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Iodine(III)-Mediated Intramolecular Cyclization of Hydroxy Allylsilanes: Synthesis of 5- or 6-Membered β-Methylene Cyclic Ethers[1)]

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Oxidative cyclization of hydroxy allylsilanes utilizing the combination of a hypervalent organoiodine compound and a Lewis acid was studied. The allylsilanes **4**, prepared from the γ-lactones **1** *via* conversion to the bis(trimethylsilylmethyl)carbinols **3**, on treatment with iodosylbenzene in the presence of boron trifluoride-etherate in an ethereal solution, afforded the 6-membered β-methylene cyclic ethers **13a** and **13b** in good yields. Similar treatment of the allylsilanes **8a** and **8b** gave the 5-membered cyclic ethers **13c** and **13d**. On the other hand, oxidative cyclization of the carboxylic acid **12** gave a poor yield of the lactone **21** and the major product was found to be the rearranged γ-keto acid **22**. Regioselectivity in the iodine(III)-mediated cyclization of **8a** is discussed.

Keywords——iodine(III)-mediated cyclization; allyliodine(III) compound; β-methylene cyclic ether; iodosylbenzene; allylsilane; rearrangement

In a series of studies on the reaction of organometal (group IVb) compounds, we have reported a new method for the allylation reactions of aromatic compounds, alcohols, carboxylic acids, nitriles, and the nitrate group.[2)] As a key step of the allylation reactions, allylmetal (group IVb) compounds were converted into highly reactive allyl cationic species, allylthallium(III) compounds, *via* the reaction with thallium(III) salts such as thallium(III) trifluoroacetate, thallium(III) nitrate, and arylthallium bis(trifluoroacetate). Recently, we have found hypervalent organoiodine compounds, especially iodosylbenzene, to be alternative effective reagents for the allylation reaction and suggested allyliodine(III) species to be an active transient intermediate.[3)] As one of the applications of the iodine(III)-mediated allylation reaction, we have studied the synthesis of 5- and 6-membered cyclic ethers and δ-lactone (Chart 1).

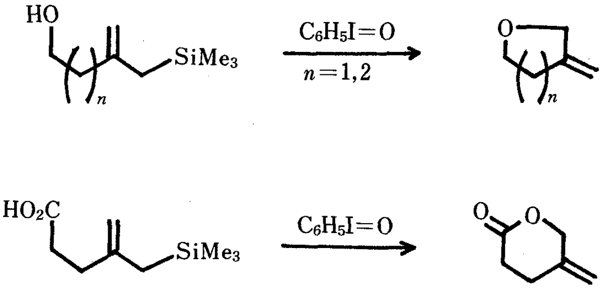


Chart 1

Synthesis of Allylsilanes

The hydroxy allylsilanes **4** seemed to be attractive compounds for investigation of the iodine(III)-mediated intramolecular allylation reaction of a hydroxy group. Many routes to allylsilanes are known, but none of them seem to be effective for the synthesis of **4**.[4] Hence, a new and efficient method for the synthesis of **4** was required. We expected that reaction of the readily available γ-lactone **1** with *ca.* 2 eq of trimethylsilylmethylmagnesium chloride might afford the bis(trimethylsilylmethyl)carbinol derivative **3** *via* the ketone **2**.[5] The hydroxy allylsilane **4** should be produced smoothly by the β-elimination of **3**.[6] Treatment of the γ-lactone **1a** with an excess amount (4 eq) of trimethylsilylmethylmagnesium chloride in diethyl ether at reflux for 2 h gave rise to the alcohol **3a**, which was shown to be labile, and was subjected to β-elimination in the presence of silica gel in chloroform without further purification to yield the desired hydroxy allylsilane **4a** (41%). Similar treatment of the γ-lactone **1b** afforded the allylsilane **4b** in 45% yield.

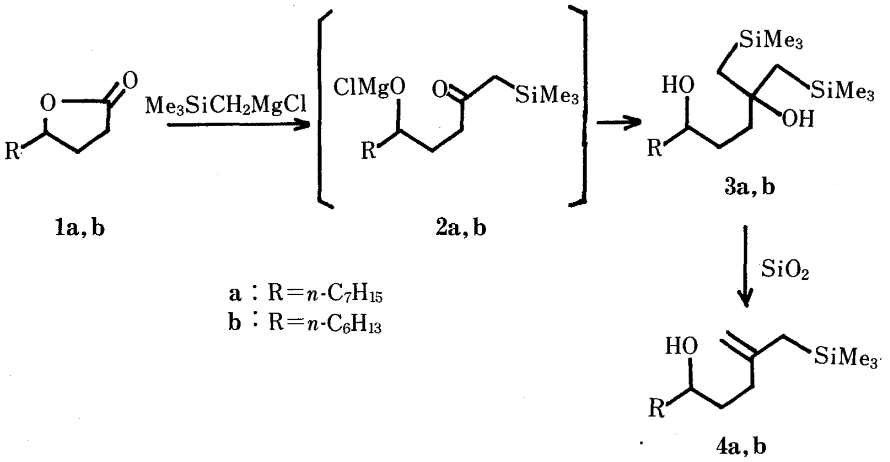


Chart 2

Syntheses of the hydroxy allylsilanes **8a** and **8b** were carried out in a straightforward fashion by using the procedure developed by Trost and Chan.[7] Generation of the dianion of the homo-allylic alcohol **5** [2 eq of *n*-butyllithium and 2 eq of tetramethylethylenediamine (TMEDA) in hexane] followed by bis-silylation with chlorotrimethylsilane gave the siloxy allylsilane **7a**. Chemoselective protodesilylation of **7a** using 10% sulfuric acid in tetrahydrofuran (THF) resulted in the formation of the desired hydroxy allylsilane **8a** in 57% yield (from **5**). Allylsilane **8b** was also prepared from the alcohol **6** in 46% yield.[8]

For comparison of the reactivity of allylsilyl and allylgermyl groups in the iodine(III)-mediated oxidative cyclization, we then prepared the hydroxy allylgermane **8c**: bis-germylation of the dianion derived from **5** with chlorotrimethylgermane, followed by the selective hydrolysis of the germyl ether moiety of **7c** using silica gel in chloroform, afforded **8c** in good yield.

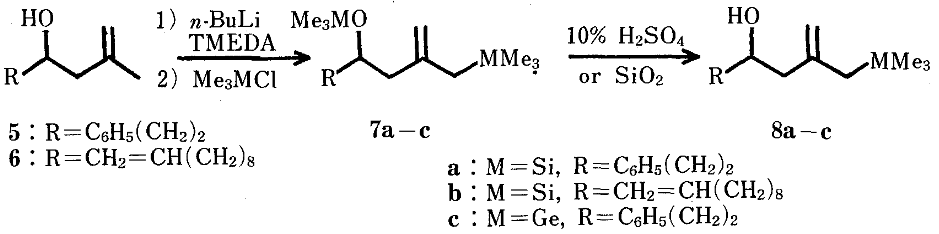
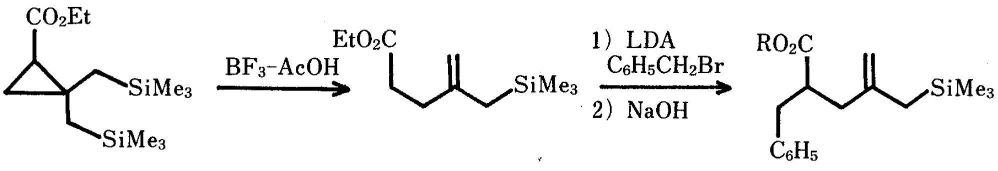


Chart 3

Furthermore, we carried out the synthesis of the allylsilane **12**, containing a suitably substituted carboxy-group, in order to evaluate the possibility of the iodine(III)-mediated oxidative lactonization. The ester **10**,[9] prepared from the cyclopropane **9** by silicone-promoted ring opening using a Lewis acid catalyst, was converted into the acid **12** *via* successive treatment with lithium diisopropylamide (LDA) and benzyl bromide and then with sodium hydroxide in methanol.



9 **10** **11**: R=Et
12: R=H

Chart 4

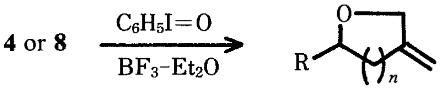
Iodine(III)-Mediated Oxidative Cyclization of Allylsilanes

Hydroxy allylsilanes obtained as described above were subjected to oxidative cyclization by using iodosylbenzene. We found that iodosylbenzene itself is not reactive enough for nucleophilic attack of allylsilanes.[3,10] Thus, for the allylation reaction of alcohols with allylmetal (group IVb) compounds, the activation of iodosylbenzene with a Lewis acid was required. Boron trifluoride-etherate was shown to be one of the most effective Lewis acids.

The hydroxy allylsilane **4a**, on treatment with iodosylbenzene in dichloromethane at −20 °C in the presence of BF_3–Et_2O, gave the β-methylene cyclic ether **13a** in 24% yield. The use of ether solvents proved to be much more effective than the use of dichloromethane or hexane. Thus, **4a** and **4b** afforded the ethers **13a** and **13b** in 63 and 65% yields, respectively, by using dioxane as the reaction solvent. The results of cyclization are summarized in Table I.

In a similar manner, the oxidative cyclization of **8a** and **8b** proceeded smoothly in dioxane to give the 5-membered cyclic ethers **13c** and **13d**. Chemoselectivity of the cyclization

Table I. Synthesis of β-Methylene Cyclic Ethers



13a: $n=2$, $R=n\text{-}C_7H_{15}$
13b: $n=2$, $R=n\text{-}C_6H_{13}$
13c: $n=1$, $R=C_6H_5(CH_2)_2$
13d: $n=1$, $R=CH_2=CH(CH_2)_8$

Run	Alcohol	Solvent	Reaction conditions[a]	Product	Yield[b] %
1	**4a**	CH_2Cl_2	−20 °C (1 h)	**13a**	24[c]
2	**4a**	Et_2O	−20 °C (2 h) then 0 °C (2 h)	**13a**	58
3	**4a**	THF	−70 °C (4 h) then −20 °C (2 h)	**13a**	53
4	**4a**	Dioxane	r.t. (3 h)	**13a**	63
5	**4b**	Dioxane	r.t. (2 h)	**13b**	65
6	**8a**	THF	0 °C (5 h)	**13c**	19
7	**8a**	DME	0 °C (1.5 h)	**13c**	52
8	**8a**	Dioxane	r.t. (2 h)	**13c**	68
9	**8b**	Dioxane	r.t. (4 h)	**13d**	40
10	**8c**	Dioxane	r.t. (4 h)	**13c**	38[d]

a) r.t.: room temperature. *b*) Isolated yield. *c*) ^{1}H-NMR yield. *d*) The alcohol **5** was also obtained in 39% yield.

was observed: the isolated double bond of **8b** was kept intact.[11]

When the hydroxy allylgermane **8c** was subjected to the cyclization, the 5-membered ether **13c** was obtained in 38% yield. The low yield of **13c** may be attributable to instability of the allylgermane moiety of **8c** under the acidic reaction conditions. In fact, the protodegermylation of **8c** was observed and the homo-allylic alcohol **5** was obtained in an amount equal to that of the ether **13c**.

One of the most plausible reaction mechanisms for the cyclization of hydroxy allylsilanes is shown in Chart 5. The iodine of iodosylbenzene activated by coordination of the Lewis acid (BF_3–Et_2O) to the oxygen becomes a highly electron deficient center. Then nucleophilic attack of the allylsilyl group of hydroxy allylsilanes may produce the highly reactive allyliodine(III) species **14** as a transient intermediate. The allyl group of **14** can now act as an allyl cation equivalent species and be attacked by the hydroxy group, yielding the cyclic ether **13**. At this stage, iodobenzene and trimethylsilanol will be released and the latter may be converted into hexamethyldisiloxane under acidic conditions.[12]

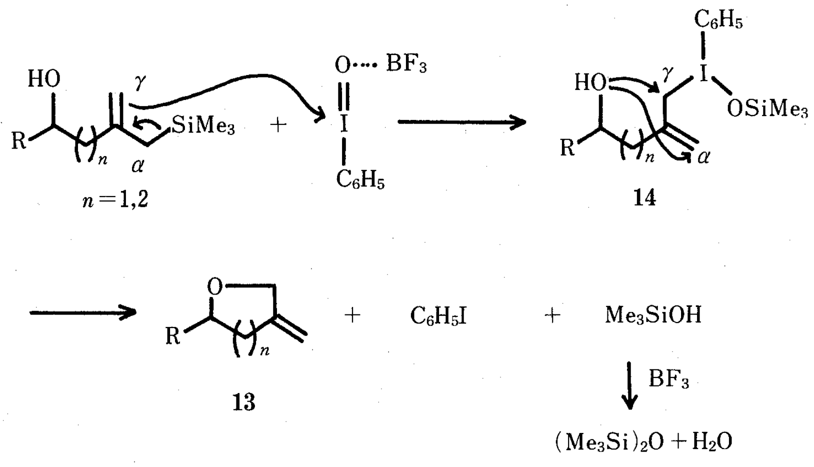
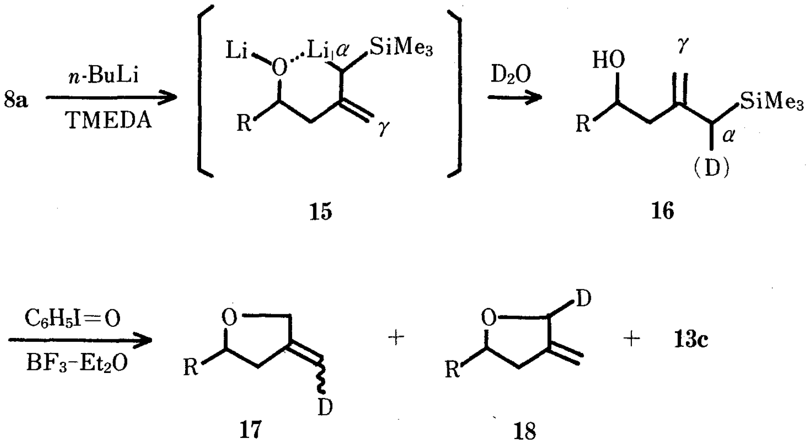


Chart 5

Reaction of allylsilanes with a variety of electrophiles has been well established to occur at the γ-carbon in a completely regioselective manner.[4] Thus, it is reasonable to assume that the carbon–iodine bond of **14** is formed at the γ-carbon of the allylsilyl group. Subsequent intramolecular attack of the hydroxy group of **14**, however, may occur on either the α- or γ-carbon or on both carbons. We decided to prepare the regioselectively deuterium-labeled allylsilane **16** in order to clarify the regiochemistry of the iodine(III)-mediated cyclization. Treatment of the allylsilane **8a** with *n*-butyllithium (2 eq) in THF in the presence of TMEDA (2 eq) at room temperature and then quenching of the resulting dianion with deuterium oxide produced the mono-deuterated allylsilane **16** in 33% yield. Analysis of the 400-MHz proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **16** showed the regioselective incorporation of deuterium on the α-carbon of the allylsilyl group of **8a**; the deuterium content was found to be 74% (see Experimental). α-Triphenylsilylallyl lithium was reported to react with water at the γ-position predominantly.[13] Formation of the α-deuterated **16** may be reasonably explained by considering the intramolecular coordination of the dianion **15**.

Oxidative cyclization of **16** gave rise to a mixture of the ethers **17** (deuterated at the vinylic position), **18** (deuterated at the allylic position), and non-deuterated **13c** in 52% yield. The ratio of mono-deuterated **17** and **18** to **13c** was determined to be 72 : 28 from the ^{1}H-NMR spectrum of the mixture. The results show that almost all of the deuterium of **16** was retained during the cyclization. Most importantly, the ratio of **17** to **18** was found to be 75 : 25. As had been expected, stereoselectivity of the cyclization was not observed: both **17** and **18**

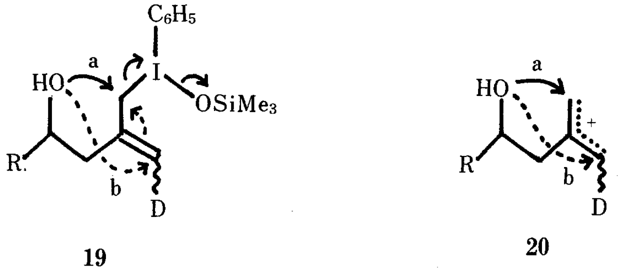


R=$C_6H_5(CH_2)_2$

Chart 6

were shown to be approximately 1 : 1 stereoisomeric mixtures (see Experimental).

There may be two extreme types of possible transition states for the cyclization of **16**. One of them is the concerted reaction process **19**. Of the two possible pathways a and b in **19**, the latter leading to formation of the ether **18** is not important, because it is a disfavoured 5-*endo*-trigonal ring-forming process.[14] The stepwise reaction process *via* the formation of the allyl cation **20** should also be considered. In this case, pathways a and b may be equally effective, since the secondary α-deuterium kinetic isotope effect on the cyclization of **20** is expected to be small.[15] On the basis of the above arguments, the results obtained in the cyclization of **16** can be reasonably explained by assuming a transition state in which the breaking carbon–iodine bond is considerably ionic. In other words, the transition state of this reaction is considered to be located at an intermediate step between **19** and **20**.



R=$C_6H_5(CH_2)_2$

Chart 7

As a model experiment directed toward the synthesis of nepetalactone[16] and gastrolactone,[17] we investigated intramolecular oxidative cyclization of the carboxylic acid **12**. The desired γ-methylene-δ-lactone **21**, however, was obtained in only 20% yield by the reaction of **12** with iodosylbenzene and boron trifluoride-etherate in dioxane. The major product of the reaction was found to be the rearranged ketone **22**: the presence of the carboxylic acid and carbonyl group was readily apparent in the infrared (IR) spectrum. In the 400 MHz ^{1}H-NMR spectrum of **22**, the methyl signal of the trimethylsilyl group appeared at δ -0.03, and two H_a and two H_b protons resonated at δ 0.70 and 2.31 as an AA′XX′ type signal. Detailed decoupling experiments and conversion of the product to the methyl ester **23** by the reaction with diazomethane confirmed the structure of **22**.

Although the reaction process leading to the rearranged γ-keto acid **22** is not yet clear,

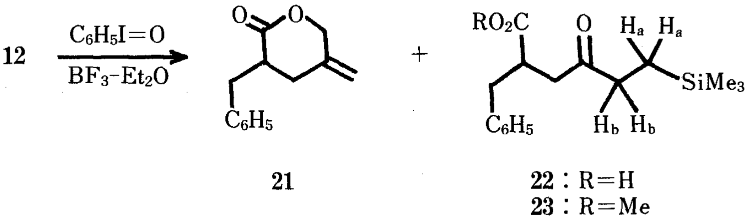
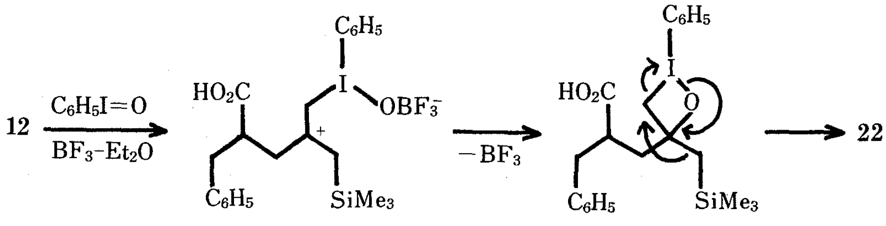


Chart 8

the sequence shown in Chart 9 seems to be plausible.[18] Allylsilane has been shown to react with electrophiles *via* generation of the cation stabilized by the neighboring carbon–silicon bond.[4,19] Hence transient formation of the zwitter ion **24**, followed by cyclization, may give rise to the reactive 4-membered cyclic compound **25**. Successive 1,2-rearrangement[20] of the trimethylsilylmethyl group of **25**, with concomitant loss of iodobenzene, would produce the ketone **22**.



24 **25**

Chart 9

Thus, a new general method for the synthesis of 5- and 6-membered β-methylene cyclic ethers was established.

Experimental

IR spectra were recorded with a JASCO IR-A-1 spectrophotometer. ^{1}H-NMR spectra were obtained with Hitachi R40, JEOL JNM-FX 100, and JEOL JNM-GX 400 spectrometers. Chemical shifts are reported relative to internal tetramethylsilane. Mass spectra (MS) were determined on a Hitachi RMU-7L spectrometer. Preparative thin layer chromatography (TLC) was carried out on precoated plates of silica gel (Merck, Silica gel F-254). Kieselgel 60 (Merck) was used.

Materials——Iodosylbenzene was prepared by oxidation of iodobenzene with peracetic acid, followed by hydrolysis with sodium hydroxide.[21] Boron trifluoride-etherate was freshly distilled from calcium hydride under nitrogen.

Synthesis of 5-Hydroxy-2-(trimethylsilylmethyl)-1-dodecene (4a)——A solution of γ-undecalactone (**1a**) (1.5 g, 8.1 mmol) in diethyl ether (3 ml) was added to a stirred solution of trimethylsilylmethylmagnesium chloride (1.17 M in diethyl ether) (28.7 ml, 32.4 mmol) at room temperature under nitrogen, and the solution was refluxed for 2 h. After being cooled, the reaction mixture was quenched with cold water and extracted with diethyl ether. The organic layer was washed with brine and dried. The solvent was evaporated off to give the crude product **3a**, which was used without further purification. The crude product **3a** was dissolved in chloroform (10 ml). Silica gel (5 g) was added to the solution and the mixture was stirred for 2 h at room temperature. Filtration and then evaporation left an oil, which was chromatographed on a column of silica gel using ethyl acetate–hexane (2 : 8) to give the hydroxy allylsilane **4a** (898 mg, 41%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3630, 3500, 1635, 1250, 1160, 860. MS *m/e*: 270 (M$^+$), 255 (base peak), 216, 215, 201, 182, 179, 170, 141, 128. High-resolution MS: Found 270.2354. Calcd for $C_{16}H_{34}OSi$ (M$^+$) 270.2376. ^{1}H-NMR (CDCl$_3$) δ: 0.03 (9H, s, SiMe$_3$), 0.8—1.0 (3H), 1.1—1.8 (16H), 1.9—2.2 (2H, m, CCH$_2$C=C), 3.45—3.75 (1H, m, C$\underline{H}$OH), 4.55, 4.65 (each 1H, m, C=CH$_2$). *Anal.* Calcd for $C_{16}H_{34}OSi$: C, 71.04; H, 12.67. Found: C, 71.17; H, 12.44.

5-Hydroxy-2-(trimethylsilylmethyl)-1-undecene (4b)——γ-Decalactone **1b** (1.7 g, 10 mmol) was converted to the hydroxy allylsilane **4b** (1.15 g, 45%) by the same method as described for the synthesis of the allylsilane **4a**. **4b**;

colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3630, 3500, 1635, 1250, 1160, 860. MS *m/e*: 256 (M$^+$), 253, 241, 211, 201, 171, 128 (base peak), 73. High-resolution MS: Found 256.2160. Calcd for $C_{15}H_{32}OSi$ (M$^+$) 256.2220. ^{1}H-NMR ($CDCl_3$) δ: 0.03 (9H, s, $SiMe_3$), 0.8—1.0 (3H), 1.1—1.8 (14H), 1.9—2.2 (2H, m, $CCH_2C=C$), 3.4—3.8 (1H, m, $C\underline{H}OH$), 4.54, 4.64 (each 1H, m, $C=CH_2$). *Anal.* Calcd for $C_{15}H_{32}OSi$: C, 70.24; H, 12.57. Found: C, 70.36; H, 12.61.

Synthesis of 4-Hydroxy-6-phenyl-2-(trimethylsilylmethyl)-1-hexene (8a)——Reaction of β-phenylpropionaldehyde (4 g, 30 mmol) with 2-methyl-2-propenylmagnesium chloride (30 mmol) in diethyl ether (40 ml) afforded the alcohol **5** (2.8 g, 49%). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3600, 1645, 1600, 1055, 900. MS *m/e*: 190 (M$^+$), 172, 134 (base peak), 116, 91, 90. ^{1}H-NMR ($CDCl_3$) δ: 1.6—2.0 (2H, m), 1.75 (3H, d, $J=1.5$ Hz, Me), 2.05—2.35 (2H, m, $CH_2C=C$), 2.65—2.95 (2H, m, $C\underline{H}_2C_6H_5$), 3.6—3.9 (1H, m, $C\underline{H}OH$), 4.78, 4.87 (each 1H, m, $C=CH_2$), 7.1—7.3 (5H, C_6H_5). *Anal.* Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.97; H, 9.61. *n*-Butyllithium (1.55 M in hexane) (8.4 ml, 13 mmol) was added to a stirred solution of **5** (1.23 g, 6.5 mmol) and TMEDA (1.5 g, 13 mmol) in hexane (15 ml) at −78 °C under nitrogen, and the mixture was stirred for 4 h at −20 °C. The resulting dianion solution was cooled to −78 °C and then chlorotrimethylsilane (2.1 g, 19.5 mmol) was added dropwise. After being stirred for 1 h at −78 °C and for an additional 15 h at room temperature, the reaction mixture was quenched with cold brine and extracted with diethyl ether. The organic layer was washed with brine and dried. The solvent was evaporated off to give the crude product **7a**, which was dissolved in THF (50 ml). A 10% aqueous sulfuric acid solution (2 ml) was added to the solution at 0 °C and the mixture was stirred for 0.5 h at 0 °C. After the addition of cold water, the mixture was extracted with diethyl ether. A usual work-up left an oil, which was separated by silica gel column chromatography [hexane–ethyl acetate (10 : 1)] to afford the allylsilane **8a** (981 mg, 57% yield based on **5**) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3600, 1630, 1605, 1255, 1160, 1075, 860. MS *m/e*: 262 (M$^+$), 247, 229, 207 (base peak), 172, 156, 143, 128, 116, 73. 400 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.03 (9H, s, $SiMe_3$), 1.48, 1.56, (each 1H, AB type, $J=13$ Hz, CH_2Si), 1.75—1.85 (2H, m, $C\underline{H}_2CH_2C_6H_5$), 2.05 (1H, dd, $J=13$, 9 Hz, one of $CCH_2C=C$), 2.16 (1H, dd, $J=13$, 3 Hz, one of $CCH_2C=C$), 2.70 (1H, ddd, $J=14$, 9, 7 Hz, one of $C\underline{H}_2C_6H_5$), 2.83 (1H, ddd, $J=14$, 10, 6 Hz, one of $C\underline{H}_2C_6H_5$), 3.68—3.77 (1H, m, $C\underline{H}OH$), 4.69, 4.70 (each 1H, $C=CH_2$), 7.15—7.35 (5H, C_6H_5). *Anal.* Calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.99. Found: C, 73.07; H, 9.96.

4-Hydroxy-2-(trimethylsilylmethyl)-1,13-tetradecadiene (8b)——Reaction of 10-undecenyl aldehyde (3 g, 17.8 mmol) with 2-methyl-2-propenylmagnesium chloride (17.8 mmol) in diethyl ether (150 ml) afforded the alcohol **6** (2 g, 50%). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3600, 1645, 1000, 910. MS *m/e*: 224 (M$^+$), 206, 169, 150, 149, 109, 95 (base peak), 80. ^{1}H-NMR ($CDCl_3$) δ: 1.2—2.4 (21H), 3.55—3.9 (1H, m, $C\underline{H}OH$), 4.7—5.2 (4H, $2\times C=CH_2$), 5.6—6.05 (1H, m, $CH=C$). *Anal.* Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.11; H, 12.68. The alcohol **6** (1.57 g, 7 mmol) was converted to the hydroxy allylsilane **8b** (955 mg, 46%) *via* the formation of **7b** by the same method as described for the synthesis of **8a**. **8b**: colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3600, 1635, 1250, 1160, 1000, 920, 855. MS *m/e*: 295 (M$^+$), 241 (base peak), 225, 205, 142, 94, 73. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (9H, s, $SiMe_3$), 1.1—1.6 (16H), 1.85—2.25 (4H), 3.5—3.8 (1H, m, $C\underline{H}OH$), 4.71 (2H, s, $C=CH_2$), 4.8—5.1 (2H, m, $CH=C\underline{H}_2$), 5.5—6.0 (1H, m, $C\underline{H}=CH_2$). *Anal.* Calcd for $C_{18}H_{36}OSi$: C, 72.90; H, 12.24. Found: C, 73.37; H, 12.21.

4-Hydroxy-6-phenyl-2-(trimethylgermylmethyl)-1-hexene (8c)——*n*-Butyllithium (1.55 M in hexane) (3.9 ml, 6 mmol) was added to a stirred solution of **5** (571 mg, 3 mmol) in hexane (15 ml) containing TMEDA (697 mg, 6 mmol) at −78 °C under nitrogen, and the solution was stirred for 4 h at −20 °C. The solution was cooled to −78 °C and then chlorotrimethylgermane (1.1 g, 7.5 mmol) was added. After being stirred for 1 h at −78 °C and for an additional 15 h at room temperature, the mixture was quenched with cold brine and extracted with diethyl ether. A usual work-up left an oil, which was dissolved in chloroform (5 ml). Silica gel (1 g) was added to the solution and the mixture was stirred for 1 h at room temperature. Filtration and then evaporation left an oil, which was chromatographed on a column of silica gel using hexane–ethyl acetate (7 : 1) to give the allylgermane **8c** (686 mg, 63%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3590, 1630, 1605, 1500, 1460, 1260, 1145, 1070, 880. MS *m/e*: 308 (M$^+$), 293, 253 (base peak), 119. High-resolution MS: Found 308.1159. Calcd for $C_{16}H_{26}GeO$ (M$^+$) 308.1193. ^{1}H-NMR ($CDCl_3$) δ: 0.16 (9H, s, $GeMe_3$), 1.66 (2H, s, CH_2Ge), 1.7—2.2 (4H), 2.6—2.9 (2H, m, $C\underline{H}_2C_6H_5$), 3.55—3.9 (1H, m, $C\underline{H}OH$), 4.67 (2H, s, $C=CH_2$), 7.1—7.4 (5H, C_6H_5).

2-(Phenylmethyl)-4-(trimethylsilylmethyl)-4-pentenoic Acid 12——A solution of the ester **10** (75 mg, 0.4 mmol) in THF (0.5 ml) was added dropwise at −78 °C under nitrogen to a solution of LDA, prepared from diisopropylamine (45 mg, 0.44 mmol) and butyllithium (1.55 M in hexane) (0.28 ml, 0.44 mmol) in THF (1 ml) at 0 °C for 0.5 h. The mixture was stirred for 1 h at −78 °C. After the addition of a solution of benzyl bromide (71 mg, 0.4 mmol) and hexamethylphosphoric triamide (HMPA) (72 mg, 0.4 mmol) in THF (0.5 ml) at −78 °C, the cooling bath was removed and the mixture was allowed to warm to room temperature. The reaction mixture was quenched with an aqueous solution of ammonium chloride and extracted with ether. A usual work-up left an oil, which was separated by preparative TLC [hexane–ethyl acetate (9 : 1)] to afford the ester **11** (92 mg, 75%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1740, 1640, 1605, 1380, 1230, 1040, 855. MS *m/e*: 304 (M$^+$), 289, 259, 249 (base peak), 213, 181, 131, 95, 91, 73. High-resolution MS: Found 304.1838. Calcd for $C_{18}H_{28}O_2Si$ (M$^+$) 304.1856. ^{1}H-NMR ($CDCl_3$) δ: −0.02 (9H, s, $SiMe_3$), 1.12 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.56 (2H, CH_2Si), 2.1—3.1 (5H), 4.02 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 4.56, 4.62 (each 1H, $C=CH_2$), 7.0—7.4 (5H, C_6H_5). Sodium hydroxide (40 mg, 1 mmol) was added to a solution of **11** (59 mg, 0.2 mmol) in methanol (1 ml) and the mixture was stirred for 5 h at room temperature. The mixture was poured into water, acidified with 2% hydrochloric acid, and extracted with chloroform. A usual work-up left an oil, which was purified by preparative TLC [hexane–ethyl acetate (1 : 1)] to give the acid **12** (38.4 mg, 73%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3300—2500, 1715, 1630, 1600, 1250, 1075, 1040, 850. MS *m/e*: 276 (M$^+$), 261, 257, 220, 205 (base peak), 185, 169, 131, 95, 91, 75, 73. ^{1}H-NMR (CDCl$_3$) δ: 0.4 (9H, s, SiMe$_3$), 1.54 (2H, CH$_2$Si), 2.15—2.4 (2H, m, CCH$_2$C=C), 2.8—3.1 (3H, $C\underline{H}C\underline{H}_2C_6H_5$), 4.64, 4.70 (each 1H, C=CH$_2$), 7.1—7.4 (5H, C$_6$H$_5$), 9.9 (1H, br s, CO$_2$H). *Anal.* Calcd for $C_{16}H_{24}O_2Si$: C, 69.52; H, 8.75. Found: C, 69.47; H, 8.61.

General Procedure for Synthesis of *β*-Methylene Cyclic Ethers 13——Boron trifluoride-etherate (2 mmol) was added dropwise to a stirred suspension of the alcohol **4** (or **8**) (1 mmol) and iodosylbenzene (1 mmol) in the solvent described in Table I, under nitrogen. The reaction conditions are given in the table. The reaction mixture was poured into an aqueous solution of NaHCO$_3$ and extracted with pentane. The organic layer was washed with brine and dried. The solvent was evaporated off to give an oil, which was purified by preparative TLC [hexane–ethyl acetate (9 : 1)] to give the cyclic ether **13**. The yields are given in Table I.

6-Heptyl-3-methylenetetrahydropyran (13a)[22]——Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1650, 1460, 1380, 1330, 1130, 1055, 900. MS *m/e*: 196 (M$^+$), 183, 125, 96 (base peak), 72, 55. ^{1}H-NMR (CDCl$_3$) δ: 0.7—1.05 (3H, Me), 1.1—2.0 (14H), 2.2—2.5 (2H, m, CCH$_2$C=C), 3.2—3.5 (1H, m, CHO), 3.94, 4.20 (each 1H, AB type, J=13 Hz, CH$_2$O), 4.77 (2H, s, C=CH$_2$). *Anal.* Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.70; H, 12.19.

6-Hexyl-3-methylenetetrahydropyran (13b)——Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1660, 1460, 1375, 1335, 1250, 1070, 900. MS *m/e*: 182 (M$^+$), 138, 112, 97 (base peak), 67, 56. ^{1}H-NMR (CDCl$_3$) δ: 0.8—1.0 (3H, Me), 1.1—2.0 (12H), 2.2—2.5 (2H, m, CCH$_2$C=C), 3.2—3.55 (1H, m, CHO), 3.95, 4.20 (each 1H, AB type, J=12 Hz, CH$_2$O), 4.77 (2H, s, C=CH$_2$). *Anal.* Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.91; H, 11.92.

5-(2-Phenylethyl)-3-methylenetetrahydrofuran (13c)——Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1680, 1600, 1495, 1455, 1045, 890. MS *m/e*: 188 (M$^+$, base peak), 170, 154, 130, 118, 105, 90, 82, 65. 400 MHz ^{1}H-NMR (CDCl$_3$) δ: 1.78—1.87, 1.91—2.01 (each 1H, m, $C\underline{H}_2CH_2C_6H_5$), 2.18—2.27, 2.59—2.68 (each 1H, m, CCH$_2$C=C), 2.63—2.82 (2H, m, $C\underline{H}_2C_6H_5$), 3.94 (1H, tt, J=8, 6 Hz, CHO), 4.24, 4.40 (each 1H, AB type, J=13 Hz, CH$_2$O), 4.90, 4.96 (each 1H, quint, J=2 Hz, C=CH$_2$), 7.15—7.32 (5H, m, C$_6$H$_5$). *Anal.* Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.94; H, 8.61.

5-(9-Decenyl)-3-methylenetetrahydrofuran (13d)——Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1680, 1650, 1470, 1120, 1045, 920, 895. MS *m/e*: 222 (M$^+$, base peak), 205, 178, 148, 109, 94, 82, 66. ^{1}H-NMR (CDCl$_3$) δ: 1.2—2.4 (17H), 2.45—2.8 (1H), 3.7—4.05 (1H, m, CHO), 4.05—4.5 (2H, CH$_2$O), 4.8—5.1 (4H, 2×C=CH$_2$), 5.55—6.05 (1H, m, $C\underline{H}=CH_2$). *Anal.* Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.18; H, 11.82.

Synthesis of Deuterated Allylsilane 16——Butyllithium (1.55 M in hexane) (0.27 ml, 0.42 mmol) was added to a stirred solution of **8a** (55 mg, 0.21 mmol) in THF (2 ml) containing TMEDA (49 mg, 0.42 mmol) at 0 °C under nitrogen and the solution was stirred for 4 h at room temperature. The resulting solution of the dianion **15** was quenched with an excess of deuterium oxide and extracted with diethyl ether. A usual work-up left an oil, which was purified by preparative TLC [hexane–ethyl acetate (10 : 1)] to give the allylsilane **16** (18 mg, 33% yield). 400 MHz ^{1}H-NMR (CDCl$_3$) δ: 0.03 (9H, s), 1.45—1.60 (total 1.26H, CH$_2$Si), 1.75—1.85 (2H, m), 2.05 (1H, dd, J=14, 9 Hz), 2.16 (1H, dd, J=14, 3 Hz), 2.70 (1H, ddd, J=14, 9, 7 Hz), 2.83 (1H, ddd, J=14, 9, 6 Hz), 3.68—3.77 (1H, m), 4.69, 4.70 (each 1H), 7.15—7.35 (5H).

Oxidative Cyclization of 16——According to the general procedure for the synthesis of β-methylene cyclic ethers **13**, the allylsilane **16** (18 mg, 0.068 mmol) was treated with iodosylbenzene (15 mg, 0.068 mmol) and boron trifluoride-etherate (20 mg, 0.14 mmol) in dioxane (2 ml) for 5 h at room temperature. A mixture of the cyclic ethers **13c**, **17**, and **18** (6.6 mg, 52%) was separated by preparative TLC. The mixture of **13c**, **17**, and **18**: 400 MHz ^{1}H-NMR (CDCl$_3$) δ: 1.78—1.87, 1.91—2.01 (each 1H), 2.18—2.27, 2.59—2.68 (each 1H), 2.63—2.82 (2H), 3.94 (1H, tt, J=8, 6 Hz), 4.21—4.27, 4.36—4.44 (each 0.91H, CH$_2$O), 4.87—4.93, 4.94—4.99 (each 0.73H, C=CH$_2$), 7.15—7.32 (5H).

Oxidative Cyclization of the Carboxylic Acid 12——Boron trifluoride-etherate (18 mg, 0.126 mmol) was added dropwise to a stirred suspension of **12** (35 mg, 0.126 mmol) and iodosylbenzene (28 mg, 0.126 mmol) in dioxane (50 ml) at room temperature and the mixture was stirred for 2 d. The reaction mixture was poured into water and extracted with diethyl ether. A usual work-up left an oil. On preparative TLC [chloroform–ethyl acetate (9 : 1)], the δ-lactone **21** (5 mg, 20%) and the γ-keto acid **22** (13 mg, 35%) were isolated. **21**: Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1745, 1650, 1600, 1380, 1140, 905. MS *m/e*: 202 (M$^+$), 187, 169, 156, 141, 129, 115, 111, 91. High-resolution MS: Found 202.0977. Calcd for $C_{13}H_{14}O_2$ (M$^+$) 202.0992. ^{1}H-NMR (CDCl$_3$) δ: 2.0—3.1 (4H, m, $C\underline{H}_2C\underline{H}C\underline{H}_2$), 3.2—3.5 (1H, m, CHC=O), 4.70, 4.84 (each 1H, AB type, J=13 Hz, CH$_2$O), 4.98, 5.08 (each 1H, s, C=CH$_2$), 7.1—7.5 (5H, C$_6$H$_5$). **22**: Colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3300—2700, 1720, 1600, 835. MS *m/e*: 292 (M$^+$), 277, 259, 231, 144, 91, 73 (base peak). High-resolution MS: Found 292.1506. Calcd for $C_{16}H_{24}O_3Si$ (M$^+$) 292.1493. 400 MHz ^{1}H-NMR (CDCl$_3$) δ: −0.03 (9H, s, SiMe$_3$), 0.63—0.77, 2.24—2.39 (each 2H, AA′XX′ type, CH$_2$CH$_2$Si), 2.46 (1H, dd, J=18, 4 Hz), 2.75 (1H, dd, J=14, 9 Hz), 2.82 (1H, dd, J=18, 9 Hz), 3.11 (1H, dd, J=14, 6 Hz), 3.18—3.27 (1H, m, $C\underline{H}CO_2H$), 7.15—7.35 (5H, C$_6$H$_5$).

Methylation of the Acid 22——A solution of diazomethane in diethyl ether was added dropwise to a solution of **22** (3.5 mg) in diethyl ether (0.5 ml) at 0 °C, and the solution was allowed to stand for 0.5 h at room temperature. The solvent was evaporated off to give an oil, which was purified by preparative TLC [hexane–ethyl acetate (9 : 1)] to afford the ester **23** (3 mg, 82%) as a colorlesss oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1740, 1730, 1600, 1265, 1100, 1010, 860, 840. MS *m*/*e*: 306 (M^+), 291, 259, 231, 163, 144, 73 (base peak). High-resolution MS: Found 306.1668. Calcd for $C_{17}H_{26}O_3Si$ (M^+) 306.1652. 400 MHz ^{1}H-NMR ($CDCl_3$) δ: −0.03 (9H, s, $SiMe_3$), 0.63—0.76, 2.23—2.38 (each 2H, AA'XX' type, CH_2CH_2Si), 2.43 (1H, dd, $J=18, 4$ Hz), 2.72 (1H, dd, $J=14, 8$ Hz), 2.83 (1H, dd, $J=18, 9$ Hz), 3.02 (1H, dd, $J=14, 6$ Hz), 3.15—3.23 (1H, m, $C\underline{H}CO_2Et$), 3.65 (3H, s, OMe), 7.13—7.32 (5H, C_6H_5).

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