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SYNTHESIS AND REACTION OF BROMOALLYLSILANE: A SHORT ACCESS TO β,γ–DISUBSTITUTED α-METHYLENE-γ–BUTYROLACTONE

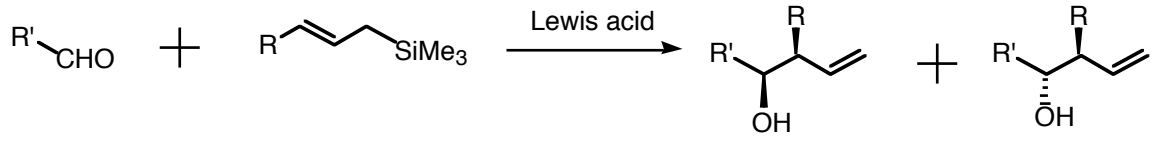
Jun'ichi Uenishi* and Masashi Ohmi

Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8412, Japan
E-mail: juenishi@mb.kyoto-phu.ac.jp

Abstract — (*Z*)-β-Bromoallylsilanes (**1a-c**) were prepared by a stereoselective Ni-catalyzed cross-coupling reaction of 1,1-dibromo-4-phenylbutene (**4**) with silylmethylmagnesium halide. Sakurai-Hosomi reaction of **1a** with aldehyde gave *syn*-3-alkyl-2-bromo-4-hydroxyalkene (**2a, 2c,** and **2e**) and that with acetal gave *syn*-4-alkoxy-3-alkyl-2-bromoalkene (**2b** and **2d**) stereoselectively. The products with formyl function reacted with a Ni-carbonyl complex to give β,γ-disubstituted α-methylene-γ–butyrolactones (**3**) in good yields. Pd-catalyzed cross-coupling reaction of **1a-c** or **4** with silylmethylmagnesium halide gave 1,1-bis(silylmethyl)-1-alkenes (**1d-i**), which reacted with dimethyl acetal to generate more functionalized allylsilane (**6**).

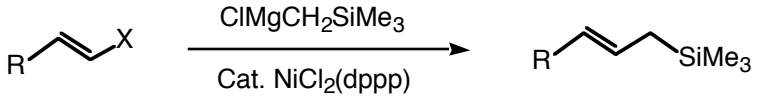
Introduction

Sakurai-Hosomi reaction of substituted allylsilane with aldehyde is an important carbon-carbon bond-forming reaction for creating a branched homoallyl functional unit (Scheme 1). The reaction has been widely used in organic synthesis, and various allylsilanes have been prepared.[1] However, β-bromoallylsilane has not been prepared except the simple one,[2] and it has therefore rarely been used in organic synthesis.[3] The reaction of haloalkene with a Grignard reagent in the presence of a transition metal catalyst,known as Kumada-Tamao-Corriu coupling, is used for the preparation of alkyl substituted alkene,[4] and this reaction has been employed as a convenient method for the preparation of allylsilanes (Scheme 2).[5]

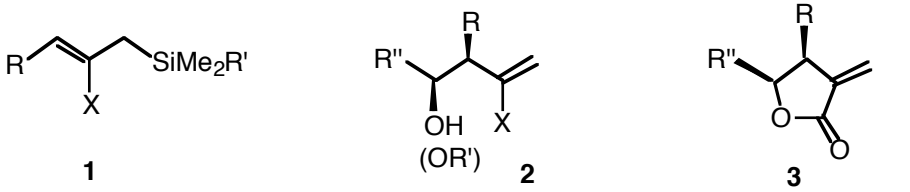


Scheme 1

major isomer minor isomer



Scheme 2



X = Br, $CH_2SiR''_3$
R = $PhCH_2CH_2$
R' = Me, Ph, OPr^i

X = Br
R = $PhCH_2CH_2$
R'' = Ph, Pr^i, C_8H_{17}

R = $PhCH_2CH_2$
R'' = Ph, Pr^i

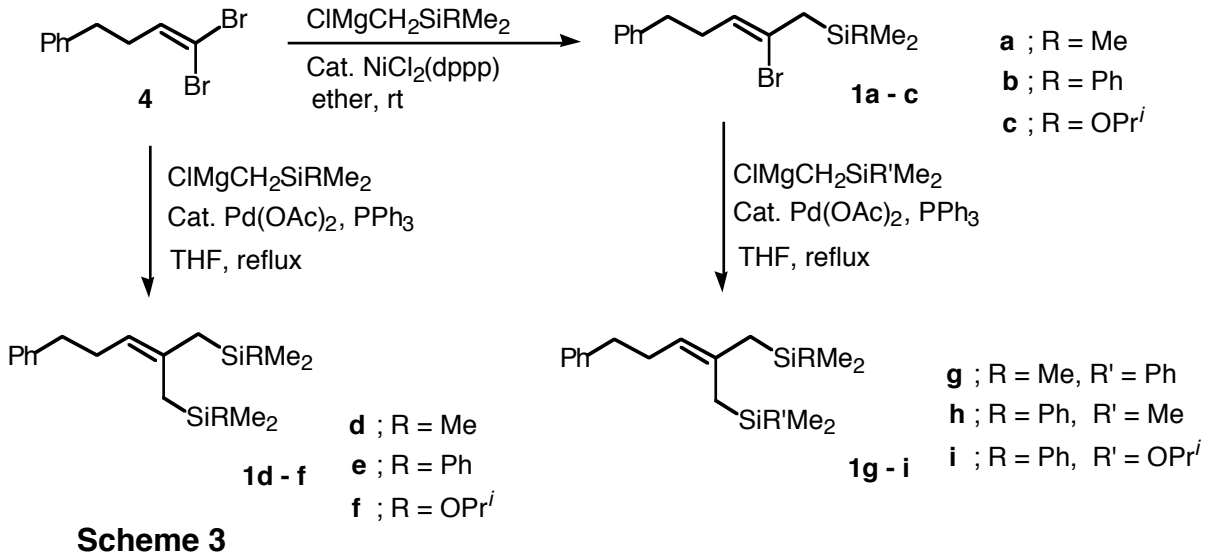
Figure 1

We have reported stereoselective Pd-catalyzed hydrogenolysis and cross-coupling reactions of 1,1-dibromo-1-alkene.[6] Since these reactions prefer to occur at the *trans* carbon-bromine bond of 1,1-dibromo-1-alkene, (*Z*)-bromoalkene is obtained stereoselectively.[7] During the course of this study, we have thought that the reaction of 1,1-dibromo-1-alkene with a trimethylsilylmethyl Grignard reagent by Kumada-Tamao-Corriu coupling would give β-bromoallylsilane (**1a**) stereoselectively. If that is the case, the Sakurai-Hosomi reaction of **1** with aldehyde will be able to give homoallylic alcohol having a vinyl bromide unit like compound (**2**). In this paper, we report the first general preparation of (*Z*)-β-bromoallylsilane and its synthetic application to β,γ-disubstituted α-methylene-γ-butyrolactone (**3**) *via* bromo-substituted homoallylic alcohol (**2**).

Preparation of Allylsilane from 1,1-Dibromo-1-alkene

(*Z*)-Bromoallylsilane (**1a**) was prepared by a $NiCl_2$(dppp) catalyzed cross-coupling reaction of 1,1-dibromo-4-phenylbutene (**4**) with trimethylsilylmethylmagnesium chloride in ether at room temperature. Under this condition, the cross-coupling took place at the *trans* position stereoselectively to give a (*Z*)-isomer (**1a**) exclusively in 89% yield, and a bistrimethylsilylmethylated product (**1d**) was not formed. The stereochemistry of **1a** was confirmed by the result of nOe experiments of ^{1}H NMR spectrum, in which 5.7% enhancement of the vinyl proton appeared at 5.43 ppm was observed upon irradiation of silylmethylene (CH_2Si) protons appeared at 2.09 ppm. In the same manner, a (dimethyl)phenylsilyl derivative (**1b**) was obtained in 83% yield. The reaction with (dimethyl)isopropoxy-silylmethylmaganesium chloride did not proceed in ether but proceeded in THF to give **1c** in 32% yield along with a bissilylmethylated product (**1f**) in 6% yield. On the other hand, 1,1-bis(silylmethyl)-1-alkenes (**1d-f**) were formed by a Pd-catalyzed cross-coupling reaction of **4** with an excess of silylmethylmagnesium chloride in refluxing THF. The compounds (**1d-f**) were obtained in 93, 73 and 67% yields, respectively, as shown in Scheme 3. If the second coupling of **1a** took place stereospecifically with a different silylmethyl Grignard

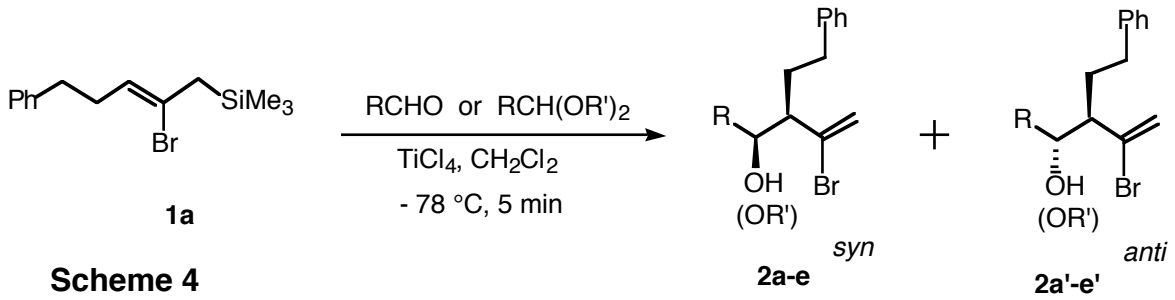
reagent, 1,1-bis(silylmethyl)-1- alkenes having different silylmethyl groups could be obtained. In fact, the reaction of **1a** with (dimethyl)phenylsilylmethylmagnesium chloride in the presence of a Pd catalyst in refluxing THF gave a (*Z*)-isomer (**1g**) preferentially over an (*E*)-isomer (**1h**) in a 10:1 ratio in 71% combined yield. On the other hand, when **1b** was used instead of **1a** with trimethylsilylmethylmagnesium chloride, **1h** was produced as a major product over **1g** in 77% yield with a 10:1 ratio. Therefore, stereocontrolled synthesis of 1,1-bis(silylmethyl)-1-alkenes having different silyl groups was possible. In a similar manner, **1i** was obtained by the reaction of **1b** with (dimethyl)isopropoxysilylmethylmaganesium chloride in 68% combined yield along with (*Z*)-isomer in a 10:1 ratio.



Scheme 3

Reaction of Allylsilanes with Aldehyde and Acetal

First, we examined the reaction of **1a** with benzaldehyde. The reaction was conducted in CH_2Cl_2 at –78 °C in the presence of $TiCl_4$. A mixture of *syn* isomer (**2a**) and *anti* isomer (**2a'**) was obtained selectively in a 10:1 ratio in 79% yield. These homoallylic alcohols were separable by HPLC. $TiCl_4$ was found to be the



Scheme 4

best among Lewis acids, such as $SnCl_4$, BF_3 etherate, $ZnBr_2$ and TMSOTf. The stereochemistry was rationally explained by the mechanism of Sakurai-Hosomi reaction, and eventually confirmed by the result of nOe experiments after leading to lactones (**3**) at a later stage. When benzaldehyde dimethyl acetal was used, the diastereoselectivity of **2b** and **2b'**decreased slightly to 5.3:1. The reaction with isobutanal gave a *syn* isomer (**2c**) exclusively in 78% yield, and the reaction with isobutanal diethyl acetal gave a mixture of

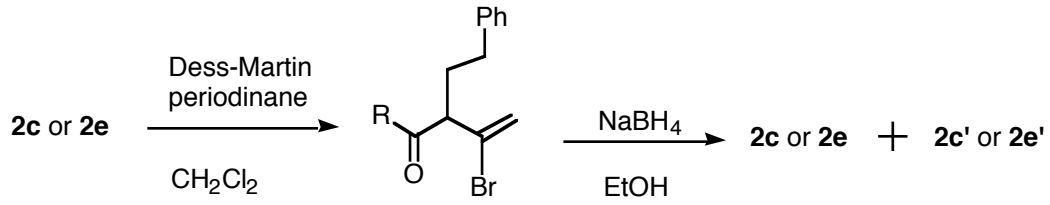
2d and **2d'** in 97% yield in an 8.7:1 ratio. The reaction with nonyl aldehyde gave **2e** in 80% yield as a single isomer. These results are summarized in Table 1 and they indicate that aliphatic aldehyde or its acetal tends to give a higher diastereoselectivity than does aromatic aldehyde or its acetal.

Table 1. Reactions of (*Z*)-β-Bromoallylsilane (**1a**) with RCHO and $RCH(OR')_2$

entry	aldehyde or acetal	R	R'	Product	Yield (%)	*syn* : *anti*[a)]
1	PhCHO	Ph	H	**2a+2a'**	79	10 : 1
2	$PhCH(OMe)_2$	Ph	Me	**2b+2b'**	74	5.3 : 1
3	Pr^iCHO	Pr^i	H	**2c+2c'**	78	>10 : 1
4	$Pr^iCH(OEt)_2$	Pr^i	Et	**2d+2d'**	97	8.7 : 1
5	$C_8H_{17}CHO$	C_8H_{17}	H	**2e+2e'**	80	>10 : 1

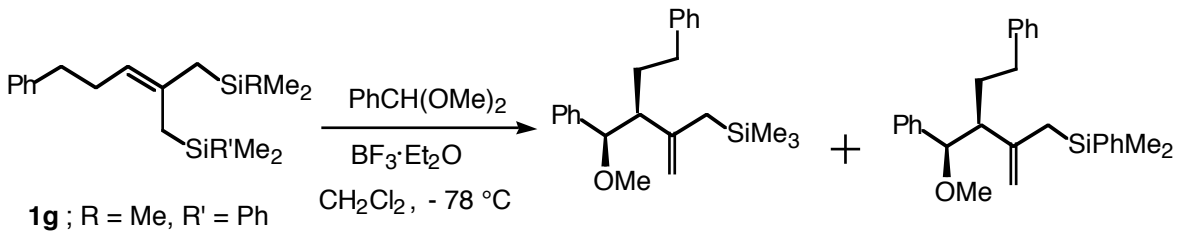
a, The isomeric ratio was determined by proton nmr of crude products

An *anti* isomer (**2c'**) was obtained as a major isomer in two steps from **2c** through the corresponding ketone (**5c**). Thus, oxidation of **2c** with a Dess-Martin oxidant followed by reduction with $NaBH_4$ in ethanol gave a mixture of *syn* : *anti* alcohols (**2c** and **2c'**) with a 1:6 ratio in 60% yield. Similarly, **2e'** was predominantly obtained with a 1:3 ratio in 61% yield. They were separable by HPLC.



5c ; R = Pr^i
5e ; R = C_8H_{17}

Scheme 5



1g ; R = Me, R' = Ph
1h ; R = Ph, R' = Me
1d ; R = Me, R' = Me

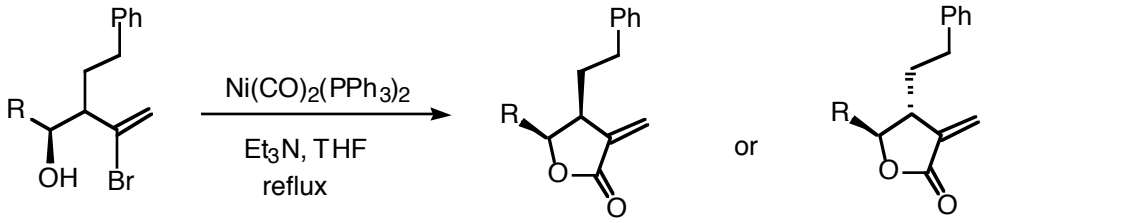
6a **6b**

Scheme 6

Although the reaction of 1,1-bis(silylmethyl)-1-alkenes (**1g**) or (**1h**) with aldehyde gave complex mixtures including protodesilylated compound, the reaction of a 10:1 mixture of **1g** and **1h** with benzaldehyde dimethyl acetal was promoted by BF_3 etherate in CH_2Cl_2 to give a mixture of **6a** and **6b** in 42% yield non-selectively. Characteristic chemoselectivity by trimethylsilylallylsilyl and (diemthyl)phenylsilyl-allylsilyl functionality could not be observed. Similarly, the reaction of a 1:10 mixture of **1g** and **1h** also afforded **6a** and **6b** in 60% yield with a 1:1 ratio. Under the same reaction conditions, **1d** gave **6a** along with inseparable protodesilylated product with a 6:5 ratio.

Synthesis of α-Methylene-γ-butyrolactone[8]

Finally, when **2a** was treated with $Ni(CO)_2(PPh_3)_2$ in the presence of triethylamine in THF, α-methylene-γ-butyrolactone (***cis*-3a**) was obtained in 71% yield.[9] The *cis* relationships of β,γ-substituents were determined by nOe experiments of ^1H NMR spectrometry. Between the two protons located at β,γ-positions, 8.8% enhancement was observed upon irradiation of each β,γ-proton. While, ***trans*-3a** was yielded from an *anti* isomer (**2a'**) in 71% yield. The relative structure was also determined by nOe experiments, in which enhancement was observed between γ-proton and methylene protons of the phenethyl group. Similarly, a *syn* isomer (**2c**) afforded ***cis*-3c** in 68% yield stereospecifically. Since this reaction sequence leading to β,γ-disubsituted α-methylene-γ-butyrolactone is extremely short and stereoselective, (*Z*)-β-bromoallylsilane will be a general synthetic unit for the efficient preparation of α-methylenelactones, particularly those possessing *anti*-cancer activity.



2a ; R = Ph (*syn*)
2a' ; R = Ph (*anti*)
2c ; R = Pr^i (*syn*)

***cis*-3a** ; R = Ph (*cis* only) ***trans*-3a** ; R = Ph (*trans* only)
***cis*-3c** ; R = Pr^i (*cis* only)

Scheme 7

In conclusion, (*Z*)-β-bromoallylsilanes were prepared from 1,1-dibromo-1-alkene stereoselectively by Kumada-Tamao-Corriu coupling. The Sakurai-Hosomi reaction with aldehyde followed by carbolactonization with $Ni(CO)_2(PPh_3)_2$ gave β,γ-disubstituted α-methylene-γ-butyrolactones in two steps in excellent yields. 1,1-Bis(silylmethyl)-1-alkenes were obtained by Pd-catalyzed cross-coupling reaction of either 1,1-dibromo-1-alkene or (*Z*)-β-bromoallylsilane with silylmethylmagnesium halide, of which reaction with dimethyl acetal gave functionalized allylsilane (**6**).

EXPERIMENTAL

All melting points were taken with Yanagimoto micro hot-stage apparatus and were uncorrected. ^1H NMR spectra were recorded on a JEOL JNM-AL-300 (300 MHz) spectrometer in $CDCl_3$ with tetramethylsilane

as an internal standard. MS spectra were obtained on JMS-GC mate, and JMS-SX 102A QQ instruments. IR spectra were recorded on JASCO FT/IR-410 instrument. All air- or moisture-sensitive reactions were carried out in flame-dried glassware under Ar or N_2 atmosphere. THF and ether were distilled freshly over sodium/benzophenone ketyl under nitrogen atmosphere, and CH_2Cl_2 was dried over P_2O_5, and they were distilled before the use. Thin layer chromatography (TLC) was performed with Merck $60F_{254}$ precoated silica gel plates. Column chromatography was carried out using Merck silica gel 60 (70-230 mesh) for gravity column.

Preparation of Bromoallylsilane (1a-1c). To a mixture of **4** (2.04 g, 6.9 mmol) and $NiCl_2$(dppp) (374 mg, 0.69 mmol) in ether (120 mL) was dropped ethereal solution of silylmagnesium chloride (1M solution, 13.8 mL) was added at rt. The mixture was stirred overnight. Then, the mixture was poured into sat. NH_4Cl and extracted with hexane. The organic extract was washed with water, dried over $MgSO_4$, and evaporated. The residual oil was purified by column chromatography on silica gel eluted with hexane to give **1a-c**. For the reaction of **1c**, THF was used instead of ether.

(*Z*)-2-Bromo-5-phenyl-1-trimethylsilyl-2-pentene (**1a**). *Rf* = 0.81 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.08 (9H, s), 2.09 (2H, d, *J* = 0.7 Hz), 2.45-2.52 (2H, m), 2.69-2.74 (2H, m), 5.43 (1H, t, *J* = 6.8 Hz), 7.18-7.35 (5H, m); ^{13}C NMR (75 MHz) δ -1.4 (3C), 32.8, 33.3, 34.9, 124.8, 125.3, 125.8, 128.3 (2C), 128.4 (2C), 141.6; MS (EI) *m/z* 296 (M^+); HRMS (EI) *m/z* Calcd for $C_{14}H_{21}BrSi$: 296.0596 (M^+). Found: 296.0592.

(*Z*)-2-Bromo-1-(dimethyl)phenylsilyl-5-phenyl-2-pentene (**1b**). *Rf* = 0.39 (1% ether in hexane); ^{1}H NMR (300 MHz) δ 0.40 (6H, s), 2.33 (2H, d, *J* = 1.1 Hz), 2.47-2.50 (2H, m), 2.64-2.68 (2H, m), 5.40 (1H, td, *J* = 7.0, 1.1 Hz), 7.19-7.42 (8H, m), 7.52-7.55 (2H, m); ^{13}C NMR (75 MHz) δ -2.9 (2C), 32.1, 33.3, 34.8, 124.5, 125.8, 125.8, 127.7 (2C), 128.3 (2C), 128.4 (2C), 129.1, 133.6 (2C), 138.0, 141.5; MS (EI) *m/z* 358 (M^+); HRMS (EI) *m/z* Calcd for $C_{19}H_{23}BrSi$: 358.0752 (M^+). Found: 358.0758.

(*Z*)-2-Bromo-1-(dimethyl)isopropoxysilyl-5-phenyl-2-pentene (**1c**). *Rf* = 0.58 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.18 (6H, s), 1.14 (6H, d, *J* = 6.1 Hz), 2.16 (2H, d, *J* = 0.9 Hz), 2.41-2.51 (2H, m), 2.66-2.73 (2H, m), 3.94-4.08 (1H, m), 5.51 (1H, tt, *J* = 6.8, 0.9 Hz), 7.15-7.22 (3H, m), 7.24-7.31 (2H, m); ^{13}C NMR (75 MHz) δ -1.2 (2C), 25.7 (2C), 33.0, 33.4, 34.7, 65.2, 124.0, 125.9, 125.9, 128.3 (2C), 128.4 (2C), 141.5; MS (EI) *m/z* 340 (M^+); HRMS (EI) *m/z* Calcd for $C_{16}H_{25}OBrSi$: 340.0858 (M^+). Found: 340.0856.

Preparation of 1d, 1e, and 1f. To a mixture of **4** (2.8 g, 9.65 mmol) and $Pd(OAc)_2$ (216 mg, 0.97 mmol) in THF (90 mL) was added PPh_3 (498 mg, 1.9 mmol), and ethereal or THF solution of silylmagnesium chloride (1M solution, 20 mL) was added at rt. The mixture was refluxed for 2.5 h. After cooling, the mixture was poured into sat. NH_4Cl and extracted with hexane. The organic extract was washed with water, dried over $MgSO_4$, and evaporated. The residual oil was purified by column chromatography on silica gel to give 1,1-bis(silylmethyl)-1-alkenes.

1,1-Bis[(trimethylsilyl)methyl]-4-phenyl-1-pentene (**1d**). Trimethylsilylmethylmagnesium chloride was used. Eluent for column chromatography; hexane. Yield 93%. *Rf* = 0.83 (3% *t*-BuOMe in hexane); ^{1}H

NMR (300 MHz) δ 0.04 (9H, s), 0.08 (9H, s), 1.44 (2H, s), 1.51 (2H, s), 2.25-2.33 (2H, m), 2.65-2.70 (2H, m), 4.90 (1H, t, J = 7.0 Hz), 7.20-7.36 (5H, m); ^{13}C NMR (75 MHz) δ -1.2 (3C), -0.6 (3C), 23.8, 29.4, 30.7, 36.6, 118.8, 125.6, 128.2 (2C), 128.4 (2C), 134.8, 142.7; MS (EI) *m/z* 304 (M^+); HRMS (EI) *m/z* Calcd for $C_{18}H_{32}Si_2$: 304.2043 (M^+). Found: 304.2040.

1,1-Bis{[(dimethyl)phenylsilyl]methyl}-4-phenyl-1-pentene(1e). [(Dimethyl)phenylsilyl]-methylmagnesium chloride was used. Eluent for column chromatography; 1% *t*-BuOMe in hexane. Yield 73%. *Rf* = 0.58 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.25 (6H, s), 0.26 (6H, s), 1.58 (2H, s), 1.62 (2H, s), 2.13-2.18 (2H, m), 2.52-2.58 (2H, m), 4.89 (1H, d, J = 6.8 Hz), 7.14-7.50 (15H, m); ^{13}C NMR (75 MHz) δ -2.8 (2C), -2.4 (2C), 23.0, 28.4, 30.5, 36.3, 120.4, 125.6, 127.6 (2C), 127.7 (2C), 128.2 (2C), 128.4 (2C), 128.8, 128.9, 133.5 (2C), 133.5, 133.6 (2C), 139.5, 139.5, 142.5; MS (EI) *m/z* 428 (M^+); HRMS (EI) *m/z* Calcd for $C_{28}H_{36}Si_2$: 428.2356 (M^+). Found: 428.2344.

1,1-Bis{[(dimethyl)isopropoxysilyl]methyl}-4-phenyl-1-pentene (1f). [(Dimethyl)isopropoxysilyl]methylmagnesium chloride in THF solution was used. Eluent for column chromatography; 3% *t*-BuOMe in hexane. Yield 67%. *Rf* = 0.21 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.11 (6H s), 0.16 (6H, s), 1.16 (6H, d, J = 1.9 Hz), 1.18 (6H, d, J = 1.8 Hz), 1.58 (2H, s), 1.64 (2H, s), 2.25-2.33 (2H, m), 2.63-2.68 (2H, m), 3.97-4.07 (2H, m), 4.96 (1H, t, J = 6.8 Hz), 7.16-7.31 (5H, m); ^{13}C NMR (75 MHz) δ -1.3 (2C), -0.8 (2C), 24.0, 25.8 (2C), 25.8 (2C), 29.4, 30.6, 36.3, 64.8, 64.9, 120.2, 125.6, 128.2 (2C), 128.3 (2C), 132.8, 142.5; MS (EI) *m/z* 392 (M^+); HRMS (EI) *m/z* Calcd for $C_{22}H_{40}O_2Si_2$: 392.2567 (M^+). Found: 392.2561.

Preparation of 1g, 1h, and 1i. To a mixture of **1a** and/or **1b** (0.67 mmol) and $Pd(OAc)_2$ (15 mg, 0.067 mmol) in THF (6.7 mL) was added PPh_3 (38 mg, 0.134 mmol) and ethereal or THF solution of silylmagnesium chloride (1M solution, 2-4 mL) was added at rt. The mixture was stirred at rt for 7 h and refluxed for an additional half hour. After cooling, the mixture was poured into sat. NH_4Cl and extracted with hexane. The organic extract was washed with water, dried over $MgSO_4$, and evaporated. The residual oil was purified by column chromatography on silica gel eluted with hexane to give **1g-1i**.

(*Z*)-1-(Dimethyl)phenylsilyl-5-phenyl-2-(trimethylsilyl)methyl-2-pentene (1g). [(Dimethyl)phenylsilyl]methylmagnesium chloride in ether solution was used. After GPC chromatography purification, a mixture of **1g** and **1h** was obtained in 71% yield as a 10:1 mixture. **1g;** *Rf* = 0.55 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ -0.05 (9H, s), 0.31 (6H, s), 1.32 (2H, s), 1.69 (2H, s), 2.11-2.19 (2H, m), 2.56 (2H, dd, J = 8.1, 7.7 Hz), 4.86 (1H, dd, J = 7.0, 6.6 Hz), 7.13-7.38 (8H, m), 7.42-7.56 (2H, m); ^{13}C NMR (75 MHz) δ -2.3 (2C), -1.2 (3C), 23.1, 29.3, 30.6, 36.5, 119.6, 125.5, 127.7 (2C), 128.2 (2C), 128.4 (2C), 128.9, 133.5 (2C), 134.1, 139.6, 142.5; MS (EI) *m/z* 366 (M^+); HRMS (EI) *m/z* Calcd for $C_{23}H_{34}Si_2$: 366.2199 (M^+). Found: 366.2198.

(*E*)-1-(Dimethyl)phenylsilyl-5-phenyl-2-(trimethylsilyl)methyl-2-pentene (1h). Trimethylsilylmethylmagnesium chloride in ether solution was used. After GPC chromatography purification, a mixture of **1g** and **1h** was obtained in 77% yield as a 1:10 mixture of *E*:*Z* isomers. **1h;** *Rf* = 0.55 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.02 (9H, s), 0.29 (6H, s), 1.40 (2H, s), 1.66 (2H, s), 2.21-2.28

(2H, m), 2.61 (2H, dd, J = 8.4, 7.4 Hz), 4.88 (1H, t, J = 7.0 Hz), 7.18-7.40 (8H, m), 7.48-7.53 (2H, m); ^{13}C NMR (75 MHz) δ -2.8 (2C), -0.7 (3C), 23.7, 28.5, 30.7, 36.5, 119.7, 125.6, 127.6 (2C), 128.2 (2C), 128.4 (2C), 128.8, 133.6 (2C), 134.1, 139.6, 142.6; MS (EI) m/z 366 (M^+); HRMS (EI) m/z Calcd for $C_{23}H_{34}Si_2$: 366.2199 (M^+). Found: 366.2203.

(*Z*)-1-(Dimethyl)isopropoxysilyl-2-[(dimethyl)phenylsilyl]methyl-5-phenyl-2-pentene (1i). [(Dimethyl)isopropoxysilyl]methylmagnesium chloride in THF solution was used. After GPC chromatography purification, a mixture of **1i** and its *E*-isomer was obtained in 68% yield as a 10:1 mixture. Only the data for the major isomer was described. **1i;** Rf = 0.36 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.14 (6H, s), 0.31 (6H, s), 1.15 (6H, d, J = 6.4 Hz), 1.49 (2H, s), 1.74 (2H, s), 2.25-2.32 (2H, m), 2.61-2.66 (2H, m), 3.94-4.00 (1H, m), 4.91 (1H, dd, J = 7.0, 6.6 Hz), 7.19-7.39 (8H, m), 7.51-7.56 (2H, m); ^{13}C NMR (75 MHz) δ -2.8 (2C), -0.7 (2C), 24.0, 25.8 (2C), 28.4, 30.6, 36.4, 64.9, 120.3, 125.6, 127.6 (2C), 128.2 (2C), 128.4 (2C), 128.8, 133.1, 133.6 (2C), 139.6, 142.5; MS (EI) m/z 410 (M^+); HRMS (EI) m/z Calcd for $C_{25}H_{38}OSi_2$: 410.2461 (M^+). Found: 410.2456.

A Typical Reaction of Bromoallylsilane with Aldehyde and Acetal

To a mixture of bromoallylsilane (0.34 mmol) in CH_2Cl_2 (3.4 mL) and aldehyde or acetal (0.4 mmol) was added $TiCl_4$ (1M solution in CH_2Cl_2, 0.37 mL) at –78 °C, and the mixture was stirred for 5 min. Then sat. $NaHCO_3$ was added to the mixture and extracted with EtOAc. Organic phase was washed with brine and dried over $MgSO_4$. Solvent was removed and the residue was purified by column chromatography on silica gel to give the product. As an eluent for chromatography, 20% EtOAc in hexane was used for **2a** and **2a'**, **2c** and **2c'**, and **2e** and **2e'**, and 5% EtOAc in hexane for **2b** and **2b'**, and **2d** and **2d'**.

3-Bromo-2-phenethyl-1-phenyl-3-buten-1-ol (2a and **2a').** Yield 79% (*syn* : *anti* = 10 : 1) as an colorless oil. The diasteteoisomers were separated by HPLC. **2a;** Rf = 0.46 (20% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 1.84-1.99 (2H, m), 2.18-2.31 (1H, m), 2.39-2.49 (1H, m), 2.55 (1H, ddd, J = 11.0, 8.1, 3.3 Hz), 3.70 (1H, ddd, J = 14.3, 10.3, 4.4 Hz), 4.72 (1H, dd, J = 8.1, 2.9 Hz), 5.35-5.38 (2H, m), 7.14-7.37 (10H, m); ^{13}C NMR (75 MHz) δ 30.3, 33.1, 56.9, 76.0, 120.1, 125.8, 126.5 (2C), 127.8, 128.2 (2C), 128.3 (2C), 128.4 (2C), 135.0, 141.8, 142.6; IR (neat) 3398 cm^{-1}; MS (EI) m/z 330 (M^+); HRMS (EI) m/z Calcd for $C_{18}H_{19}OBr$: 330.0619 (M^+). Found: 330.0611. **2a';** Rf = 0.42 (20% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 1.19-1.31 (1H, m), 1.60-1.74 (1H, m), 2.09 (1H, br s), 2.28 (1H, ddd, J = 14.3, 9.5, 7.3 Hz), 2.48 (1H, ddd, J = 11.0, 9.2, 3.3 Hz), 2.61 (1H, ddd, J = 14.3, 10.3, 4.8 Hz), 4.56 (1H, d, J = 9.2 Hz), 5.77 (1H, d, J = 1.5 Hz), 5.86 (1H, d, J = 1.5 Hz), 6.98 (2H, d, J = 7.0 Hz), 7.13-7.38 (8H, m); ^{13}C NMR (75 MHz) δ 30.3, 32.8, 56.8, 75.5, 121.5, 125.8, 127.3 (2C), 128.3, 128.3 (2C), 128.5 (2C), 128.6 (2C), 136.0, 141.2, 141.3; IR (neat) 3437 cm^{-1}; MS (FAB) m/z 353 (M^++Na); HRMS (FAB) m/z Calcd for $C_{18}H_{19}OBrNa$: 353.0517 (M^++Na). Found: 353.0516.

3-Bromo-1-methoxy-2-phenethyl-1-phenyl-3-butene (2b and **2b').** Yield 74% (*syn* : *anti* = 5.3 : 1) as an colorless oil. **2b;** Rf = 0.46 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 1.79-1.94 (1H, m), 2.27-2.55 (3H, m), 2.61-2.73 (1H, m), 3.15 (3H, s), 4.06 (1H, d, J = 9.2 Hz), 5.25 (2H, s), 7.15-7.34 (10H, m); ^{13}C NMR (75 MHz) δ 31.2, 33.3, 56.8, 57.0, 85.4, 120.3, 125.7, 127.4 (2C), 127.8, 128.0 (2C), 128.3 (2C),

128.5 (2C), 135.0, 140.1, 142.1; MS (CI) *m/z* 313 (M^+-OMe); HRMS (CI) *m/z* Calcd for $C_{18}H_{18}Br$: 313.0591 (M^+-OMe). Found: 313.0599. **2b';** *Rf* = 0.40 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 1.14-1.28 (1H, m), 1.52-1.68 (1H, m), 2.25 (1H, ddd, *J* = 13.9, 9.9, 7.3 Hz), 2.48 (1H, ddd, *J* = 11.0, 9.2, 3.7 Hz), 2.57 (1H, ddd, *J* = 13.9, 9.9, 4.4 Hz), 3.15 (3H, s), 4.05 (1H, d, *J* = 9.2 Hz), 5.65 (1H, d, *J* = 1.5 Hz), 5.73 (1H, d, *J* = 1.5 Hz), 6.96 (2H, d, *J* = 7.3 Hz), 7.17-7.39 (8H, m) ; ^{13}C NMR (75 MHz) δ 30.1, 32.8, 55.5, 56.9, 85.0, 119.6, 125.8, 128.0 (2C), 128.1 (2C), 128.2, 128.4 (2C), 128.4 (2C), 136.5, 139.4, 141.4; MS (CI) *m/z* 313 (M^+-OMe); HRMS (CI) *m/z* Calcd for $C_{18}H_{18}Br$: 313.0591 (M^+-OMe). Found: 313.0586.

5-Bromo-2-methyl-4-phenyl-5-hexen-3-ol (**2c** and **2c'**). Yield 78% (*syn* : *anti* = >10 : 1) as an colorless oil. **2c;** *Rf* = 0.26 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 0.83 (3H, d, *J* = 7.0 Hz), 0.92 (3H, d, *J* = 7.0 Hz), 1.43 (1H, br s), 2.70-2.91 (2H, m), 2.10 (1H, dddd, *J* = 13.6, 10.3, 7.0, 3.3 Hz), 2.31 (1H, ddd, *J* = 11.4, 8.1, 3.3 Hz), 2.43 (1H, ddd, *J* = 13.6, 9.9, 7.0 Hz), 2.65-2.78 (1H, m), 3.41-3.50 (1H, m), 5.58 (1H, d, *J* = 1.5 Hz), 5.70 (1H, d, *J* = 1.5 Hz), 7.14-7.32 (5H, m); ^{13}C NMR (75 MHz) δ 14.4, 20.3, 29.9, 30.7, 33.2, 52.7, 77.4, 119.2, 125.8, 128.3 (2C), 128.5 (2C), 136.1, 142.0; IR (neat) 3436 cm^{-1}; MS (FAB) *m/z* 319 (M^++Na); HRMS (FAB) *m/z* Calcd for $C_{15}H_{21}OBrNa$: 319.0673 (M^++Na). Found: 319.0676. Spectroscopic data for **2c'** is described in the next experimental section.

5-Bromo-2-methyl-3-ethoxy-4-phenethyl-5-hexene (**2d** and **2d'**). Yield 97% (*syn* : *anti* = 8.7 : 1) as an colorless oil. **2d;** *Rf* = 0.39 (3% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.78 (3H, d, *J* = 6.6 Hz), 0.89 (3H, d, *J* = 6.9 Hz), 1.06 (3H, t, *J* = 7.0 Hz), 1.61-1.83 (2H, m), 1.91-2.03 (1H, m), 2.26-2.39 (2H, m), 2.59 (1H, ddd, *J* = 13.6, 11.0, 4.4 Hz), 3.03 (1H, dd, *J* = 9.8, 2.6 Hz), 3.51 (2H, q, *J* = 7.0 Hz), 5.47 (1H, d, *J* = 1.5 Hz), 5.62 (1H, d, *J* = 1.5 Hz), 7.08-7.24 (5H, m); ^{13}C NMR (75 MHz) δ 15.0, 15.7, 20.9, 30.5, 31.0, 33.5, 53.1, 69.7, 85.7, 119.0, 125.7, 128.3 (2C), 128.5 (2C), 136.8, 142.3; MS (CI) *m/z* 325 (M^++H); HRMS (CI) *m/z* Calcd for $C_{17}H_{26}OBr$: 325.1167 (M^++H). Found: 325.1168.

2-Bromo-3-phenethyl-1-dodecen-4-ol (**2e** and **2e'**). Yield 80% (*syn* : *anti* = >10 : 1) as an colorless oil. **2e;** *syn*; *Rf* = 0.46 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 0.88 (3H, t, *J* = 6.6 Hz), 1.19-1.60 (15H, m), 1.73-1.88 (1H, m), 2.01-2.22 (2H, m), 2.43 (1H, ddd, *J* = 13.9, 9.9, 7.3 Hz), 2.72 (1H, ddd, *J* = 13.9, 9.9, 4.8 Hz), 3.59 (1H, brs), 5.59 (1H, d, *J* = 1.1 Hz), 5.69 (1H, d, *J* = 1.1 Hz), 7.14-7.31 (5H, m); ^{13}C NMR (75 MHz) δ 14.1, 22.7, 25.5, 29.3, 29.5, 29.5, 30.4, 31.9, 33.2, 34.9, 55.4, 73.2, 119.5, 125.8, 128.3 (2C), 128.5 (2C), 135.9, 141.9; IR (neat) 3389 cm^{-1}; MS (FAB) *m/z* 389 (M^++Na); HRMS (FAB) *m/z* Calcd for $C_{20}H_{31}OBrNa$: 389.1456 (M^++Na). Found: 389.1454. Spectroscopic data for **2e'** is described in the next experimental section.

Preparation of 2c' and 2e'

A mixture of alcohol (**2c** or **2e**, 0.2 mmol) and Dess-Martin periodinane (214 mg, 0.3 mmol) was stirred in CH_2Cl_2 (2 ml) for 1 h at rt. An excess of oxidant was decomposed by the addition of sat. $Na_2S_2O_3$. The reaction mixture was extracted with ether and the extract was washed with sat. $NaHCO_3$, water and brine. The crude product was dissolved in ethanol (2 mL) and an excess of $NaBH_4$ was added at rt. The mixture

was diluted with water, and extracted with EtOAc. The extract was dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexane to give alcohol.

5-Bromo-2-methyl-4-phenyl-5-hxene-3-ol (**2c'**). *Rf* = 0.26 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 0.81 (3H, d, *J* = 7.0 Hz), 1.00 (3H, d, *J* = 7.0 Hz), 1.53 (1H, br s), 1.62-1.89 (3H, m), 2.23-2.34 (1H, m), 2.35-2.50 (1H, m), 2.71 (1H, dd, *J* = 13.9, 9.1, 5.5 Hz), 3.42 (1H, ddd, *J* = 8.5, 3.3 Hz), 5.70 (1H, d, *J* = 1.1 Hz), 5.76 (1H, d, *J* = 1.1 Hz), 7.15-7.33 (5H, m); ^{13}C NMR (75 MHz) δ 14.7, 20.4, 29.1, 30.6, 33.1, 52.9, 75.7, 121.0, 125.9, 128.4 (2C), 128.4 (2C), 136.6, 141.6; IR (neat) 3477 cm^{-1}; MS (FAB) *m/z* 297 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{15}H_{22}OBr$: 297.0854 (M^++H). Found: 297.0861.

2-Bromo-3-phenethyl-1-dodecen-4-ol (**2e'**). *Rf* = 0.46 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 0.88 (3H, t, *J* = 7.0 Hz), 1.26-1.85 (17H, m), 2.21 (1H, ddd, *J* = 12.5, 8.1, 4.8 Hz), 2.37-2.51 (1H, m), 2.71 (1H, ddd, *J* = 14.3, 9.6, 5.5 Hz), 3.53-3.64 (1H, m), 5.69 (1H, d, *J* = 1.5 Hz), 5.75 (1H, d, *J* = 1.5 Hz), 7.15-7.30 (5H, m); ^{13}C NMR (75 MHz) δ 14.1, 22.7, 25.4, 29.2, 29.5, 29.7, 30.9, 31.9, 33.2, 33.8, 55.4, 72.0, 121.0, 125.9, 128.4 (2C), 128.4 (2C), 135.9, 141.7; IR (neat) 3435 cm^{-1}; MS (FAB) *m/z* 389 (M^++Na); HRMS (FAB) *m/z* Calcd for $C_{20}H_{31}OBrNa$: 389.1456 (M^++Na). Found: 389.1448.

Reaction of 1,1-Bis(silylmethyl)-1-alkene with Acetal. To a mixture of **1g** or **1h** (1 mmol) and benzaldehyde dimethyl acetal (1 mmol) in CH_2Cl_2 (10 mL) was added dropwise BF_3 etherate (1M CH_2Cl_2 solution, 10 mL) at –78 °C slowly, and the mixture was stirred for 5 min at the same temperature. The reaction mixture was quenched with sat. $NaHCO_3$, and extracted with EtOAc. The organic extract was washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexane to give **6a** and **6b**.

Compound (6a) *Rf* = 0.71 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ -0.02 (9H, s), 1.17 (1H, d, *J* = 14.7 Hz), 1.35 (1H, d, *J* = 14.7 Hz), 1.73-1.90 (1H, m), 2.06-2.21 (1H, m), 2.30 (1H, ddd, *J* = 10.3, 7.4, 3.7 Hz), 2.49 (1H, ddd, *J* = 13.6, 11.7, 5.5 Hz), 2.69 (1H, ddd, *J* = 13.6, 11.7, 4.8 Hz), 3.20 (3H, s), 4.06 (1H, d, *J* = 7.4 Hz), 4.72 (1H, s), 4.73 (1H, s), 7.13-7.36 (10H, m); ^{13}C NMR (75 MHz) δ -0.9 (3C), 26.2, 31.5, 34.1, 54.2, 57.0, 87.1, 110.5, 125.5, 127.2, 127.6 (2C), 127.9 (2C), 128.2 (2C), 128.4 (2C), 141.1, 143.1, 146.7; MS (EI) *m/z* 352 (M^+); HRMS (EI) *m/z* Calcd for $C_{23}H_{32}OSi$: 352.222 (M^+). Found: 352.2218.

Compound (6b) *Rf* = 0.57 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 0.22 (3H, s), 0.23 (3H, s), 1.43 (1H, d, *J* = 15.0 Hz), 1.57 (1H, d, *J* = 15.0 Hz), 1.65-1.82 (1H, m), 1.94-2.11 (1H, m), 2.16-2.38 (2H, m), 2.54 (1H, ddd, *J* = 12.3, 12.1, 4.8 Hz), 3.15 (3H, s), 4.00 (1H, d, *J* = 7.0 Hz), 4.69 (1H, d, *J* = 1.1 Hz), 4.72 (1H, d, *J* = 1.1 Hz), 7.05-7.46 (15H, m); ^{13}C NMR (75 MHz) δ -2.5, -2.4, 25.1, 31.3, 33.9, 54.0, 57.0, 87.0, 111.5, 125.5, 127.2, 127.5 (2C), 127.7 (2C), 127.9 (2C), 128.2 (2C), 128.3 (2C), 128.9 (2C), 133.6, 139.2, 141.0, 143.0, 146.1; MS (EI) *m/z* 414 (M^+); HRMS (EI) *m/z* Calcd for $C_{28}H_{34}OSi$: 414.2379 (M^+). Found: 414.2372.

Carbolactonization Reaction

A mixture of homoallylic alcohol (0.3 mmol), $Ni(CO)_2(PPh_3)_2$ (290 mg, 0.46 mmol) and triethylamine (0.08 ml, 0.6 mmol) in THF (3 mL) was refluxed for 30 min. After cooling, 10% HCl was added to the reaction mixture, and the mixture was extracted with ether. The ethereal extract was washed with brine and dried over $MgSO_4$. Solvent was evaporated and the residue was purified by silica gel column chromatography eluted with 20% EtOAc in hexane to give lactone.

3-Methylene-4-phenethyl-5-phenyldihydrofuran-2-one (***cis*-3a**). Yield 71% as an colorless crystals, mp 52-53 ℃ (hexane); *Rf* = 0.16 (6% *t*-BuOMe in hexane); ^{1}H NMR (300 MHz) δ 1.31-1.44 (1H, m), 1.52-1.65 (1H, m), 2.38-2.58 (2H, m), 3.29 (1H, qdd, *J* = 7.4, 2.6, 2.4 Hz), 5.62 (1H, d, *J* = 7.7 Hz), 5.64 (1H, d, *J* = 2.4 Hz), 6.37 (1H, d, *J* = 2.4 Hz), 6.92 (2H, d, *J* = 7.4 Hz), 7.11-7.42 (8H, m); ^{13}C NMR (75 MHz) δ 30.8, 32.4, 43.7, 82.0, 122.1, 126.1, 126.4 (2C), 128.2 (2C), 128.5 (2C), 128.6 (3C), 135.8, 139.0, 140.7, 170.4; IR (neat) 1766 cm^{-1}; MS (EI) *m/z* 278 (M^+); HRMS (EI) *m/z* Calcd for $C_{19}H_{18}O_2$: 278.1307 (M^+). Found: 278.1311; *Anal*. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52: Found: C, 82.03; H, 6.72.

3-Methylene-4-phenethyl-5-phenyldihydrofuran-2-one (***trans*-3a**). Yield 71% as an colorless crystals, mp 93-94 ℃ (hexane); *Rf* = 0.45 (20% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 2.02-2.12 (2H, m), 2.60-2.78 (2H, m), 3.00-3.09 (1H, m), 5.19 (1H, d, *J* = 5.2 Hz), 5.66 (1H, d, *J* = 2.0 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 7.06 (2H, d, *J* = 8.4 Hz), 7.13-7.41 (8H, m); ^{13}C NMR (75 MHz) δ 32.5, 35.3, 47.1, 84.2, 122.6, 126.0 (2C), 126.3, 128.2 (2C), 128.6 (2C), 128.8, 128.9 (2C), 138.7, 139.3, 140.6, 170.1; IR (neat) 1766 cm^{-1}; MS (EI) *m/z* 278 (M^+); HRMS (EI) *m/z* Calcd for $C_{19}H_{18}O_2$: 278.1307 (M^+). Found: 278.1311; *Anal*. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.72: Found: C, 81.85; H, 6.75.

5-Isopropyl-3-methylene-4-phenyldihydrofuran-2-one (***cis*-3c**). Yield 68% as an colorless crystals, mp 48-49 ℃ (hexane); *Rf* = 0.14 (10% EtOAc in hexane); ^{1}H NMR (300 MHz) δ 0.92 (3H, d, *J* =7.0 Hz), 1.02 (3H, d, *J* = 6.6 Hz), 1.61-1.75 (1H, m), 1.88-2.05 (2H, m), 2.55 (1H, ddd, *J* = 13.9, 9.6, 6.6 Hz), 2.77 (1H, ddd, *J* = 13.9, 9.9, 5.5 Hz), 2.90-2.99 (1H, m), 4.03 (1H, dd, *J* = 8.8, 5.9 Hz), 5.58 (1H, d, *J* = 1.6 Hz), 6.24 (1H, d, *J* = 1.6 Hz), 7.15-7.33 (5H, m); ^{13}C NMR (75 MHz) δ 18.5, 18.9, 28.1, 28.3, 32.3, 42.1, 86.1, 121.0, 126.2, 128.3 (2C), 128.6 (2C), 140.1, 140.8, 170.6; IR (neat) 1766 cm^{-1}; MS (EI) *m/z* 244 (M^+); HRMS (EI) *m/z* Calcd for $C_{16}H_{20}O_2$: 244.1463 (M^+). Found: 244.1468; *Anal*. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25: Found: C, 78.56; H, 8.42.

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