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Asymmetric Total Synthesis of Syringolide 1, a Nonproteinaceous Elicitor

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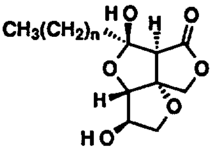
Abstracts: An asymmetric synthesis of syringolide 1, one of the elicitors produced by *Pseudomonas syringae* pv. *tomato*, is described. It was synthesized from 2-(1-oxoethyl)-2-buten-4-olide *via* 1,4-addition of alkenyl cuprate, asymmetric dihydroxylation, and intramolecular Michael reaction.

The plants have acquired various chemical defense mechanisms against attack of pathogens.[1] The chemical defenses have been gradually elucidated by the recent progress of biochemistry, and it has been revealed that the plants recognize chemical signals and then the activation of defense responses is initiated. Hypersensitive defense response (HR) is the phenomenon, which involves the localized cell death in the infected tissues and subsequent accumulation of phytoalexins around the cells. The phytoalexins are not found in healthy plant tissues and their production is induced by elicitor. There had been two reports that the association of the production of elicitor with the avirulence gene (*avr D*) was affirmed.[2] These elicitors were characterized as proteins themselves, produced by *avr D*. In 1993, Keen *et al.* isolated novel nonproteinaceous elicitors, syringolides 1 (1a) and 2 (1b) from *Pseudomonas syringae* pv. *tomato*.[3] The compounds induce a hypersensitive response in specific soybean cultivars that carry a resistance gene, *Rpg4*. Syringolides are produced by the action of *avr D*, whereas the direct protein product of *avr D* failed in the elicitor activity. Since these elicitors constitute the first isolation of their class and have features in common with antigens that are recognized by the immune systems of vertebrates, syringolides attract considerable chemical and biological interests. In order to clarify the action of elicitors, the establishment of the synthetic route and the provision of the radiolabelled compounds have been required. Therefore, several groups including us have synthesized syringolides and their related compound, syributin, until now.[4] In this paper, we mention the details of our

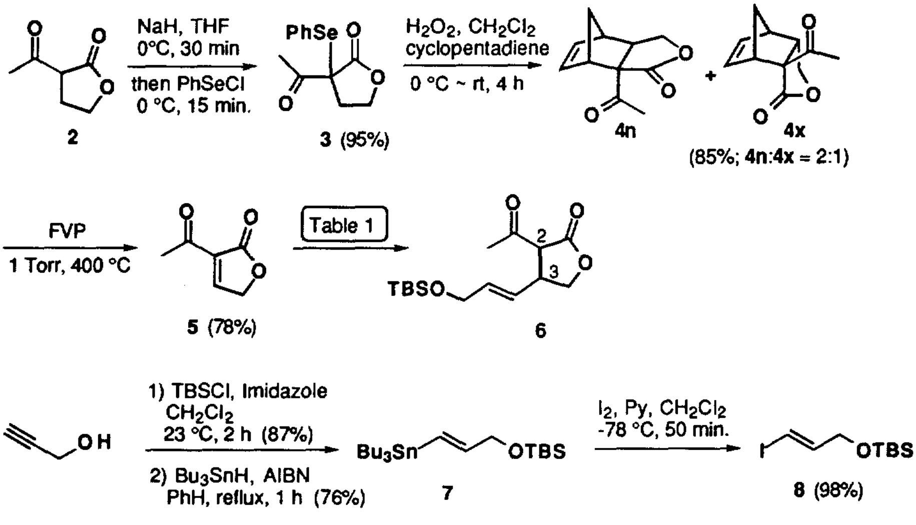


Syringolide 1 (**1a**; n=4)
Syringolide 2 (**1b**; n=6)

asymmetric synthesis of syringolide 1 (**1a**). Our synthetic strategy is 1,4-addition of an organocopper reagent to 2-acetyl-2-buten-4-olide (**5**), followed by an asymmetric dihydroxylation and an intramolecular Michael reaction.

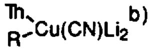
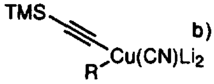
Results and Discussion

Compound **5** was prepared from commercially available 2-acetyl-4-butanolide (**2**). In the early papers,[5] **5** was synthesized from **2** in a two-step sequence [selenylation and oxidative elimination]. Although this procedure was attempted several times, overoxidation occurred immediately and none of **5** was obtained, and thus we made a detour. According to the method of Büchi,[6] the oxidative elimination of **3** in the presence of cyclopentadiene presented Diels-Alder adducts **4n** and **4x** in 85% combined yield. The subsequent flash vacuum thermolysis furnished compound **5** in a good yield even in a gram scale. Next, the 1,4-additon reactions of some organocopper reagents to the butenolide were explored (Table 1). Alkenyl compounds, **7** and **8**, were readily prepared from propargyl alcohol.[7] When the reactions were carried out using alkenylstannane **7**, the transmetalation was not completed and the respective yields of the desired compound **6** were less than 30% (entries 1-3). On the other hand, treatment with the cuprates, prepared from alkenyliodide **8**, resulted in moderate yield of **6** (entries 4-7). Using higher ordered alkenylcuprates, **5** was converted into **6** in 31-47% yield (entries 4-6). The best yield was obtained when the reaction was executed employing lithium alkenylcyanocuprate, prepared by the addition of the alkenyl iodide to *t*-BuLi, affording **6** in 49% yield (entry 7). The 2,3-substituents of **6** have *trans*-configuration and it was suggested from ^{1}H-NMR spectra in $CDCl_3$ that the keto and enol tautomers existed in the ratio of 14:1.



Scheme 1.

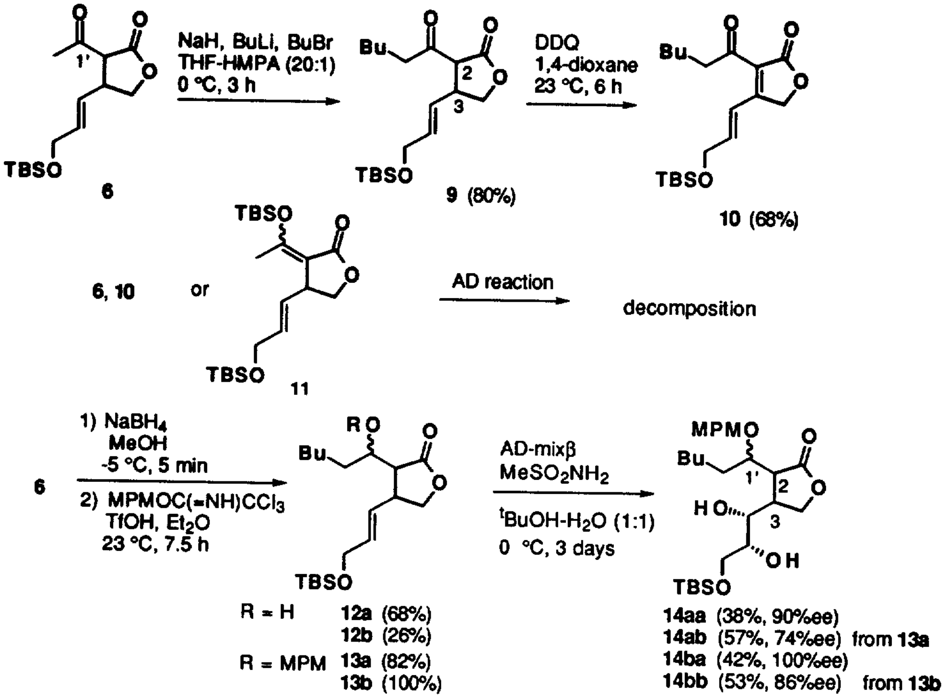
Table 1. 1,4-Addition of **5**.

entry	reagent	solvent	condition	yield
1	 $\mathrm{R(Me)Cu(CN)Li_2}$ a)	THF	-78 °C, 20 min.	25%
2	$\mathrm{R_2Cu(CN)Li_2}$ a)	THF	-78 °C, 20 min.	30%
3	$\mathrm{RCu{\cdot}BF_3}$ a)	THF	-78 °C, 2 h	decomp.
4	 $\mathrm{Th(R)Cu(CN)Li_2}$ b)	$\mathrm{THF\text{-}Et_2O}$ (2:5)	-78 °C ~ rt, 1 h	22%
5	 TMS, R, Cu(CN)Li$_2$ b)	THF	-78 °C, 20 min.	31%
6	$\mathrm{R_2Cu(CN)Li_2}$ b)	THF	-78 ~ -48 °C, 40 min.	47%
7	RCu(CN)Li c)	THF	-78 °C, 10 min.	49%

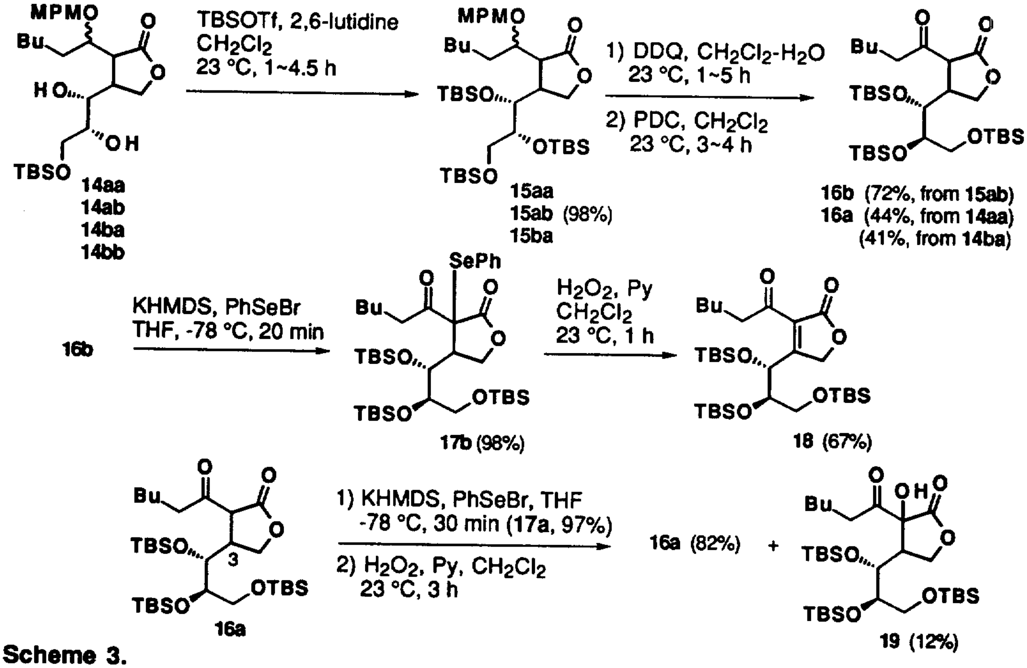
R = $\mathrm{TBSOCH_2CH{=}CH\text{-}}$. a) Prepared from alkenylstannane. b) The corresponding lithium compound was prepared by the addition of *t*-BuLi to alkenyl iodide. c) The corresponding lithium compound was prepared by the addition of the alkenyl iodide to *t*-BuLi.

The dianion of **6**, prepared by treatment with NaH and BuLi, was exposed to BuBr to afford 2,3-*trans*-compound **9** in 80% yield (Scheme 2). Oxidative elimination of **9** with DDQ gave conjugate diene **10** in 68% yield. Then, Sharpless asymmetric dihydroxylation (AD)[8] was investigated. In general, the oxidation of disubstituted olefins would proceed much faster than that of tetrasubstituted ones, and their enantioexcess yield would be high. Therefore, we selected compound **10** as a substrate of the AD reaction, though the dihydroxylation resulted in failure due to its lability. Treatment of compound **6** also gave a complex mixture. Since the enol olefin in the keto-enol equilibrium of **6** might be oxidized faster than the double bond in the side chain, the undesired oxidation would occur. It was verified by the evidence that the AD reaction of silyl enol ether **11** afforded similar decomposition products. Compound **6** was then reduced to give a mixture of diastereomers at C-1', **12a** (66%) and **12b** (26%). These alcohols were led to the corresponding MPM-ethers (**13a** and **13b**), respectively. AD reaction of compound **13a** proceeded smoothly to present compounds **14aa** (38%, 90%ee) and **14ab** (57%, 74%ee)[9]. Similarly, **13b** was converted into **14ba** (42%, 100%ee) and **14bb** (53%, 86%ee) (Scheme 2). Although the absolute stereochemistries at C-1', 2, and 3 of these products (**14aa**-**14bb**) were not determined, the relative stereochemistries of C-2 and 3 were found to be *trans*. The respective enantiomeric ratios were determined by ^{1}H-NMR analysis of their bis-MTPA esters.

Protection of **14ab** with TBSOTf and 2,6-lutidine afforded compound **15ab** (98%). Subsequent removal of the MPM group with DDQ and oxidation with PDC, gave compound **16b** in 85 % yield (Scheme 3). Similarly, the other two isomers, **14aa**, **14ba**, were converted to **16a**, but the transformation of **14bb** was unsuccessful. The phenylselenylation (KHMDS, PhSeBr, THF) of **16b** provided compound **17b**, which was subsequently oxidized to give an α,β-unsaturated ketone **18** in 65% yield. While **16a** was convertible into the phenylselenyl compound **17a** in good yield, the oxidative elimination of **17a** resulted in the regeneration of **16a** and formation of **19**. Various efforts to transform **16a** into **18** led to fruitless results probably due to *anti* relationship between the phenylselenyl group and the adjacent hydrogen atom at C-3 (Scheme 3).



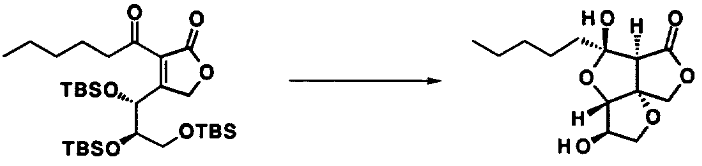
Scheme 2.



Scheme 3.

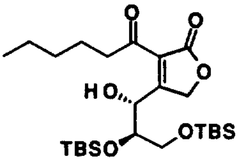
Detachment of the TBS group in **18** and the subsequent intramolecular Michael reaction were troublesome because of the lability of the products. Table 2 indicates the results of the investigation. Treatment of **18** with Bu_4NF gave decomposition products (entry 1). The moderate neutral conditions, such as HF-Py afforded a complex mixture. Exposure to acidic agents, such as HCl-THF, HF-THF-CH_3CN, or AcOH-THF-H_2O, gave also unsuccessful results (enties 3-5). When **18** was treated with SiF_4,[10] an unexpected acetal compound **21** was obtained quantitatively (enty 7), of which the structure was determined by ^{1}H-NMR, ^{13}C-NMR, and HMBC spectra. Reaction with $PdCl_2(CH_3CN)_2$ or KF/18-crown-6 gave an alcohol **20** (and/or acetal **21**) (entries 6 and 8). Eventually, we found that exposing **18** to PTS in THF-H_2O (10:1) afforded directly **1a** in 16% yield. The spectroscopic data (^{1}H- and ^{13}C-NMR and IR) of the synthetic sample of **1a** were in agreement with those reported by Kuwahara et al.[4b] The optical rotation of our synthetic sample was $[\alpha]_D^{22}$ -60 (*c* 0.03, $CHCl_3$) {lit.[4b] $[\alpha]_D^{24}$ -83.7 (*c* 0.15, $CHCl_3$)}, since we used compound **14ab**, which was estimated to be 87%ee. In conclusion, we accomplished the asymmetric synthesis of syringolide 1 from commercially available 2-(1-oxoethyl)-4-butanolide in 13 steps.

Table 2. Removal of the TBS groups of 18.



18 **1a**

entry	reagent	solvent	time	temp.	results
1	TBAF	THF	1 day	23 °C	decomp.
2	HF-Py	THF	36 h	23 °C	decomp.
3	46% HF aq.	CH_3CN	1 day	23 °C	decomp.
4	36% HCl aq.	THF	1 day	23 °C	decomp.
5	THF-AcOH-H_2O (8:3:1)	-	1 day	55 °C	**18**, 76%
6	KF, 18-crown-6	CH_3CN	8 h	23 °C	**20**, 42%
7	SiF_4	CH_3CN	3 h	23 °C	**21**, 100%
8	$PdCl_2(CH_3CN)_2$	H_2O-acetone (1:100)	30 h	23 °C	**20**, 27% **21**, 18%
9	PTS•H_2O	acetone-H_2O (2.5:1)	2 days	23 °C	**1**, 13% **21**, 6%
10	PTS•H_2O	THF-H_2O (10:1)	5 days	23 °C	**1**, 16% **21**, 23%
11	PTS•H_2O	THF	2 days	23 °C	**1**, 12%



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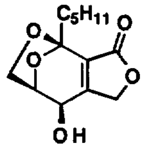

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Experimental

Solvents and reagents were dried and distilled before use. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. CH_2Cl_2, Pyridine, and Et_3N were distilled from CaH_2. DMSO were distilled under reduced pressure from CaH_2. EtOH and MeOH were distilled from their magnesium alkoxides. Normal reagent-grade solvents were used for flash chromatography and extraction. All reactions were monitored by tlc with precoated SiO_2 plates (E. Merck, silica gel 60 F_{254} Art. 5715). Visualization was achieved *via* UV light and a 5.6% ethanolic *p*-anisaldehyde solution containing 5.6% of concentrated H_2SO_4-heat. For flash chromatography was utilized SiO_2 (YMG, silica gel SIL-60-400/230W). HPLC was run with a Waters Associates 600 liquid chromatography equipped with a JASCO UNIDEC-100 UV spectrophotometer. Recycling preparative HPLC was performed with a Japan Analytical Industry LC-908. Melting points were determined in open capillary tubes and are uncorrected. IR spectra were obtained on a Hitachi model 270-30 infrared spectrophotometer in neat state or in $CHCl_3$ solution. The ^{1}H-NMR spectra were recorded on a JEOL model EX-400 and α-400 (400 MHz) spectrometer in $CDCl_3$. The ^{13}C-NMR spectra were measured on a JEOL model α-400 (100 MHz) spectrometer in $CDCl_3$. Chemical shifts (δ) are reported with tetramethylsilane (δ = 0.00 ppm) or $CHCl_3$ (δ = 7.26 ppm) as internal standards. Splitting patterns are designated as "s, d, t, q, m, and br"; indicating "singlet, doublet, triplet, quartet, multiplet, and broad", respectively. Optical rotations were recorded on JASCO model DIP-360 digital polarimeter using $CHCl_3$ as a solvent. Low- and high-resolution mass spectra (LRMS and HRMS) were obtained on a JEOL model JMS-HX-110 mass spectrometer under EI and fast atom bombardment (FAB) conditions. All reactions were carried out under anhydrous conditions and argon atmosphere, unless otherwise noted.

3-(*tert*-Butyldimethylsiloxy)-1-iodopropene (8): To a stirred solution of propenylstannane **7** (5.05 g, 10.9 mmol), prepared by the method of the previous paper,[7] in CH_2Cl_2 (100 ml) were added iodine (3.06 g, 12.1 mmol) and pyridine (1.15 ml, 14.2 mmol) at -78 °C. After stirring for 50 min, the mixture was treated with satd aq. $Na_2S_2O_5$ (60 ml) and the aq. layer was extracted with CH_2Cl_2 (2 × 50 ml). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was diluted with Et_2O (80 ml) and aq. KF (16 g/80 ml), and the mixture was stirred vigorously for 12 h. The precipitate was filtered off and the filtrate was extracted with ether (30 ml). The extract was dried over $MgSO_4$ and concentrated *in vacuo*. The crude compound was purified by distillation (84 °C, 1.8 Torr) to give compound **8** (2.69 g, 9.02 mmol, 83%) as a colorless oil. **8**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.07 (6H, s), 0.90 (9H, s), 4.41 (2H, dd, J = 2.0, 4.6 Hz), 6.29 (1H, dt, J = 14.2, 2.0 Hz), and 6.60 (1H, dt, J = 4.6, 14.2 Hz); IR (neat), vmax 2956, 2932, 2890, 2854, 1611, 1467, 1392, 1257, 1128, 1098, 837, and 777 cm^{-1}.

(1'*E*)-2-Acetyl-3-[3'-(*tert*-butyldimethylsiloxy)-1'-propenyl]-4-butanolide (6): To a mixture of *t*-BuLi (1.56 mol/l solution in pentane, 17.0 ml, 26.5 mmol) and THF (18 ml) was added a solution of **8** (3.41 g, 11.4 mmol) in THF (35 ml) at -78 °C over 20 min and the mixture was stirred at that temperature for 2 h. The vinyl lithium solution was thus prepared. This solution was added dropwise to a suspension of CuCN (1.18 g, 13.2 mmol) in THF (40 ml) over 10 min and the mixture was stirred at -78 °C for 50 min. To the mixture was added a solution of **5** (1.15 g, 9.10 mmol) in THF (15 ml) at -78 °C, and stirring was continued for additional

10 min. The reaction mixture was quenched by a mixture of satd aq. NH_4Cl-25% NH_3 (9:1) (70 ml), and extracted with ether (2 × 50 ml). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was subjected to column chromatography (SiO_2, 9% EtOAc in hexane) to furnish the desired compound **6** (1.31 g, 4.39 mmol, 48%) as a colorless oil. **6**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.06 (6H, s), 0.90 (9H, s), 2.44 (3H, s), 3.51 (1H, d, *J* = 9.2 Hz), 4.14-4.31 (1H, m), 4.01 (1H, dd, *J* = 8.6, 8.9 Hz), 4.20 (2H, dd, *J* = 1.5, 6.6 Hz), 4.46 (1H, dd, *J* = 8.2, 8.6 Hz), 5.59 (1H, ddt, *J* = 1.5, 11.7, 23.6 Hz), and 5.75 (1H, dt, *J* = 6.6, 23.6 Hz); IR (neat), νmax 2956, 2982, 2856, 1776, 1724, 1610, 1466, 1362, 1252, 838, 812, and 778 cm^{-1}; EI-MS-HR, calcd. for $C_{14}H_{23}O_4Si$ (M^+-CH_3) 283.1366, found 283.1339; calcd. for $C_{11}H_{17}O_4Si$ (M^+-C_4H_9) 241.0896, found 241.0904.

(1'*E*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1'-propenyl]-2-hexanoyl-4-butanolide (9): To a suspension of NaH (60 % dispersion in oil, 375.3 mg, 9.38 mmol) in THF (18 ml) and HMPA (2.69 mmol, 15.5 mmol) was added a solution of **6** (2.10 g, 7.03 mmol) in THF (8 ml) at 0 °C over 6 min. After stirring at the same temperature for 40 min, BuLi (a solution of 1.68 mmol/l in hexane, 4.6 ml, 7.73 mmol) was added dropwise over 10 min, and the mixture was stirred for 10 min. Butyl bromide (1.02 ml, 9.49 mmol) was then added and the reaction mixture was stirred for additional 40 min. The reaction was quenched by satd aq. NH_4Cl (20 ml), and the aq. layer was extracted with ether (3 × 20 ml). Drying over $MgSO_4$, concentration *in vacuo*, and the flash chromatography (SiO_2, 5% EtOAc in hexane to 13% EtOAc in hexane) gave compound **9** (2.00 g, 5.64 mmol, 80%) as a colorless oil. **9**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.06 (6H, s), 0.90 (9H, s), 0.84-1.00 (4H, m), 1.22-1.38 (3H, m), 1.56-1.64 (2H, m), 2.55 (1H, dt, *J* = 17.8, 7.3 Hz), 2.94 (1H, dt, *J* = 17.8, 7.4 Hz), 3.50 (1H, d, *J* = 9.2 Hz, H-2), 3.66-3.80 (1H, m), 4.00 (1H, t, *J* = 8.9 Hz), 4.14 (2H, dd, *J* = 1.0, 4.3 Hz), 4.46 (1H, dd, *J* = 7.9, 8.9 Hz), 5.52-5.67 (1H, m), and 5.74 (1H, dt, *J* = 15.5, 4.3 Hz); IR (neat), νmax 2932, 2806, 1776, 1722, 1647, 1467, 1341, 1254, 837, and 777 cm^{-1}; EI-MS-HR, calcd. for $C_{18}H_{31}O_4Si$ (M^+-CH_3) 339.1991, found 339.1971.

(1'*E*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1'-propenyl]-2-(1"-hydroxyhexanoyl)-4-butanolide (12a) and (12b): A mixture of **9**, $NaBH_4$ (464 mg, 12.3 mmol), and methanol (120 ml) was stirred at -5 °C for 70 min. Dilution with satd aq. NH_4Cl (40 ml) and water (70 ml), followed by extraction with EtOAc (3 × 70 ml), drying over $MgSO_4$, and solvent removal gave a crude oil. The oil was subjected to flash chromatography (SiO_2, 12.5% EtOAc in hexane-20% EtOAc in hexane) to furnish compound **12a** (2.98 g, 8.36 mmol, 68%) as a colorless oil and **12b** (1.14 g, 3.20 mmol, 26%) as a colorless oil. **12a**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.07 (6H, s), 0.91 (9H, s), 0.83-0.97 (3H, m), 1.10-1.68 (8H, m), 2.41 (1H, dd, *J* = 6.1, 5.5 Hz), 3.04-3.16 (1H, m), 3.17 (1H, br d, *J* = 4.0 Hz), 3.72-3.80 (1H, m), 3.89 (1H, dd, *J* = 8.9, 9.9 Hz), 4.16 (2H, dd, *J* = 4.3, 1.7 Hz), 4.38 (1H, t, *J* = 8.9 Hz), 5.54 (1H, ddt, *J* = 15.2, 8.4, 1.7 Hz), and 5.76 (1H, dt, *J* = 15.2, 4.3 Hz); IR (neat), νmax 3508, 2926, 2734, 1767, 1470, 1257, 966, 840, and 777 cm^{-1}; EI-MS-HR, calcd. for $C_{18}H_{33}O_4Si$ (M^+-CH_3) 341.2148, found 341.2134. **12b**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.07 (6H, s), 0.91 (9H, s), 0.84-0.97 (3H, m), 1.19-1.66 (8H, m), 2.11 (1H, br d, *J* = 5.9 Hz), 2.54 (1H, dd, *J* = 10.1, 2.8 Hz), 3.32-3.49 (1H, m), 3.89 (1H, t, *J* = 9.2 Hz), 4.15 (2H, dd, *J* = 4.3, 1.7 Hz), 4.13-4.25 (1H, m), 4.37 (1H, dd, *J* = 9.2, 8.6 Hz), 5.62 (1H, ddt, *J* = 15.2, 8.6, 1.7 Hz), and 5.76 (1H, dt, *J* = 15.2, 4.3 Hz); IR (neat), νmax 3478, 2932, 2860, 1767, 1467, 1341, 1257, 975, 837, and 777 cm^{-1}; FAB-MS-HR, calcd. for $C_{19}H_{37}O_4Si$ (M^++H) 357.2461, found 357.2485.

(1'*E*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1'-propenyl]-2-[1"-(4-methoxyphenylmethoxy)hexanoyl]-4-butanolide (13a): To a solution of **12a** (1.00 g, 2.80 mmol) in ether (25 ml) were added 4-methoxybenzyl 2,2,2-trichloroacetimidate (1.16 ml, 5.61 mmol) and trifluoromethanesulfonic acid (0.02 mol/l solution in ether, 42 µl, 0.84 µmol). After stirring at 23 °C for 7.5 h, a solution of trifluoromethanesulfonic acid in ether (250 µl, 5.00 µmol) was added, and stirring was continued for additional 3 h. The reaction mixture was diluted with satd aq. $NaHCO_3$ (10 ml), extracted with ether (2 × 10 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, PhH-1.6% EtOAc in PhH) to provide compound **13a** (1.09 g, 2.29 mmol, 82%) as a colorless oil. **13a**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.06 (6H, s), 0.88 (3H, t, *J* = 6.6 Hz), 0.90 (9H, s), 1.22-1.38 (6H, m), 1.62-1.76 (2H, m), 2.68 (1H, dd, *J* = 9.2, 3.3 Hz), 3.11-3.22 (1H, m), 3.70 (1H, dt, *J* = 3.3, 6.8 Hz), 3.80 (3H, s), 3.90 (1H, t, *J* = 8.6 Hz), 4.10 (2H, br d, *J* = 2.6 Hz), 4.35 (1H, t, *J* = 8.6 Hz), 4.42 (1H, d, *J* = 11.4 Hz), 4.50 (1H, d, *J* = 11.4 Hz), 5.52 (1H, dt, *J* = 15.2, 4.0 Hz), 5.60 (1H, dd, *J* = 15.2, 6.6 Hz), 6.87 (2H, d, *J* = 8.6 Hz), and 7.24 (2H, d, *J* = 8.6 Hz); IR (neat), νmax 2932, 2860, 1779, 1617, 1587, 1515, 1470, 1251, 837, and 777 cm^{-1}; EI-MS-HR, calcd. for $C_{27}H_{44}O_5Si$ (M^+) 476.2958, found 476.2987.

(1'*E*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1'-propenyl]-2-[1"-(4-methoxyphenylmethoxy)hexanoyl]-4-butanolide (13b): As described above, **12b** (1.14 g, 3.21 mmol) was converted into 4-methoxyphenybenzyl ether **13b** (1.62 g, 3.21 mmol, 100%) as a colorless oil. **13b**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.06 (6H, s), 0.87 (3H, t, *J* = 6.6 Hz), 0.90 (9H, s), 1.19-1.30 (6H, m), 2.13-2.28 (2H, m), 2.52 (1H, dd, *J* = 8.6, 2.0 Hz, H-2), 3.37-3.45 (1H, m), 3.80 (3H, s), 3.89 (1H, t, *J* = 8.6 Hz), 4.04 (1H, br dt, *J* = 2.0, 7.4 Hz), 4.13 (2H, d, *J* = 3.6 Hz), 4.37 (1H, dd, *J* = 8.6, 8.9 Hz), 4.47 (2H, s), 5.62 (1H, br dd, *J* = 2.0, 7.4 Hz), 5.72 (1H, dt, *J* = 15.2, 3.6 Hz), 6.86 (2H, d, *J* = 8.4 Hz), and 7.23 (2H, d, *J* = 8.4 Hz); IR (neat), νmax 2932, 2860, 1776, 1617, 1587, 1515, 1467, 1248, 837, and 777 cm^{-1}; EI-MS-HR, calcd. for $C_{27}H_{44}O_5Si$ (M^+) 476.2958, found 476.2948.

(1'*R*,2'*R*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1',2'-(dihydroxyl)propyl]-2-[1"-(4-methoxyphenylmethoxy)-hexyl]-butanolide (14aa) and (14ab): To a stirred mixture of **13a** (1.05 g, 2.20 mmol) in *t*-BuOH (11.5 ml) and water (11.5 ml) were added AD-mix β (4.65 g) and methanesulfonamide (321.5mg) at 0 °C. After stirring at the same temperature for 16.5 h , Na_2SO_3 (4.96 g) was added and the mixture was stirred at 23 °C for 2.5 h, extracted with EtOAc (3 × 50 ml), and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was diluted with CH_2Cl_2, then filtered through Celite. Concentration *in vacuo* and flash chromatography (SiO_2, 25% EtOAc in hexane) afforded compound **14aa** (421 mg, 0.825 mmol, 38%) as a colorless oil and compound **14ab** (637 mg, 1.247 mmol, 57%) as a colorless oil. **14aa**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.07 (3H, s), 0.08 (3H, s), 0.86 (3H, t, *J* = 6.8 Hz), 0.90 (9H, s), 1.25-1.46 (6H, m), 1.56-1.67 (2H, m), 2.56 (1H, d, *J* = 7.6 Hz), 2.86-2.94 (2H, m), 3.41 (1H, br dt, *J* = 7.6, 6.0 Hz), 3.60 (1H, br dd, *J* = 5.6, 2.0 Hz), 3.67 (2H, dd, *J* = 6.0, 2.0 Hz), 3.81 (3H, s), 3.89 (1H, br t, *J* = 8.8 Hz), 3.98 (1H, dt, *J* = 9.2, 2.8 Hz), 4.29 (1H, d, *J* = 2.0 Hz), 4.39 (1H, br dd, *J* = 8.4, 8.8 Hz), 4.56 (2H, d, *J* = 1.6 Hz), 6.88 (2H, d, *J* = 8.8 Hz), and 7.26 (2H, d, *J* = 8.8 Hz); IR (neat), νmax 3406, 2932, 2860, 1770, 1614, 1587, 1518, 1470, 1251, 1176, 837, and 780 cm^{-1}; FAB-MS-HR, calcd. for $C_{27}H_{45}O_7Si$ (M^+-H) 509.2934, found 509.2957. **14ab**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.09 (6H, s), 0.87 (3H, t, *J* = 6.8 Hz), 0.90 (9H, s), 1.23-1.38 (6H, m), 1.42-1.52 (2H, m), 2.67 (1H, d, *J* = 6.1 Hz), 2.73 (1H, dq, *J* = 4.8, 8.8 Hz), 3.02 (1H, d, *J* = 4.8 Hz), 3.12 (1H, dd, *J* = 5.8, 8.8 Hz), 3.53-3.56 (1H, m), 3.67 (1H, dd, *J* = 4.6, 10.1 Hz), 3.72 (1H, dd, *J* = 4.0, 10.1 Hz), 3.78 (1H, dd, *J* = 2.0, 4.8 Hz), 3.80 (3H, s), 3.85-3.89 (1H, m), 4.34 (2H, dd, *J* = 8.8, 2.8 Hz), 4.47 (1H, d, *J* = 11.2 Hz), 4.54 (1H, d, *J* = 11.2 Hz), 6.87 (2H, d, *J* = 8.6 Hz), and 7.26 (2H, d, *J* = 8.6 Hz); IR (neat), νmax 3496, 2932, 2860, 1767, 1617, 1587, 1515, 1470, 1251, 1176, 837, and 780 cm^{-1}; FAB-MS-HR, calcd. for $C_{27}H_{45}O_7Si$ (M^+-H) 509.2934; found 509.2965.

(1'*R*,2'*R*)-3-[3'-(*tert*-Butyldimethylsiloxy)-1',2'-(dihydroxyl)propyl]-2-[1"-(4-methoxyphenylmethoxy)-hexyl]-butanolide (14ba) and (14bb): Analogously described above, **13b** (1.50 g, 3.15 mmol) was transformed

into compound 14ba (671.5 mg, 1.315 mmol, 42%) and compound 14bb (856.8 mg, 1.677 mmol, 53%). **14ba**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.08 (6H, s), 0.87-0.92 (12H, m), 1.26-1.41 (6H, m), 1.55-1.62 (1H, m), 1.73-1.80 (1H, m), 2.66 (1H, d, *J* = 7.2 Hz), 2.83 (1H, ddt, *J* = 8.2, 9.2, 3.4 Hz), 2.92 (1H, t, *J* = 3.4 Hz), 3.24 (1H, d, *J* = 4.4 Hz), 3.56 (1H, ddd, *J* = 1.2, 4.4, 8.2 Hz), 3.68-3.78 (3H, m), 3.80 (3H, s), 3.94 (1H, dt, *J* = 3.4, 6.4 Hz), 4.04 (1H, dd, *J* = 3.4, 9.2 Hz), 4.37 (1H, t, *J* = 9.2 Hz), 4.42 (1H, d, *J* = 10.8 Hz), 4.51 (1H, d, *J* = 10.8 Hz), 6.86 (2H, d, *J* = 8.4 Hz), and 7.22 (2H, d, *J* = 8.4 Hz); IR (neat), vmax 3472, 2932, 2860, 1767, 1617, 1587, 1515, 1470, 837, and 780 cm^{-1}; FAB-MS-HR, calcd. for $C_{27}H_{45}O_7Si$ (M^+-H) 509.2934, found 509.2954. **14bb**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.09 (6H, s), 0.86-0.94 (12H, m), 1.24-1.38 (6H, m), 1.46-1.55 (1H, m), 1.71-1.81 (1H, m), 2.70 (1H, dd, *J* = 2.6, 6.4 Hz), 2.84-2.91 (1H, m), 3.67-3.77 (4H, m), 3.80 (3H, s), 4.03 (1H, dt, *J* = 2.6, 6.6 Hz), 4.32 (1H, t, *J* = 8.6 Hz), 4.43 (1H, d, *J* = 10.6 Hz), 4.45 (1H, m), 4.49 (1H, d, *J* = 10.6 Hz), 6.86 (2H, d, *J* = 8.4 Hz), and 7.22 (2H, d, *J* = 8.4 Hz); IR (neat), vmax 3472, 2932, 2860, 1752, 1614, 1587, 1515, 1470, 837, and 780 cm^{-1}; FAB-MS-HR, calcd. for $C_{27}H_{45}O_7Si$ (M^+-H) 509.2934, found 509.2954.

Bis-MTPA ester of 14ab: A mixture of **14ab** (8.9 mg, 17.6 μmol), *R*-MTPACl (20 μl, 105 μmol), Et_3N (30 μl, 210 μmol), Et_2NH (20 μl, 176 μmol), and a catalytic amount of DMAP in CH_2Cl_2 was stirred at 23 °C for 1 h. Concentration and flash chromatography (9% EtOAc in hexane) gave Bis-MTPA ester (15.1 mg, 16.0 μmol, 91 %). ^{1}H NMR (400 MHz, $CDCl_3$), δ 0.02 (6H, s) 0.86 (9H, s), 0.88 (3H, t, *J* = 6.8 Hz), 1.24-1.36 (6H, m), 1.49-1.51 (1H, m), 1.58-1.63 (1H, m), 2.67 (1H, dd, *J* = 3.2, 7.6 Hz), 2.74 (1H, dq, *J* = 3.2, 7.6 Hz), 3.40 (3H, s), 3.41 (1H, dd, *J* = 10.4, 7.6 Hz), 3.50 (3H, s), 3.59 (1H, dd, *J* = 10.4, 7.6 Hz), 3.70 (1H, ddd, *J* = 3.2, 5.2, 8.0 Hz), 3.79-3.81 (1H, m), 3.82 (3H, s), 4.44 (2H, s), 4.38 (1H, d, *J* = 10.4 Hz), 4.98 (1H × 0.13, dt, *J* = 3.2, 6.5 Hz), 5.08 (1H × 0.87, dt, *J* = 3.2, 6.5 Hz), 5.56 (1H × 0.13, brt, *J* = 3.2 Hz), 5.61 (1H × 0.87, brt, *J* = 3.2 Hz), 6.89 (2H, d, *J* = 8.6 Hz), 7.25 (2H, d, *J* = 8.6 Hz), 7.38-7.46 (6H, m), and 7.52-7.56 (4H, m); IR (neat), vmax 3070, 2956, 2860, 1758, 1614, 1587, 1518, 1470, 837, 780, 765, 720, and 699 cm^{-1}; FAB-MS-HR calcd. for $C_{47}H_{59}F_6O_{11}Si$ (M^+-H) 941.3731, found 941.3705.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-[1''-(4-methoxyphenylmethoxy)hexyl]-4-butanolide (15ab): A mixture of **14ab** (135 mg, 0.26 mmol), 2,6-lutidine (0.28 μl, 2.4 mmol), and *t*-butyldimethylsilyl trifluoromethanesulfonate (276 μl, 1.2 mmol) in CH_2Cl_2 (3 ml) was stirred at 23 °C for 4.5 h. The mixture was diluted with brine (5 ml), and extracted with CH_2Cl_2 (2 × 5 ml), followed by drying over $MgSO_4$ and concentration *in vacuo*. The resulting residue was chromatographed on SiO_2 (5% EtOAc in hexane) to give compound **15ab** (189 mg, 0.256 mmol, 98%) as a colorless oil. **15ab**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.03 (6H, s), 0.04 (3H, s), 0.05 (3H, s), 0.06 (3H, s), 0.07 (3H, s), 0.86-0.89 (30H, m), 1.23-1.33 (6H, m), 1.51-1.57 (1H, m), 1.67-1.77 (1H, m), 2.84-2.93 (2H, m), 3.27 (1H, dd, *J* = 8.1, 10.1 Hz), 3.68-3.84 (4H, m), 3.80 (3H, s), 4.13 (1H, t, *J* = 8.4 Hz), 4.23 (1H, dd, *J* = 5.6, 8.4 Hz), 4.45 (1H, d, *J* = 12.0 Hz), 4.49 (1H, d, *J* = 12.0 Hz), 6.86 (2H, d, *J* = 8.5 Hz), and 7.22 (2H, d, *J* = 8.5 Hz); IR (neat), vmax 2932, 2860, 1776, 1614, 1587, 1515, 1470, 1248, 834, 774, and 672 cm^{-1}; FAB-MS-HR, calcd. for $C_{39}H_{73}O_7Si_3$ (M^+-H) 737.4664, found 737.4650.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-4-butanolide (16b): To a stirred mixture of **15ab** (156 mg, 0.21 mmol) in CH_2Cl_2 (3.6 ml) and water (0.2 ml) was added DDQ (72.0 mg, 0.32 mmol). After vigorous stirring at 23 °C for 4.5 h, the reaction mixture was diluted with satd aq. $NaHCO_3$ (5ml), followed by extraction with CH_2Cl_2 (2 × 4 ml) and washing with satd aq. $NaHCO_3$ (3 ml). Drying over $MgSO_4$, concentration *in vacuo*, and flash chromatography (SiO_2, 3% EtOAc in hexane) afforded an alcohol

(112 mg, 86%) as a colorless oil. **15ab**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.05 (6H, s), 0.09 (3H, s), 0.096 (3H, s), 0.102 (3H, s), 0.11 (3H, s), 0.85-0.92 (30H, m), 1.25-1.42 (6H, m), 1.50-1.73 (2H, m), 2.55 (1H, dd, *J* = 5.3, 8.6 Hz), 2.66 (1H, d, *J* = 4.9 Hz), 2.85-2.94 (1H, m), 3.31 (1H, dd, *J* = 7.6, 13.2 Hz), 3.64-3.82 (4H, m), 4.19 (1H, t, *J* = 8.6 Hz), and 4.26 (1H, t, *J* = 8.6 Hz); IR (neat), νmax 3496, 2956, 2710, 1770, 1473, 1257, 834, 777, and 669 cm^{-1}; FAB-MS-HR calcd. for $C_{31}H_{67}O_6Si_3$ (M^++H) 619.4245, found 619.4275.

A mixture of this alcohol (192 mg, 0.31 mmol), MS-4A (200 mg), and PCC (143 mg, 0.66 mmol) in CH_2Cl_2 (4 ml) was stirred at 23 °C for 3 h. Dilution with 9% EtOAc in hexane (3 ml), addition of $MgSO_4$, filtration, and concentration *in vacuo* gave a crude mixture. The residue was purified by flash chromatography (SiO_2, 3% EtOAc in hexane), providing compound **16b** (163 mg, 0.26 mmol, 84%) as white crystals. **16b**: m.p. 67-72 °C; ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.04 (3H, s), 0.05 (3H, s), 0.06 (3H, s), 0.07 (3H, s), 0.08 (3H, s), 0.10 (3H, s), 0.86-0.91 (30H, m), 1.28-1.32 (6H, m), 1.54-1.63 (2H, m), 2.57 (1H, dt, *J* = 17.8, 7.3 Hz), 2.93 (1H, dt, *J* = 17.8, 7.4 Hz), 3.31-3.35 (2H, m), 3.61-3.67 (1H, m), 3.71-3.76 (2H, m) 3.83 (1H, d, *J* = 7.6 Hz), 4.17 (1H, dd, *J* = 6.6, 8.6 Hz), and 4.31 (1H, t, *J* = 8.6 Hz); IR (neat), νmax 2932, 2860, 1776, 1725, 1470, 1257, 837, and 669 cm^{-1}; FAB-MS-HR, calcd. for $C_{31}H_{65}O_6Si_3$ (M^++H) 617.4089, found 617.4119.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-4-butanolide (16a) from 14aa: By the procedure described for **14ab**, **14aa** (618 mg, 1.21 mmol) was converted to an alcohol (914mg), a part of which (28.0 mg) was purified by SiO_2 chromatography (9% EtOAc in hexane) to give a pure sample (14.8 mg, the yield was evaluated 66% from **14aa**). This alcohol (31.4 mg, 0.051 mmol) was transformed into compound **16a** (20.7 mg, 0.034 mmol, 67%). **15aa**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.01 (6H, s), 0.03 (6H, s), 0.07 (6H, s), 0.83-0.91 (30H, m), 1.25-1.41 (6H, m), 1.73-1.80 (1H, m), 1.93-2.03 (1H, m), 2.77 (1H, ddd, *J* = 7.3, 9.5, 14.7 Hz), 2.92 (1H, dd, *J* = 2.2, 9.5 Hz), 3.56 (1H, dd, *J* = 8.8, 13.2 Hz), 3.65-3.70 (4H, m), 3.74 (1H, ddd, *J* = 2.2, 4.4, 8.8 Hz), 3.79 (3H, s), 4.33 (1H, d, *J* = 11.4 Hz), 4.41 (1H, dd, *J* = 1.5, 7.3 Hz), 4.57 (1H, d, *J* = 11.4 Hz), 6.84 (2H, d, *J* = 8.4 Hz), and 7.21 (2H, d, *J* = 8.4 Hz); IR (neat), νmax 2932, 2860, 1776, 1617, 1587, 1518, 1470, 1251, 834, 777, 717, and 669 cm^{-1}; FAB-MS-HR, calcd. for $C_{39}H_{73}O_7Si_3$ (M^+-H) 737.4664, found 737.4634. **16a**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.03 (3H, s), 0.04 (3H, s), 0.05 (6H, s), 0.06 (3H, s), 0.10 (3H, s), 0.81-0.90 (30H, m), 1.25-1.37 (6H, m), 1.58-1.65 (2H, m), 2.63 (1H, dt, *J* = 18.3, 7.4 Hz), 2.95 (1H, dt, *J* = 18.3, 7.6 Hz), 3.58-3.77 (6H, m), and 4.52 (1H, dd, *J* = 2.5, 8.1 Hz); IR (neat), νmax 2932, 2860, 1772, 1724, 1650, 1472, 1258, 838, and 672 cm^{-1}.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-4-butanolide (16a) from 14ba: Analogously, **14ba** (672 mg, 1.31 mmol) was converted to an alcohol (567mg, 0.916 mmol, 70%). This alcohol (552 mg, 0.892 mmol) was oxidized to **16a** (326 mg, 0.528 mmol, 59%). **15ba**: ^{1}H-NMR (400 MHz, $CDCl_3$), δ 0.05 (6H, s), 0.060 (3H, s), 0.062 (3H, s), 0.095 (3H, s), 0.099 (3H, s), 0.86-0.90 (30H, m), 1.26-1.40 (6H, m), 1.63-1.72 (1H, m), 1.87-2.00 (1H, m), 2.58 (1H, br dt, *J* = 3.7, 9.2 Hz), 3.12 (1H, dd, *J* = 6.0, 9.2 Hz), 3.52 (1H, dd, *J* = 9.2, 13.6 Hz), 3.65-3.72 (3H, m), 3.80 (3H, s), 3.85 (1H, dd, *J* = 3.7, 10.6 Hz), 3.95 (1H, dt, *J* = 11.2, 6.0 Hz), 4.40 (1H, d, *J* = 10.8 Hz), 4.52 (1H, d, *J* = 10.8 Hz), 4.67 (1H, br s), 6.85 (2H, d, *J* = 8.8 Hz), and 7.21 (2H, d, *J* = 8.8 Hz); IR (neat), νmax 2932, 2860, 1776, 1617, 1587, 1518, 1470, 1251, 837, 777, 717, and 669 cm^{-1}; FAB-MS-HR, calcd. for $C_{39}H_{73}O_7Si_3$ (M^+-H) 737.4664, found 737.4652.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-2-phenylselenyl-4-butanolide (17b): To a solution of **16b** (132 mg, 0.214 mmol) in THF (2 ml) was added dropwise KHMDS (0.5 M solution in PhMe, 510 μl, 0.26 mmol) at -78 °C over 5 min. After stirring for 1 h, a solution of PhSeBr (0.5 ml) was added, and stirring was continued at the same temperature for additional 20 min. The reaction

mixture was diluted with satd aq. NH_4Cl (2 ml), extracted with ether (3 × 2 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, hexane-2% EtOAc in hexane) to furnish compound 17b (162 mg, 0.210 mmol, 98%) as a colorless oil. **17b**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.03-0.11 (18H, m), 0.75-0.94 (30H, m), 1.09-1.39 (4H, m), 1.49-1.69 (2H, m), 2.70 (1H, ddd, *J* = 6.1, 8.7, 19.1 Hz), 2.90 (1H, ddd, *J* = 6.3, 8.7, 19.1 Hz) 3.05 (1H, d, *J* = 5.6 Hz), 3.44 (1H, dd, *J* = 5.8, 9.9 Hz), 3.57-3.63 (1H, m), 3.73 (1H, dd, *J* = 3.0, 9.9 Hz), 4.13 (1H, d, *J* = 4.6 Hz), 4.46 (1H, d, *J* = 8.9 Hz), 4.54 (1H, dd, *J* = 5.6, 8.9 Hz), 7.29-7.39 (3H, m), and 7.54-7.59 (2H, m); IR (neat), vmax 2932, 2860, 1767, 1695, 1578, 1473, 1443, and 1257 cm^{-1}.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-2-phenylselenyl-4-butanolide (17a): By the procedure described for **16b**, **16a** (111 mg, 0.180 mmol) was converted to compound **17a** (134 mg, 0.174 mmol, 97%) as a colorless oil. **17a**: ^{1}H-NMR (270 MHz, $CDCl_3$), δ 0.03 (6H, s), 0.05 (3H, s), 0.07 (3H, s), 0.10 (6H, s), 0.81-0.93 (30H, m), 1.13-1.32 (4H, m), 1.38-1.61 (2H, m), 2.52-2.77 (2H, m), 3.25 (1H, ddd, *J* = 5.6, 7.3, 8.9 Hz), 3.56 (1H, dd, *J* = 5.9, 9.6 Hz), 3.62 (1H, dd, *J* = 7.9, 9.6 Hz), 3.82 (1H, ddd, *J* = 1.0, 5.9, 7.9 Hz), 3.97 (1H, dd, *J* = 7.3, 9.9 Hz), 4.04 (1H, dd, *J* = 5.6, 9.9 Hz), 4.41 (1H, dd, *J* = 1.0, 8.9 Hz), 7.29-7.43 (3H, m), and 7.59-7.66 (2H, m); IR (neat), vmax 3058, 2932, 2860, 1767, 1704, 1578, 1473, 1443, and 1257 cm^{-1}.

(1'*R*,2'*R*)-3-[1',2',3'-tris(*tert*-Butyldimethylsiloxy)propyl]-2-hexanoyl-4-butenolide (18): A mixture of **17b** (162 mg, 0.21 mmol), pyridine (60 µl, 0.74 mmol), H_2O_2 (34.5% aq. solution, 56 µl, 0.62 mmol) in CH_2Cl_2 (2 ml) was stirred at 0 °C for 1 h. The reaction mixture was diluted with brine (2 ml) and extracted with ether (3 × 2 ml). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-2% EtOAc in hexane) to furnish compound **18** (85.9 mg, 67%) as white crystals. **18**: m.p. 54-60 °C; ^{1}H-NMR ($CDCl_3$, 270 MHz), δ -0.17 (3H, s), -0.04 (3H, s), 0.01 (3H, s), 0.08 (3H, s), 0.11 (3H, s), 0.12 (3H, s), 0.84-0.93 (30H, m), 1.23-1.37 (4H, m), 1.54-1.68 (2H, m), 2.95 (2H, t, *J* = 7.3 Hz), 3.47 (1H, dd, *J* = 5.0, 10.2 Hz), 3.67 (1H, dd, *J* = 8.6, 9.9 Hz), 3.90 (1H, ddd, *J* = 2.1, 5.0, 8.6 Hz), 4.89 (1H, d, *J* = 1.0, 20.1 Hz), 5.05, (1H, dd, *J* = 1.0, 20.1 Hz), and 5.53 (1H, dd, *J* = 1.0, 2.1 Hz); IR (neat), vmax 2932, 2860, 1773, 1692, and 1623 cm^{-1}.

(1*R*,7*R*,8*R*)-7-Hydroxy-4,10,11-trioxa-1-pentyltricyclo[6.2.1.0]undec-2(6)-en-3-one (21): A solution of **18** (25.9 mg, 42.1 µmol) in acetonitrile (1 ml) was stirred under the atmosphere of SiF_4 at 25 °C for 3.5 h. The mixture was diluted with acetate buffer (pH 5.0, 1 ml), and the aq. phase was extracted with EtOAc (5 × 2 ml). Drying over $MgSO_4$ and concentration *in vacuo* afforded compound **21** (11.2 mg, 100%). **21**: ^{1}H-NMR ($CDCl_3$, 270 MHz), δ 0.83-0.94 (3H, m), 1.24-1.49 (6H, m), 1.99-2.12 (1H, m), 2.20-2.36 (1H, m), 4.05 (1H, br dd, *J* = 8.6, 6.1Hz), 4.10 (1H, dd, *J* = 8.6, 2.3 Hz), 4.64 (1H, ddd, *J* = 6.1, 4.3, 2.3 Hz), 4.76 (1H, br d, *J* = 8.1 Hz), 4.99 (1H, d, *J* = 8.1 Hz), and 5.10 (1H, br d, *J* = 4.3 Hz); ^{13}C-NMR (Acetone-d_6, 67.5 MHz), δ 14.1, 23.0, 23.3, 31.9, 32.6, 64.3, 67.0, 69.5, 76.3, 104.6,128.4, 165.1, and 170.0; IR (neat), vmax 3448, 2960, 2936, 2868, 1756, 1660, and 1466 cm^{-1}.

Syringolide 1 (1a): To a stirred mixture of **18** (52.5 mg, 85.4 µmol), THF (2 ml), and water (0.2 ml) was added *p*-TsOH·H_2O (640 mg, 3.36 mmol). After stirring at 23 °C for 42 h, the mixture was diluted with EtOAc (2 ml), washed with satd aq. $NaHCO_3$ (3 ml), and extracted with EtOAc (5 × 2 ml). Drying over $MgSO_4$, concentration *in vacuo*, and recycling preparative HPLC afforded syringolide 1 (**1a**) (3.8 mg, 14.1 µmol, 16%) as white crystals. **1a**: m.p. 112-114 °C; $[\alpha]_D^{22}$ -60 (*c* 0.03, $CHCl_3$); ^{1}H-NMR (Acetone-d_6, 270 MHz), δ 0.89 (3H, t, *J* = 6.9 Hz), 1.27-1.37 (4H, m), 1.44-1.54 (1H, m), 1.56-1.67 (1H, m), 1.85-1.92 (2H, m), 3.09 (1H, s), 3.83 (1H, dd, J = 3.0, 9.9 Hz), 3.95 (1H, dd, J = 1.2, 9.9 Hz), 4.15, (1H, br t, J = 10.2 Hz), 4.32 (1H, d, J = 10.2 Hz), 4.32 (1H, br s), 4.49 (1H, br s), 4.67 (1H, d, J = 10.2 Hz), and 5.38 (1H, d, J = 2.0 Hz); ^{13}C-NMR (Acetone-d_6, 100 MHz), δ 14.2, 23.1, 24.0, 32.6, 39.3, 59.6, 74.9, 75.4, 75.6, 92.2, 99.0, 108.8, and 172.6; IR ($CHCl_3$), νmax 3604, 2954, 2938, 2860, 1773, 1470, 1380, 1239, 1185, 1071, 1041, 975, and 915 cm^{-1}.

References and Notes

1) Murai, A. *Pesticide Science and Biotechnology* ed. by R. Greenhalgh and T. R. Roberts, Blackwell, London, p. 81-88 (1987).

2) a) Culver, J. N.; Dawson, W. O. *Molec. Plant-Microbe. Interact.* 1991, *4*, 458; b) Van den Ackerveken, G. F. J. M.; Van Kan, J. A. L.; Dewit, P. J. G. M. M. *Plant J.* 1992, *2*, 359.

3) Smith, M. J.; Mazzola, E. P.; Sims, J. J.; Midland, S. L.; Keen, N. T; Burton, V.; Stayton, M. M. *Tetrahedron Lett.* 1993, *34*, 223.; Midland, S. L.;. Keen, N. T; Sims, J. J.; Midland, M. M.; Stayton, M. M. Burton, V.; Smith, M. J.; Mazzola, E. P.; Gragam, K. J.; Clardy, J. *J. Org. Chem.* 1993, *58*, 2940.

4) a) Wood, J. L.; Jeong, S.; Salcedo, A.; Jenkins, J. *J. Org. Chem.* 1995, *60*, 286; b) Kuwahara, S.; Moriguchi, M.; Miyagawa, K.; Konno, M.; Kodama, O. *Tetrahedron Lett.* 1995, *36*, 3201.; Kuwahara, S.; Moriguchi, M.; Miyagawa, K.; Konno, M.; Kodama, O. *Tetrahedron* 1995, *51*, 8809; c) Ishihara, J.; Sugimoto, T.; Murai, A. *SYNLETT* 1996, 335; d) Henschke, J. P.; Rickards, R. W. *Tetrahedron Lett.* 1996, *37*, 3557; e) syntheses of syributin 1 and syringolides 1 and 2: Honda, T.; Mizutani, H.; Kanai, K. *J. Org. Chem.* 1996, *61*, 9374; f) syntheses of (-)- and (+)-syringolides 1: Zeng, C.-m.; Midland, S. L.; Keen, N. L.; Sims, J. J. *J. Org. Chem.* 1997, *62*, 4780.

5) Liotta, D.; Saindane, M.; Barnum, C.; Ensley, H.; Balakrishnan, P. *Tetrahedron. Lett.* 1981, *22*, 3043.

6) Horne, D. A.; Fugmann, B.; Yakushijin, K.; Büchi, G. *J. Org. Chem.* 1993, *58*, 62.

7) Wender, P. A.; Sieburth, S. M.; Petraotis, J. J.; Singh, S. K. *Tetrahedron* 1981, *37*, 3967.

8) For a review, see; Kolb, H., C.; VanNieuwnhze, M. S.; Sharpless, K. B. *Chem. Rev.* 1994, *94*, 2483.

9) In our previous paper,[4c] we estimated the enantiomeric ratios of compound **14aa** and **14ab** to be 95%ee and 87%ee, respectively. After reconsideration, we revised the ratios to 90%ee (**14aa**) and 74%ee (**14ab**).

10) Corey, E. J.; Yi, E. Y. *Tetrahedron. Lett.* 1992, *33*, 2289.

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