REACTIONS OF 1,1-BIS(SILYLMETHYL)-1-ALKENE WITH *N*-HALOSUCCINIMIDE AND OZONE

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Abstract — Electrophilic reactions of 3-phenyl-1,1-bis(trimethylsilymethyl)-1-propene (**1**) and 1,1-bis[dimethyl(phenyl)silylmethyl]-3-phenyl-1-propene (**4**) are described. Protodesilylation of **1** with PPTS gave 2-substituted allylsilane (**2**) in excellent yield. Halogenation of **4** with *N*-halosuccimide gave a mixture of 3-halo-5-phenyl-2-silylmethyl-1-pentene (**5**) and 3-halo-5-phenyl-1,2-bis(silylmethyl)-1-pentene (**6**). The reaction of **1** and **4** with ozone gave no carbonyl compounds but gave 3-hydoxy-5-phenyl-2-silylmethyl-1-pentene (**7**).

INTRODUCTION

Allylsilane is an important and useful functional unit in organic synthesis. Various types of allylsilanes have been prepared to date.[1] Recently, we have reported the synthesis of β-bromoallylsilane and 1,1-bis(trialkylsilylmethyl)-1-alkene and their reactions with aldehydes as shown in Scheme 1.[2] Since the cation-stabilizing effect by the β-silyl group is doubly enhanced in the case of 1,1-bis(trialkylsilylmethyl)-1-alkene, the reactivity of this allylsilane is greater than that of a simple allylsilane. In fact, 1,1-bis(trimethylsilylmethyl)-1-alkene can transform to exomethylene-type allylsilane effectively by protodesilylation under weak acidic conditions.[3] This unique reactivity of doubly activated allysilane led us to examine electrophilic reactions of 1,1-bis(silylmethyl)-1-alkene with halogenation and oxidation reagents.[4]
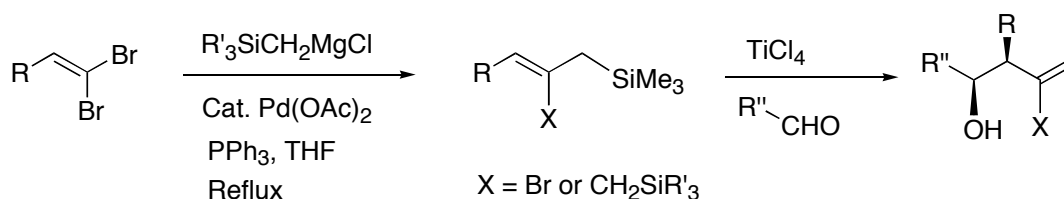
Scheme 1

Protodesilylation

The reaction of allylsilane with electrophiles is well known and useful in organic synthesis. When the electrophile is protonic acid, the reaction is a protodesilylation. 1,1-Bis(silylmethyl)-1-alkene (X = CH$_2$SiMe$_3$, in Scheme 1) is a highly electrophilic allylsilane which is activated by two trimethylsilyl groups. 3-Phenyl-1,1-bis(trimethylsilylmethyl)-1-propene (**1**) can be obtained by the double cross-coupling reaction of 1,1-dibromo-3-phenyl-1-propene with trimethylsilylmethyl Grignard reagent in the presence of a Pd catalyst. Since this allylsilane (**1**) gradually suffered protodesilylation on silica gel as shown in Scheme 2, quick elution with hexane during the purification process on column chromatography is essentially required to prevent its prodesilylation on silica gel. Nonetheless, compound (**1**) was contaminated with a small portion of the protodesilylated product (**2**). The transformation of **1** to **2** by acid is also a delicate reaction, and the use of stronger acid gave a mixture of **2** with over-protodesilylated product (**3**). Mild protodesilylation of **1** was achieved successfully with PPTS in a mixture of THF and acetonitrile for 2 days at room temperature to give **2** in quantitative yield, though it contained ~5% of further protodesilylated product (**3**). On the other hand, the reaction with PPTS in acetonitrile, CH$_2$Cl$_2$ or other protic solvents gave a mixture of **2** and **3**. Stronger acids such as in HCl or acetic acid eventually afforded **3**.
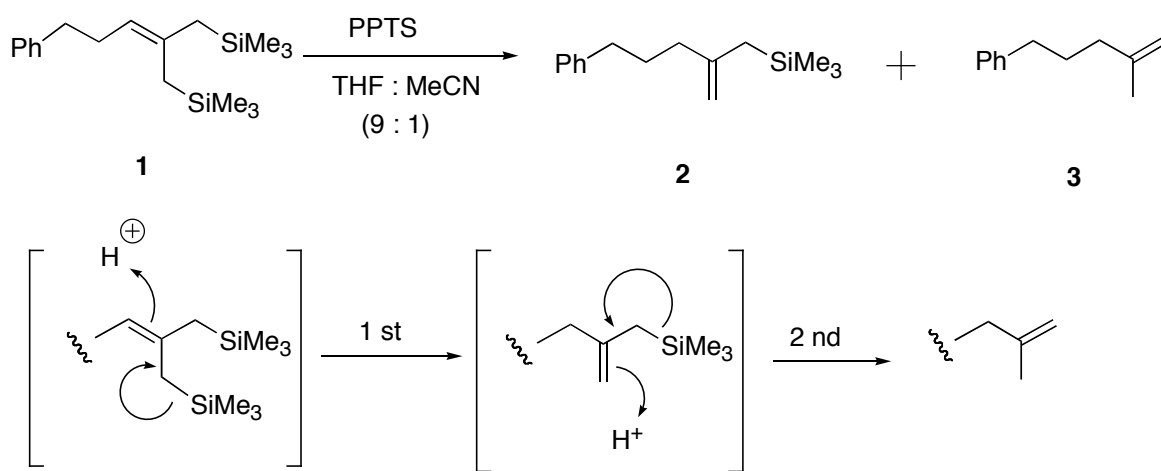

Scheme 2. Formation and Protodesilylation of 1,1-Bis(trimethylsilylmethyl)-1-alkene

Reaction with *N*-Halosuccinimide

The electrophilic reactivity of doubly activated bis(trialkylsilyl)alkene was found to be very high in protodesilylation reaction. However, the reaction of **1** with *N*-bromosuccinimide (NBS) gave complex mixtures even when the reaction was conducted at a low temperature. When the trimethylsilyl group was replaced with dimethyl(phenyl)silyl group, bromination of 1,1-bis[dimethyl(phenyl)silylmethyl]-3-phenyl-1-propene (**4**) with NBS took place at -78 °C in CH$_2$Cl$_2$ to give brominated allylsilane (**5a**) in 34% yield along with the product (**6a**) in 21% yield as a single (*Z*)-isomer.[5] On the other hand, the reaction of **4** with NBS proceeded not at -78 °C but at room temperature for 2 h to give **5b**, **6b**(*Z*) and

6b(*E*) in 13%, 10% and 10% yields, respectively.[5] The structure of **6a** was confirmed to be (*Z*)-configuration by a NOESY experiment. Thus, the olefinic proton that appeared at 5.79 ppm has a clear correlation with –CH- proton that appeared at 4.03 ppm but no correlation with diastereomeric –CH$_2$-Si protons that appeared at 2.22 and 1.93 ppm. Similar relations were observed for compound [**6b**(*Z*)], which was a polar isomer and identified to be (*Z*)-configuration. In the case of a less-polar isomer [**6b**(*E*)], when the olefinic proton that appeared at 5.27 ppm was irradiated, nOe was observed for the -CH$_2$-Si protons that appeared at 1.96 and 1.94 ppm but not for the CH proton at 4.40 ppm.

The reaction mechanism can be considered to be following. Initially, halogenation of alkene occurs at the γ-position to generate a cation which is stabilized by the two β–silyl groups. Elimination of the dimethyl(phenyl)silyl group leads to the formation of allylsilane (**5**), while that of the α-hydrogen leads to the formation of vinylsilane (**6**).[6] It is interesting that deprotonation at -78 °C gives (*Z*)-alkene stereoselectively, while that at room temperature gives a mixture. Although the chemical yields of products are not so satisfactory, product (**5**) possesses a 3-halo-2-silylmethylalkenyl unit, which has been used as a valuable building block for organic syntheses.[7]
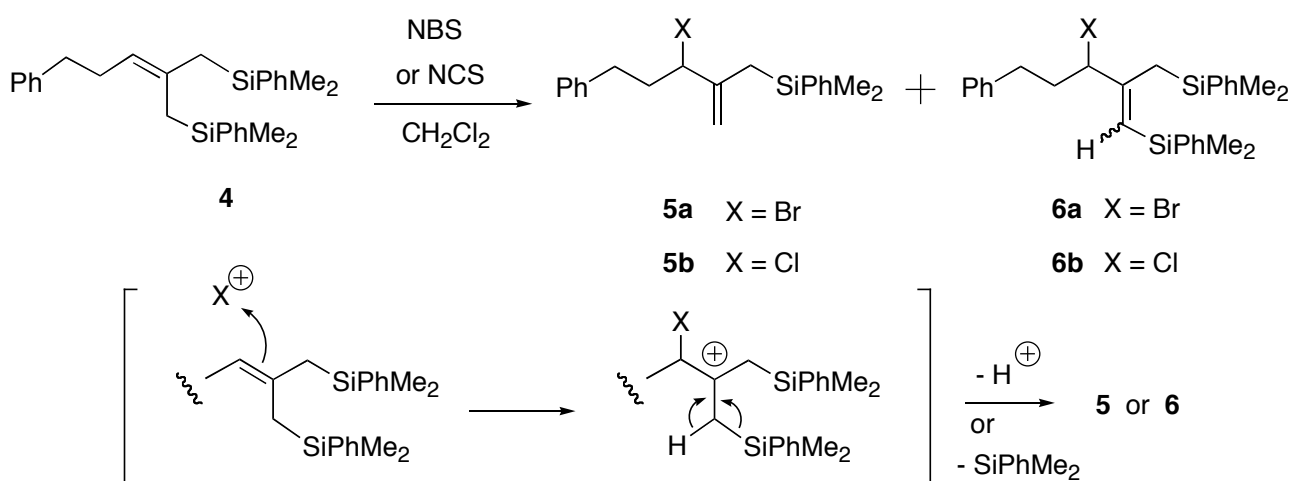
Scheme 3. Halogenation of 1,1-Bis(trialkylsilylmethy)l-1-alkene

Reaction with ozone

Oxidations of **1** or **4** with mCPBA gave complex mixtures. On the other hand, oxidation of **4** with ozone provided allylic alcohol (**7a**) in 35-45% yields without the formation of normal ozonolysis products, that is, 3-phenylpropanal and 1,3-bis[dimethyl(phenyl)silyl]-2-propanone. The structure of **7a** was confirmed by spectroscopic analysis and it was also confirmed to lead to its acetate (**8**). Compound (**1**) was also oxidized with ozone to give **7b** in 36% yield. They are unexpected products by the unusual oxidation reaction. Since the compound (**7**) also can reacted with ozone, the chemical yield of **7** could not exceed 45% at least by our hand. In fact, depending on the reaction time, over-oxidation gave complex mixtures.
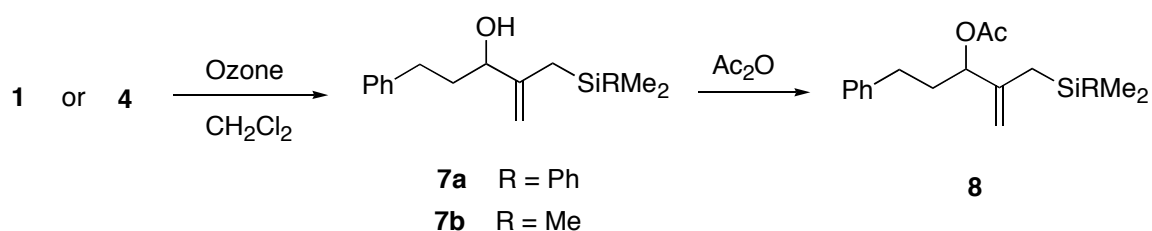
Scheme 4. Ozonization of 1,1-Bis(trialkylsilylmethyl)-1-alkene

The plausible mechanism of this unusual oxidation reaction is illustrated in Figure 1. Ozonide (**I**) is formed by the reaction of allylsilane with ozone as usual. Before the usual fragmentation takes place to lead to the formation of ozonide (**II**), desilylation gives alkene to form peroxy silyl ether (**IV**). Reduction of **IV** with dimethyl sulfide eventually affords **7a**. Alternatively, the activated allylsilane having a high HOMO level can react with ozone to form a C-O bond because of its high electrophilicity associated with the potent cation stabilizing effect of β-silyl groups to generate cation (**III**). An immediate elimination of the silyl group results in the formation of the peroxy silyl ether (**IV**), which is reduced by dimethyl sulfide to give **7a**.
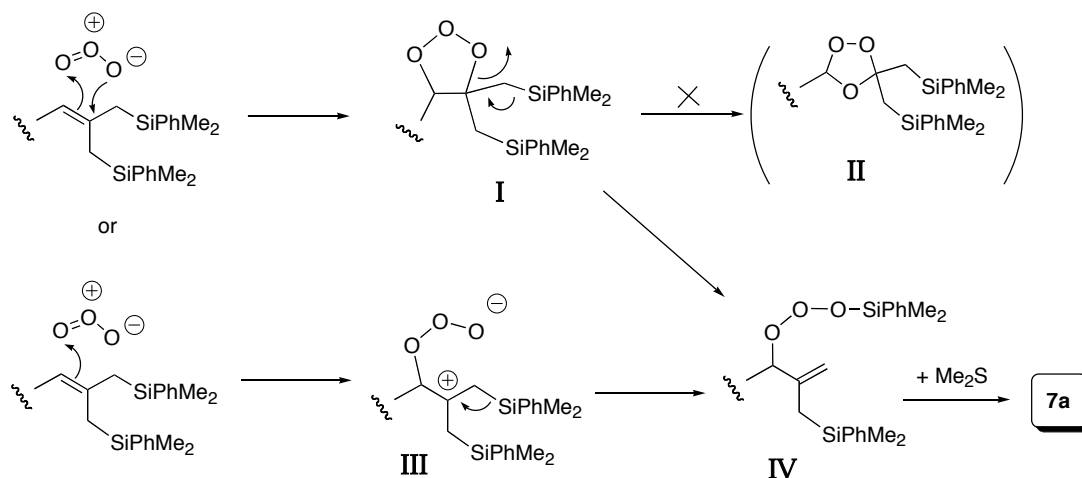

Figure 1

In conclusion, 1,1-bis(silymethyl)-1-alkene is an activated allylsilane that can react with NBS and ozone to give 2-silylmethyl substituted 3-halo- and 3-hydoxy-1-alkenes. Although the oxidation reaction with peracid was sluggish, that with ozone was relatively cleaner and gave hydroxyallylsilane by the unusual oxidation mechanism.

EXPERIMENTAL

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

Protodesilylation of 3-phenyl-1,1-bis(trimethylsilylmethyl)-1-propene (1). A mixture of **1** containing ~3% of **2** (443 mg, 1.46 mmol) and PPTS (548 mg, 2.18 mmol) in 10% acetonitrile in THF (14.5 mL) was stirred at room temperature. The reaction was monitored by reverse phase HPLC. After 2 days, saturated aq. NaHCO was added to the mixture, and the mixture was extracted with hexane. The hexane extract was washed with water and brine, dried over $MgSO_4$, and evaporated. The residual oil was purified by column chromatography on silica gel eluted with hexane to give **2** (326 mg) in 96% yield, which contained ~5% of **3**. Although compounds (**1**, **2**, and **3**) possess the same rf value and difficult to separate on silica gel column chromatography as well as medium or high pressure LC, the were able to be separatd on reverse phase HPLC using Lichrosorb RP-2 (20X250 mm)with 15% water in acetonitrille as an eluent. Retention times (1 mL/ min); **1**, 29.0 min, **2**, 9.6 min, and **3**, 3.7 min.

2 Colorless oil. Rf = 0.76 (3% t-BuOMe in hexane); ^{1}H NMR (300 MHz, C_6D_6) δ 0.00 (9H, s), 1.53 (2H, s), 1.77 (2H, quint, J = 7.3 Hz), 2.01 (2H, t, J = 7.3 Hz), 2.62 (2H, t, J = 7.3 Hz), 4.53 (1H, s), 4.61 (1H, s), 7.15-7.30 (5H, m); ^{13}C NMR (75 MHz) δ -1.3, 26.8, 29.6, 35.6, 37.7, 107.1, 125.6, 128.2, 128.4, 142.6, 147.4; MS (EI) m/z 232 (M^+), 128, 73; HRMS (EI) m/z Calcd for $C_{15}H_{24}Si$: 232.1647 (M^+). Found: 232.1662.

Reaction with *N*-bromosuccinimide. To a solution of **4** (300 mg, 0.7 mmol) in CH_2Cl_2 (7 mL) was added NBS (125 mg, 0.7 mmol) at -78 °C. The mixture was stirred for 2 h at the same temperature. Ether (25 mL) was added to the mixture and the whole was washed with water, brine and dried over $MgSO_4$. The solvent was removed and the residue was roughly purified by silica gel column chromatography eluted with hexane. Then, further purification was performed by HPLC using Phenomenex-Luna (21X250 mm) with hexane as an eluent. Retention times (15 mL/min); **5a**, 11.0 min, **6a**, 18.1 min. Pure compounds (**5a**) and (**6a**) were obtained in 34% yield (89 mg) and 21% yield (74 mg), respectively.

5a. Colorless oil. Rf = 0.2 (hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.32 (3H, s), 0.34 (3H, s), 1.87 (1 H, d, J = 14.1 Hz), 2.00 (1 H, d, J = 14.1 Hz), 2.04 (1H, dddd, J = 14.3, 9.2, 6.8, 4.8 Hz), 2.23 (1H, dtd, J =14.2, 9.2, 5.0 Hz), 2.53 (1H, ddd, J =17.5, 9.2, 6.6 Hz), 2.77 (1H, ddd, J =17.5, 9.2, 4.8 Hz), 4.14 (1H, dd, J = 9.2, 5.0 Hz), 4.77 (1H, d, J = 0.7 Hz), 5.07 (1H, s), 7.15-7.53 (10H, m); ^{13}C-NMR (75 MHz, $CDCl_3$) δ -2.89, -2.81, 22.8, 34.1, 38.4, 59.3, 117.7, 126.1, 127.8, 128.4, 128.5, 128.5(2C), 128.5, 129.2,

133.6, 138.4, 140.7, 146.5; MS (CI) m/z 372 (M⁺); HRMS (CI) m/z Calcd for $C_{20}H_{25}BrSi$: 372.0909. Found: 372.0907.

6a. Colorless oil. Rf = 0.16 (hexane). ¹H NMR (300 MHz, CDCl₃) δ 0.12 (3 H, s), 0.14 (3 H, s), 0.35 (6 H, s), 1.93 (1 H, d, J = 13.6 Hz), 2.00 (1 H, m), 2.22 (1 H, d, J = 13.6 Hz), 2.23 (1 H, m), 2.51 (1 H, m), 2.80 (1 H, ddd, J = 13.6, 9.0, 4.6 Hz), 4.03 (1 H, dd, J = 9.6, 3.9 Hz), 5.79 (1 H, s), 7.61-7.11 (15 H, m); ¹³C-NMR (75 MHz, CDCl₃) δ -2.5, -2.4, -0.99, -0.83, 26.2, 34.1, 39.1, 58.6, 121.8, 126.1, 127.8, 127.9, 128.3, 128.4, 128.5, 129.1, 133.5, 133.5, 133.8, 133.9; MS (EI) m/z 506 (M⁺); MS (EI) m/z: Calcd for $C_{28}H_{35}BrSi_2$: 506.1460. Found: 506.1456.

Reaction with *N*-chlorosuccinimide. To a solution of **4** (300 mg, 0.7 mmol) in CH_2Cl_2 (7 mL) was added NCS (123 mg, 0.7 mmol) at rt and it was stirred for 2 h at the same temperature. Ether (25 mL) was added to the mixture and the whole was washed with water, brine and dried over $MgSO_4$. The solvent was removed and the residue was purified by silica gel column chromatography eluted by hexane to give a mixture of **5b**, **6b**(*Z*) and **6b**(*E*). Further purification was performed by HPLC using the same system as described for the separation of **5a** and **6a**. Retention times (15 mL/min); **5b**, 13.5 min, **6b**(*E*), 15.4 min, **6b**(*Z*), 19.1 min. Compounds **5b** (31 mg), **6b**(*E*) (32 mg), and **6b**(*Z*) (32 mg) were obtained in 13%, 10%, and 10% yields, respectively.

5b Colorless oil. Rf = 0.20 (hexane). ¹H NMR (400 MHz, CDCl₃) δ 0.29 (3H, s), 0.31 (3H, s), 1.77 (1H, d, J = 14.7), 1.92 (1H, d, J = 14.7 Hz), 2.21-1.99 (2H, m), 2.56 (1H, ddd, J = 13.7, 9.0, 7.1 Hz), 2.75 (1H, ddd, J = 13.7, 8.8, 4.9 Hz), 4.03 (1H, dd, J = 8.8, 4.9 Hz), 5.01 (1H, s), 4.74 (1H, s), 7.51-7.14 (10H, m); MS (EI) m/z 328 (M⁺); HRMS (EI) m/z: Calcd for $C_{20}H_{25}ClSi$: 328.1414. Found: 328.1410.

6b(*E*) Colorless oil. Rf = 0.20 (hexane). ¹H NMR (400 MHz, CDCl₃) δ 0.16 (3H, s), 0.23 (3H, s), 0.36 (3H, s), 0.38 (3H, s), 1.54-1.62 (1H, m), 1.94 (1 H, d, J = 13.7 Hz), 1.96 (1H, s), 1.87-1.98 (1H, m), 2.22 (1 H, ddd, J = 13.6, 9.6, 7.1 Hz), 2.57 (1H, ddd, J = 13.6, 9.6, 4.2 Hz), 4.40 (1H, dd, J = 10.3, 3.8 Hz), 5.27 (1H, s), 7.53-6.97 (15H, m); MS (EI) m/z: 462 (M⁺); HRMS m/z: Calcd for $C_{28}H_{35}ClSi_2$: 462.1964. Found: 462.1966.

6b(*Z*) Colorless oil. Rf = 0.20 (hexane). ¹H NMR (400 MHz, CDCl₃) δ 0.13 (3H, s), 0.15 (3H, s), 0.33 (6H, s), 1.85 (1H, d, J = 13.7 Hz), 2.00-2.10 (2H, m), 2.12 (1H, d, J = 13.7 Hz), 2.45-2.53 (1H, m), 2.77 (1H, ddd, J = 13.7, 8.6, 5.3 Hz), 3.95 (1H, dd, J = 8.8, 4.4 Hz), 5.74 (1H, s), 7.52-7.12 (15H, m); MS (EI) m/z: 462 (M⁺); HRMS m/z: Calcd for $C_{28}H_{35}ClSi_2$: 462.1964. Found: 462.1957.

Reaction of 4 with ozone. Ozone gas was bubbled to a solution of alkene **4** (90 mg, 0.21 mmol) in CH_2CH_2 (2 mL) at -78 °C. After an addition of dimethyl sulfide (50 μL), the mixture was warmed up to rt. The mixture was purified directly by column chromatography on silica gel eluted with 5% EtOAc in

hexane to give **7a** (32 mg) in 45% yield. Colorless oil. Rf = 0.20 (10% AcOEt in hexane). ^{1}H-NMR (300 MHz, C_6D_6) δ 0.23 (6H, s), 1.55 (1H, dd, J = 14.0, 1.1 Hz), 1.63-1.80 (2H, m), 1.77 (1H, dd, J = 14.0, 1.1 Hz), 2.36 (1H, ddd, J = 13.9, 9.1, 5.9 Hz), 2.56 (1H, ddd, J = 13.9, 9.2, 7.0 Hz), 3.69 (1H, dd, J = 7.7, 4.8 Hz), 4.65 (1H, d, J = 1.3 Hz), 4.92 (1H, t, J = 1.3 Hz), 7.21-7.01 (8H, m), 7.57-7.37 (2H, m); ^{13}C-NMR (75 MHz, C_6D_6) δ −2.6, −0.2, 0.2, 21.7, 32.4, 37.8, 74.7, 108.1, 126.0, 127.9, 128.1, 128.3, 128.6, 128.8, 129.3, 133.9; MS (FAB) m/z: 333 (M+Na$^+$). HRMS (FAB) m/z: Calcd for $C_{20}H_{26}OSiNa$: 333.1644. Found 333.1654.

Preparation of acetate (**8**) was performed by the standard procedure with acetic anhydride in pyridine. Colorless oil. Rf = 0.54 (10% AcOEt in hexane). ^{1}H NMR (300 MHz, C_6D_6) δ 0.23 (3H, s), 0.24 (3H, s), 1.58 (1H, dd, J =14.3, 0.7 Hz), 1.74 (1H, d, J = 14.3 Hz), 1.79-1.97 (2H, m), 1.93, (3H, s), 2.34-2.55 (2H, m), 4.61 (1H, s), 4.81 (1H, s), 5.00 (1H, t, J = 6.2 Hz), 7.20 (10 H, m); ^{13}C NMR (75 MHz) δ -2.87, -2.84, 21.1, 21.7, 31.8, 34.6, 76.6, 109.9, 125.9, 127.8, 128.3, 128.3, 129.0, 133.6, 138.9, 141.5, 144.4, 170.1; IR (neat) cm^{-1}: 1737; MS (EI) m/z 352 (M$^+$); HRMS (EI) m/z Calcd for $C_{22}H_{28}O_2Si$: 352.1859. Found: 352.1856; *Anal*. Calcd for $C_{22}H_{28}O_2Si$: C, 74.95; H, 8.00. Found: C, 74.73; H, 8.18.

The reaction of **1** was carried out by the same procedure as described for **4** except the solvent for chromatography. A 2.5% AcOEt in hexane was used as an elutiing solvents instead of 5%. **7b**, 36% yield. Colorless oil. Rf = 0.37 (5% AcOEt in hexane). ^{1}H NMR (300 MHz, C_6D_6) δ 0.01 (9 H, s), 1.40 (1 H, dd, J = 13.9, 0.7 Hz), 1.62 (1 H, dd, J = 13.9, 0.7 Hz), 1.73-1.98 (2 H, m), 2.61-2.83 (2 H, m), 3.96 (1 H, dd, J = 7.7, 4.0 Hz), 4.70 (1 H, s, J = 1.0 Hz), 4.94 (1 H, m), 7.61-7.15 (5 H, m); MS (FAB) m/z 249 (M+1$^+$); HRMS (FAB) m/z Calcd for $C_{15}H_{25}Si_2O$: 249.1668. Found: 249.1661.

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