 (47), 78 (3), 77 (2), 59 (21); HRMS calcd for $C_{20}H_{34}O$: 290.2610, found: 290.2605. Elemental analysis (%) calcd for $C_{20}H_{34}O$: C 82.69, H 11.80; found: C 82.65, H 11.58.

2g: 3-Phenyloctyl phenyl sulfide: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.31–7.11 (m, 10H), 2.75–2.64 (m, 3H), 1.97–1.86 (m, 2H), 1.60–1.53 (m, 2H), 1.23–1.09 (m, 6H), 0.83–0.80 ppm (m, 3H);^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 128.64, 128.61, 128.2, 127,5 126.0, 125.5, 45.2, 36.8, 36.2, 32.0, 31.6, 27.3, 22.7, 14.2 ppm; IR (NaCl): $\tilde{\nu}$ = 3060, 3026, 2954, 2926, 2855, 1602, 1584, 1480, 1466, 1452, 1438, 1400, 1269, 1091, 1026, 737, 701, 691 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 298 ([*M*]$^+$, 42), 189 (4), 188 (27), 137 (30), 132 (43), 123 (25), 118 (13), 117 (100), 110 (9), 109 (14), 104 (13), 91 (49), 79 (3), 78 (3), 77 (6); HRMS calcd for $C_{20}H_{26}S$: 298.1755, found: 298.1761. Elemental analysis (%) calcd for $C_{20}H_{26}S$: C 80.48, H 8.78; found: C 80.42, H 8.77.

2h: Methylphenyl 3-phenyloctyl amine: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.33–7.15 (m, 7H), 6.66–6.62 (m, 1H), 6.55–6.53 (m, 2H), 3.21–3.05 (m, 2H), 2.80 (s, 3H), 2.55–2.49 (m, 1H), 1.97–1.89 (m, 1H), 1.83–1.75 (m, 1H), 1.64–1.54 (m, 2H), 1.23–1.20 (m, 6H), 0.83–0.80 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.1, 145.3, 129.1, 128.4, 127.6, 126.1, 115.8, 112.1, 51.0, 43.9, 38.1, 37.2, 32.9, 31.9, 27.2, 22.5, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3061, 3026, 2926, 2857, 1600, 1505, 1452, 1372, 1192, 1034, 747, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 295 ([*M*]$^+$, 18), 133 (1), 132 (1), 121 (9), 120 (100), 117 (1), 107 (8), 105 (4), 104 (3), 91 (5), 79 (1); HRMS calcd for $C_{21}H_{29}N$: 295.2300, found: 295.2314. Elemental analysis (%) calcd for $C_{21}H_{29}N$: C 85.37, H 9.89, N 4.74; found: C 85.31, H 10.13, N 4.67.

2i: 1-Ethoxy-3-(2-naphtyl)octane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.82–7.74 (m, 3H), 7.57 (s, 1H), 7.47–7.25 (m, 3H), 3.38–3.18 (m, 4H,) 2.88–2.80 (m, 1H), 2.06–2.00 (m, 1H), 1.92–1.87 (m, 1H), 1.69–1.68 (m, 2H), 1.21–1.11 (m, 9H), 0.83–0.81 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.9, 133.5, 132.2, 127.9, 127.6, 127.5, 126.3, 125.9, 125.8, 125.0, 68.7, 66.0, 42.7, 36.9, 36.7, 31.9, 27.2, 22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3052, 3016, 2924, 2857, 2800, 1633, 1600, 1508, 1466, 1377, 1355, 1120, 889, 818, 746, 662 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 284 ([*M*]$^+$,26), 238 (10), 213 (17), 212 (100), 182 (13), 169 (22), 168 (16), 167 (79), 155 (33), 142 (39), 141 (96), 128 (13), 59 (19); HRMS calcd for $C_{20}H_{28}O$: 284.2140, found: 284.2147.

2j: 1-Ethoxy-3-*p*-methylphenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.10–7.02 (m, 4H), 3.42–3.30 (m, 2H), 3.28–3.14 (m, 2H), 2.61 (septet-like tt, *J* = 4.9, 9.4 Hz, 1H), 2.32 (s, 3H), 1.97–1.89 (m, 1H), 1.79–1.70 (m, 1H), 1.63–1.53 (m, 2H), 1.24–1.10 (m, 9H), 0.82 ppm (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.7, 127.8, 126.6, 120.5, 110.5, 69.2, 66.0, 55.3, 35.7, 35.5, 35.0, 32.0, 27.1, 22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3019, 2927, 2858, 2800, 1513, 1456, 1378, 1124, 1020, 816, 722 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 248 ([*M*]$^+$, 7), 202 (55), 187 (54), 146 (41), 131 (95), 118 (12) 117 (18), 105 (100), 91 (9), 59 (28); HRMS calcd for $C_{17}H_{28}O$: 248.2140, found: 248.2133. Elemental analysis (%) calcd for $C_{17}H_{28}O$: C 82.20, H 11.36; found: C 82.09, H 11.30.

2k: 1-Ethoxy-3-*p*-fluorophenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.11–6.94 (m, 4H), 3.38–3.33 (m, 2H), 3.25–3.21 (m, 1H), 3.16–3.13 (m, 1H) 2.67 (septet-like tt, *J* = 4.9, 9.8 Hz, 1H), 1.99–1.90 (m, 1H), 1.75–1.51 (m, 3H), 1.23–1.10 (m, 9H), 0.82 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2 (d, *J* = 242 Hz), 141.0 (d, *J* = 2.8 Hz), 128.9 (d, *J* = 7.8 Hz), 115.0 (d, *J* = 21.1 Hz), 68.5, 66.1, 41.8, 37.0, 36.9, 31.8, 27.1, 22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3091, 2956, 2929, 2958, 1604, 1509, 1468, 1378, 1353, 1296, 1223, 1158, 1123, 1015, 834, 725, 687 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 252 ([*M*]$^+$, 0.4), 206 (36), 180 (3), 163 (2), 150 (36), 135 (100), 122 (13), 110 (59), 96 (2), 59 (26); HRMS calcd for $C_{16}H_{25}FO$: 252.1889, found: 252.1887. Elemental analysis (%) calcd for $C_{16}H_{25}FO$: C 76.15, H 9.98; found: C 76.25, H 10.00.

2l: 1-Ethoxy-3-*o*-methoxyphenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.17–7.12 (m, 2H), 6.91–6.82 (m, 2H), 3.79 (s, 3H), 3.40–3.33 (m, 2H), 3.24 (t, *J* = 7.2 Hz, 2H), 3.15 (quintet-like tt, *J* = 7.3, 7.4 Hz, 1H), 1.96–1.84 (m, 2H), 1.63–1.57 (m, 2H), 1.23–1.11 (m, 9H), 0.82 ppm (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 133.7, 127.8, 126.6, 120.5, 110.5, 69.2, 66.0, 55.3, 35.7, 35.5, 32.0, 27.1, 22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3025, 2929, 2858, 1600, 1585, 1492, 1464, 1439, 1378, 1288, 1240, 1109, 1052, 1032, 794, 753 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 264 ([*M*]$^+$, 22), 218 (9), 192 (5), 162 (14), 149 (35), 147 (63), 134 (4), 121 (100), 108 (2), 91 (20), 59 (21); HRMS calcd for $C_{17}H_{28}O_2$: 264.2089, found 264.2087. Elemental analysis (%) calcd for $C_{17}H_{28}O_2$: C 77.22, H 10.67; found: C 77.02, H 10.39.

2m: 1-Ethoxy-3-methyl-3-phenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$,25 °C, TMS): δ = 7.33–7.24 (m, 2H), 7.18–7.14 (m, 2H), 3.36–3.24 (m, 3H), 3.16–3.10 (m, 1H), 2.09–2.02 (m, 1H), 1.91–1.84 (m, 1H), 1.71–1.62 (m, 1H), 1.57–1.50 (m, 1H) 1.31 (s, 3H) 1.23–1.10 (m, 9H), 1.00–0.90 (m, 1H), 0.81 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 128.0, 126.2, 125.4, 67.5, 66.1, 43.8, 42.2, 39.6, 32.5, 24.3, 23.6,

22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3088, 3058, 3023, 2957, 2931, 2862, 2802, 1602, 1497, 1468, 1445, 1378, 1357, 1130, 1105, 1032, 763, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 248 ($[M]^+$, 2), 176 (44), 145 (1), 133 (73), 131 (15), 119 (14), 105 (100), 91 (75), 59 (62); HRMS calcd for $C_{17}H_{28}O$: 248.2140, found: 248.2145. Elemental analysis (%) calcd for $C_{17}H_{28}O$: C 82.20, H 11.36; found: C 81.92, H 11.07.

2n: 1-Ethoxy-3,3-diphenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.36–7.13 (m, 10H), 3.32 (q, *J* = 7.1 Hz, 2H), 3.13 (t, *J* = 7.8 Hz, 2H), 2.43 (t, *J* = 7.7 Hz, 2H), 2.08–2.04 (m, 2H), 1.22–1.19 (m, 4H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.05–1.00 (m, 2H), 0.799 ppm (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 127.8, 127.7, 125.6, 67.6, 66.2, 48.0, 38.1, 37.0, 32.5, 23.6, 22.5, 15.2, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3087, 3056, 2934, 2868, 2802, 1598, 1579, 1495, 1444, 1378, 1357, 1111, 1030, 754, 700, 622 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 310 ($[M]^+$, 4), 241 (2), 239 (100), 195 (55), 181 (11), 167 (74), 133 (9), 117 (45), 105 (18), 91 (71), 59 (59); HRMS calcd for $C_{22}H_{30}O$: 310.2297, found: 310.2294. Elemental analysis (%) calcd for $C_{22}H_{30}O$: C 85.11, H 9.74; found: C 84.91, H 9.60.

14: (*E*)-1-Methoxy-3,6-diphenyl-5-undecene: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.31–7.15 (m, 10H), 5.21(t, *J* = 7.1 Hz, 1H), 3.28–3.20 (m, 5H), 2.87–2.80 (m, 1H), 2.58–2.36 (m, 4H), 2.11–2.03 (m, 1H), 1.91–1.82 (m, 1H), 1.24–1.22 (m, 6H), 0.83 ppm (t, *J* = 6.6 Hz, 3H); NOE difference measurement: irradiation of methylene protons at δ = 2.42 ppm (-C*H*$_2$-*n*Bu) caused 8.6% enhancement of methylene proton at δ = 2.58 ppm (vinyl-C*H*H-benzyl), irradiation of methylene proton at δ = 2.58 ppm caused 7.4% enhancement of methylene protons at δ = 2.42 ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 143.4, 141.3, 128.3, 128.0, 127.7, 126.7, 126.6, 126.4, 70.8, 58.5, 42.9, 36.0, 35.7, 31.9, 29.8, 28.2, 22.5, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3081, 3059, 3026, 2954, 2928, 2870, 1600, 1493, 1453, 1388, 1121, 760, 699 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 336 ($[M]^+$, 0.1), 304 (2), 277 (2), 205 (2), 188 (11), 189 (65), 174 (2), 162 (3), 147 (18), 131 (27), 127 (2), 119 (10), 118 (16), 117 (100), 115 (12), 105 (10), 91 (41); HRMS calcd for $C_{24}H_{32}O$: 336.2453, found: 336.2457. Elemental analysis (%) calcd for $C_{24}H_{32}O$: C 85.66, H 9.58; found: C 85.62, H 9.47.

21: 2-Phenyloctyltetrahydrofuran: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.30–7.15 (m, 5H), 3.85–3.80 (m, 1H), 3.67–3.61 (m, 1H), 3.53–3.49 (m, 1H), 2.75 (septet-like tt, *J* = 4.9, 9.3 Hz, 1H), 1.84–1.55 (m, 7H), 1.34–1.09 (m, 7H), 0.82 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = (145.61, 145.57), (128.3, 128.2), (127.8, 127.5), (125.9, 125.8), (77.19, 77.18), (67.4, 2C) (43.4, 43.0), (43.3, 42.6), (37.4, 36.9), (31.89, 31.88), (31.8, 31.1), (27.2, 27.1), (25.64, 25.63), (22.5, 2C), (14.02, 14.01) ppm; IR (NaCl): $\tilde{\nu}$ = 3062, 3027, 2956, 2927, 2856, 1602, 1494, 1454, 1378, 1063, 759, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 246 ($[M]^+$, 10), 218 (3), 200 (1), 190 (3), 175 (11), 162 (85), 157 (17), 129 (13), 118 (21), 105 (25), 91 (79), 71 (100); HRMS calcd for $C_{17}H_{26}O$: 246.1984, found: 246.1980. Elemental analysis (%) calcd for $C_{17}H_{26}O$: C 82.87, H 10.64; found: C 82.68, H 10.35.

27: 1-Methoxy-1,3-diphenyloctane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.33–7.16 (m, 10H), 3.69 (dd, *J* = 2.9, 10.4 Hz, 1H), 3.09 (s, 3H), 2.97–2.89 (m, 1H), 2.06 (ddd, *J* = 4.2, 10.4, 14.3 Hz, 1H), 1.72 (ddd, *J* = 2.9, 11.1, 14.3 Hz, 1H),1.60–1.55 (m, 2H), 1.26–1.17 (m, 6H), 0.82 ppm (t *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4, 143.0, 128.3, 128.3, 128.1, 127.9, 127.3, 126.3, 126.0, 81.3, 56.6, 46.5, 42.5, 37.1, 31.9, 29.7, 27.2, 22.5, 14.0 ppm; IR (NaCl): $\tilde{\nu}$ = 3062, 3028, 2927, 2857, 2820, 2364, 1602, 1493, 1454, 1358, 1100, 1072, 756, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 296 ($[M]^+$, 0.5), 264 (22), 193 (17), 162 (4), 121 (100), 104 (5), 91 (12); HRMS calcd for $C_{21}H_{28}O$: 296.2140, found: 296.2145. Elemental analysis (%) calcd for $C_{21}H_{28}O$: C 85.08, H 9.52; found: C 84.79, H 9.26.

28: Triethyl(1-phenylhexyl)silane: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.26–7.03 (m7.26–7.03, 5H), 2.13 (dd, *J*,= 12.2, 3.2 Hz, 1H), 1.83–1.77 (m, 1H), 1.69–1.65 (m, 1H), 1.25–1.09 (m, 6H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.84–0.81 (m, 3H), 0.49 ppm (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 128.0, 127.9, 124.1, 34.1, 31.7, 29.7, 29.1, 22.5, 14.1, 7.5, 2.3 ppm; IR (NaCl): $\tilde{\nu}$ = 3080, 3060, 3023, 2954, 2875, 1600, 1493, 1450, 1416, 1378, 1240, 1188, 1089, 1016, 803, 722, 713, 700 cm^{-1}; MS (EI): *m*/*z* (relative intensity, %): 277 ($[M]^+$, 2), 276 (6), 247 (2), 160 (16), 135 (2), 121 (2), 116 (11), 115 (100), 107 (5), 104 (3), 87 (62), 59 (17); HRMS calcd for $C_{18}H_{32}Si$: 276.2273, found: 276.2277. Elemental analysis (%) calcd for $C_{18}H_{32}Si$: C 78.18, H 11.66; found: C 77.98, H 11.71.

29a: (*E*)-1-Phenyl-1-hexene: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.40–7.11 (m, 5H) 6.38 (d, *J* = 15.9 Hz, 1H), 6.26–6.19 (m, 1H), 2.21 (q, *J* = 6.8 Hz, 2H), 1.49–1.31 (m, 4H), 0.92 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 131.2, 129.7, 128.4, 126.7, 125.9, 32.7, 31.5, 22.3, 13.9 ppm.

29b: (*E*)-1-Phenyl-1-decene: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.40–7.15 (m, 5H), 6.37 (d, *J* = 15.6 Hz, 1H), 6.26–6.19 (m, 1H), 2.23–2.17 (m, 2H), 1.48–1.27 (m, 12H), 0.88 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 131.3, 129.7, 128.4, 126.7, 125.9, 33.1, 31.9, 29.5, 29.4, 29.3, 29.2, 22.7, 14.1 ppm; HRMS calcd for $C_{16}H_{24}$: 216.1878, found: 216.1875.

29c: (*E*)-1-(2-Naphthyl)-1-hexene: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.74 (t, *J* = 8.8 Hz, 3H), 7.64 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.42–7.35 (m, 2H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.37–6.29 (m, 1H), 2.24 (q, *J* = 7.0 Hz, 2H), 1.51–1.31 (m, 4H), 0.93 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 134.1, 133.0, 132.0, 130.2, 128.3, 128.1, 127.9, 126.4, 125.7, 125.6, 123.9, 33.2, 31.9, 22.6, 14.3 ppm; HRMS calcd for $C_{16}H_{18}$: 210.1409, found: 210.1411.

29d: (*E*)-1-*p*-Chlorophenyl-1-hexene: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.25 (s, 4H), 6.32 (d, *J* = 15.6 Hz, 1H), 6.23–6.16 (m, 1H), 2.23–2.17 (m, 2H), 1.49–1.32 (m, 4H), 0.92 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.4, 132.2, 131.9, 128.6, 128.5, 127.1, 32.7, 31.4, 22.3, 13.9 ppm; HRMS calcd for $C_{12}H_{15}Cl$: 194.0862, found: 194.0864.

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