Synthesis of the Methyl Ester of AK-Toxin II, a Host-Specific Toxin to Japanese White Pear, and Its Congeners: Structure–Toxicity Relationship of the Toxin

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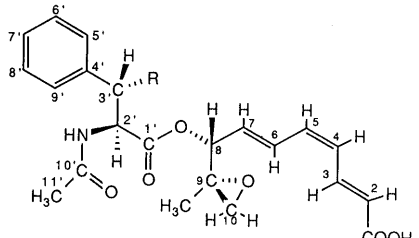
Synthesis of the methyl ester of AK-toxin II, a typical host-specific toxin, toxic to Japanese white pear, and fifteen diastereoisomers as its congeners was accomplished in optically active forms starting from vitamin C as a chiral starting material. Toxicity testing of these synthetic compounds revealed that the configurations of two chiral centers in the carboxylic acid part of the toxin have an important role in the toxicity.

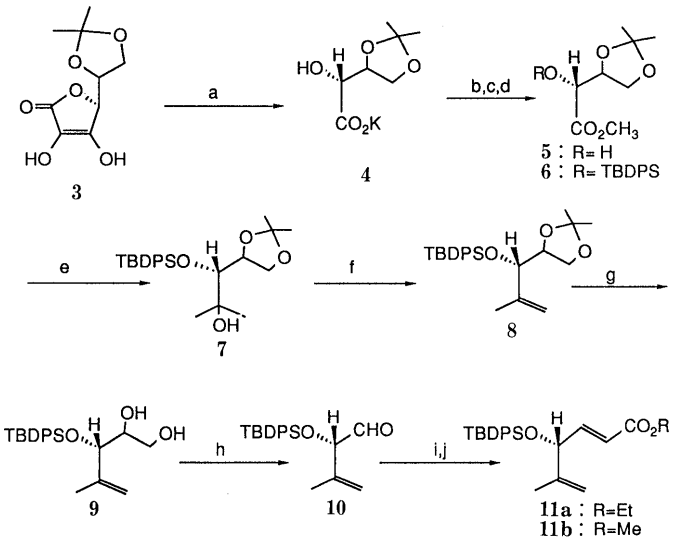
Keywords host-specific toxin; vitamin C; Wadsworth–Emmons reaction; *N*-acetyl-phenylalanine; AK-toxin II

In 1933, Tanaka[1] observed that when Japanese white pear, *Pyrus serotina* REHDER var. *culta* (Japanese name nijisseiki), was fatally infected with *Alternaria kikuchiana*, black spots appeared on the fruits and plants. He suggested that the fungus produced toxins that were only toxic to white pear, not to red pear, because the fermentation broth of the fungus exhibited toxicity only to white pear. He therefore proposed the concept of a host-specific toxin. In 1985, Ueno and his co-workers[2] isolated and characterized two host-specific toxins, AK-toxins I and II, as crystalline forms and elucidated their structures to be **1** and **2**, respectively. We have achieved the total synthesis of the methyl ester of AK-toxin II and its congeners starting from vitamin C as a chiral starting material with the aim of examining the toxicity–structure relationship of these toxins and confirming the availability of vitamin C as a convenient and cheap material for synthesis of natural products in optically active forms. We report here in detail the synthesis of the methyl ester of AK-toxin II and its congeners in optically active forms.[3]



1 : AK-toxin I R=CH_3
2 : AK-toxin II R=H

Chart 1



a) K_2CO_3, $KMnO_4$, H_2O; b) HCl, MeOH; c) CH_2N_2, ether; d) TBDPS-Cl, imidazole, pyridine; e) MeMgI, ether; f) $SOCl_2$, pyridine, CH_2Cl_2; g) CF_3COOH, MeOH; h) $NaIO_4.2H_2O$, ether; i) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, dry benzene j) $(CH_3CH_2O)_2P(O)CH_2CO_2CH_2CH_3$, NaH, dry benzene

Chart 2

Oxidation of the acetonide (**3**),[4] in aqueous potassium carbonate with potassium permanganate under a carbon dioxide atmosphere gave the potassium salt (**4**) of the carboxylic acid. Treatment of the salt with equimolar methanolic hydrogen chloride under cooling (dry ice–acetone) followed by an excess of diazomethane gave the ester (**5**) in 75% yield. Grignard reaction of the silyl-ether (**6**), obtained from (**5**) by treatment with *tert*-butyldiphenylsilyl chloride (TBDPS chloride) in pyridine in the presence of imidazole at 70 °C for 2 d, with methyl magnesium iodide gave the alcohol (**7**). Dehydration of **7** with thionyl chloride in pyridine furnished the olefin (**8**), the structure of which was confirmed by its proton nuclear magnetic resonance (^{1}H-NMR) spectrum ($CDCl_3$) exhibiting two olefinic signals at δ 4.73 as a broad singlet. Hydrolysis of the acetonide group with trifluoroacetic acid in methanol at room temperature gave the glycol (**9**). Oxidation of **9** with periodic acid in ether gave the aldehyde (**10**), which was, without further purification, subjected to a Wadsworth–Emmons reaction with triethyl phosphonoacetate in dry benzene to give the α,β-unsaturated ethyl ester (**11a**) in 65% yield from the olefin (**8**).

Epoxidation of **11a** with *m*-chloroperbenzoic acid (mCPBA) in methylene chloride gave the oxides (**12a** and **12b**) corresponding to two diastereoisomers with respect to (*R*)-(*S*) and (*R*)-(*R*) configurations at the two chiral centers in 1 : 1 ratio in 85% total yield. The structures of these oxides were proposed on the basis of ^{1}H-NMR nuclear Overhauser effect (NOE) experiments. Thus, irradiation of the signal assigned to one of the methylene protons, which has *trans* orientation to the methyl group on the oxide ring, showed 5.4% enhancement of the signal at δ 3.88 assigned to the proton on the carbon bearing the TBDPSO group. A *trans*-relationship between one of the methylene protons and the methyl group was proposed from the observation of a long-range coupling between them. Assuming a

plausible conformation in which the two oxygen groups, the epoxide and the TBDPSO groups, are separated from each other, a close proximity of the protons mentioned above might be expected in the diastereomer (**12a**) having C4-(*R*) and C5-(*S*) configuration (see Chart 3). In the ^{1}H-NMR spectrum of AK-toxin I, 14.3% enhancement (NOE) has been observed between the signal of the proton on the carbon bearing the phenylalanyloxy group and the signal of one of the methylene protons having a *trans* relationship to the tertiary methyl group. On the other hand, such proximity between the same protons can not be expected in another stereoisomer (**12b**), when the isomer has the same type of conformation. Furthermore, the (*R*)-(*S*) isomer (**12a**) showed AB-type quartets at δ 1.88 and 2.22 (J=4.8 Hz) due to the methylene protons, while the (*R*)-(*R*) isomer (**12b**) showed a singlet at δ 2.56 corresponding to methylene protons. This observation provides a useful tool to determine the structures of the oxides obtained from similar oxidation of similar compounds (*vide infra*).

Treatment of each oxide (**12c**) and (**12d**), obtained from (**11b**) by using trimethyl phosphonoacetate in the same manner as in the case of the ethyl ester (**11a**), with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) gave the respective alcohols (**13a** and **13b**) in good yields. Each alcohol was acylated with *N*-acetyl-L-phenylalanine (Ac–(L)-Phe–OH) and dicyclohexylcarbodiimide in the presence of 4-pyrrolidinopyridine[5] in anhydrous ethyl acetate, resulting in a mixture of two diastereoisomers (**14a** and **b** from **13a** and **14c** and **d** from **13b**) at the α-carbon of the phenylalanine moiety in each case. Each isomer was separated in pure form by flash chromatography and preparative thin layer chromatography. The configuration of the phenylalanyl moieties of the compounds (**14a—b**) was checked by applying an L-amino acid determination method[6] to the hydrolysate prepared from each compound with 6 N hydrochloric acid at 110 °C. An attempt was made to convert the ester (**11**) into the allyl alcohol (**15**) by treatment with TBAF but the reaction gave an inseparable mixture.

At this point, we carried out an experiment to confirm the optical purities of the epoxy-alcohols (**13a, b**) using the Mosher method.[7] Acylation of the epoxy-alcohols (**13a** and **13b**) with (+)-α-methoxy-α-trifluoromethylphenylacetyl (MTPA) chloride in the usual manner gave the corresponding esters, which were examined by ^{1}H-NMR (400 MHz), showing that the optical purities of these epoxy-alcohols were more than 99.5% enantiomeric excess.

Reduction of the ester (**11**) with diisobutylaluminum hydride (DIBAL-H) gave the allyl alcohol (**16**) in 85% yield. Oxidation of **16** with active manganese dioxide in methylene chloride gave the aldehyde (**17**) in good yield. Another Wadsworth–Emmons reaction on this aldehyde gave the ester (**18**), which was subjected to oxidation with mCPBA, giving the diastereoisomeric oxides (**19a** and **19b**) in 1 : 1 ratio in 75% total yield. The structures of these oxides were also supported by the similar shape of the signals assigned to the methylene protons of the oxide moiety in the ^{1}H-NMR spectra. Thus, the (*R*)-(*S*) (**19a**) and the (*R*)-(*R*) (**19b**) isomers exhibited an AB-type quartet and a singlet in their ^{1}H-NMR spectrum, respectively, assignable to the methylene protons of the oxide group. After deprotection of the silyl group in each epoxide with TBAF,

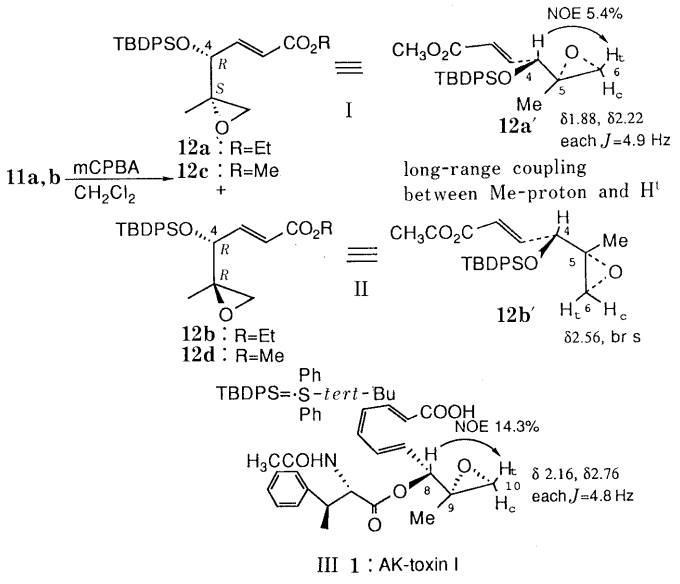
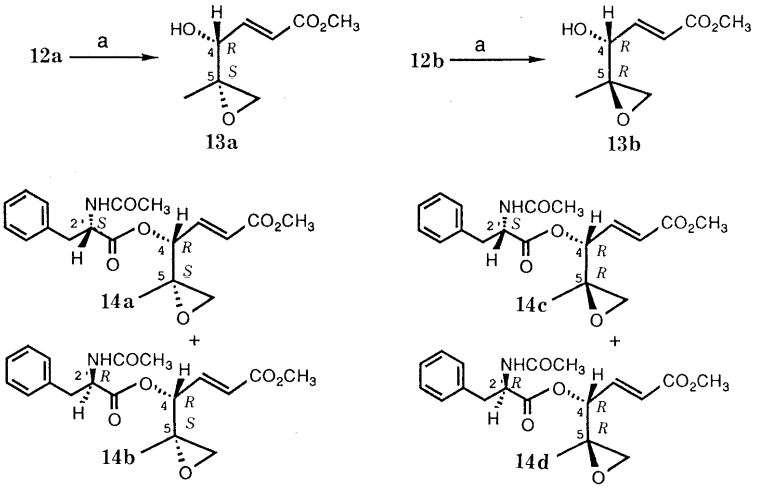


Chart 3



a) TBAF, THF; b) *N*-acetyl-L-phenylalanine, DCC, 4-pyrrolidinopyridine

Chart 4

the resulting alcohols (**20a** and **20b**) were acylated with Ac–(L)-Phe–OH in the same way as mentioned above, giving rise to a mixture of two diastereoisomeric phenylalanyl esters: **21a** and **21b** from **20a**, and **21c** and **21d** from **20b**.

The structures of all the compounds were confirmed by application of an L-amino acid determination method. Repeated reaction of the ester (**18**), reduction with DIBAL-H, manganese dioxide oxidation, and Wadsworth–Emmons reaction gave the all-*trans*-ester (**22**) in 45% overall yield. Oxidation of the ester (**22**) with mCPBA gave two isomers (**23a** and **23b**), the structures of which were discriminated in the same way as described for the oxide (**12a** and **12b**). After deprotection of the silyl group in each oxide, acylation of the resultant alcohols (**24a** and **24b**) with Ac–(L)-Phe–OH in the same manner gave two isomeric esters (**25a** and **25b**) from **24a** and **25c** and **25d** from **24b**. The configurations of the phenylalanine moieties were also determined in the same manner as in the cases mentioned above. Synthesis of twelve compounds related to AK-toxin II methyl ester for biological testing on Japanese white pear was completed. The results of the biological test of these compound are presented below.

Then, we aimed at the synthesis of the methyl ester of AK-toxin II. For this purpose, preparation of methyl 6-triphenylphosphonium-2,3-*trans*-4,5-*cis*-hexadienoate was carried out in the following way. Thus, mono-silylation of *cis*-butene-1,4-diol (**26**) with *tert*-butyldimethylsilyl (TBDMS) chloride gave the mono-siloxy compound (**27**) in 45% yield, and this was converted to the aldehyde (**28**) with manganese dioxide in methylene chloride in good yield. A Wadsworth–Emmons reaction on **28** afforded the diene (**29**). After desilylation, treatment of the alcohol (**30**) with carbon tetrabromide and triphenylphosphine[8] gave the bromide (**31**). Heating of the bromide with triphenylphosphine afforded the phosphonium bromide (**32**). Condensation

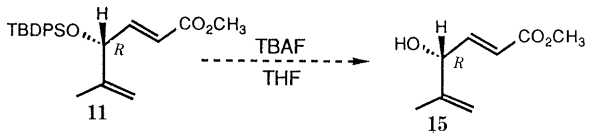
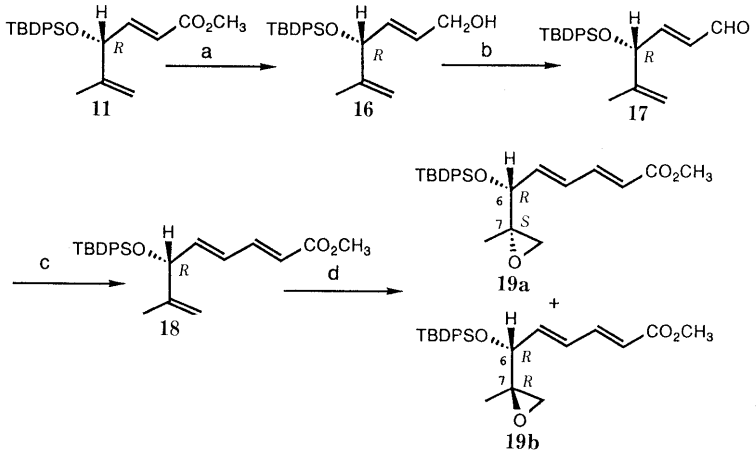


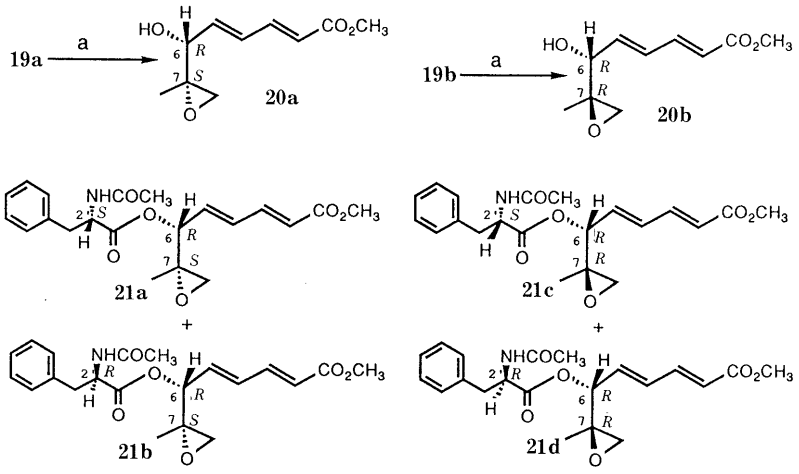
Chart 5



a) DIBAL-H, dry CH_2Cl_2; b) active MnO_2, CH_2Cl_2;

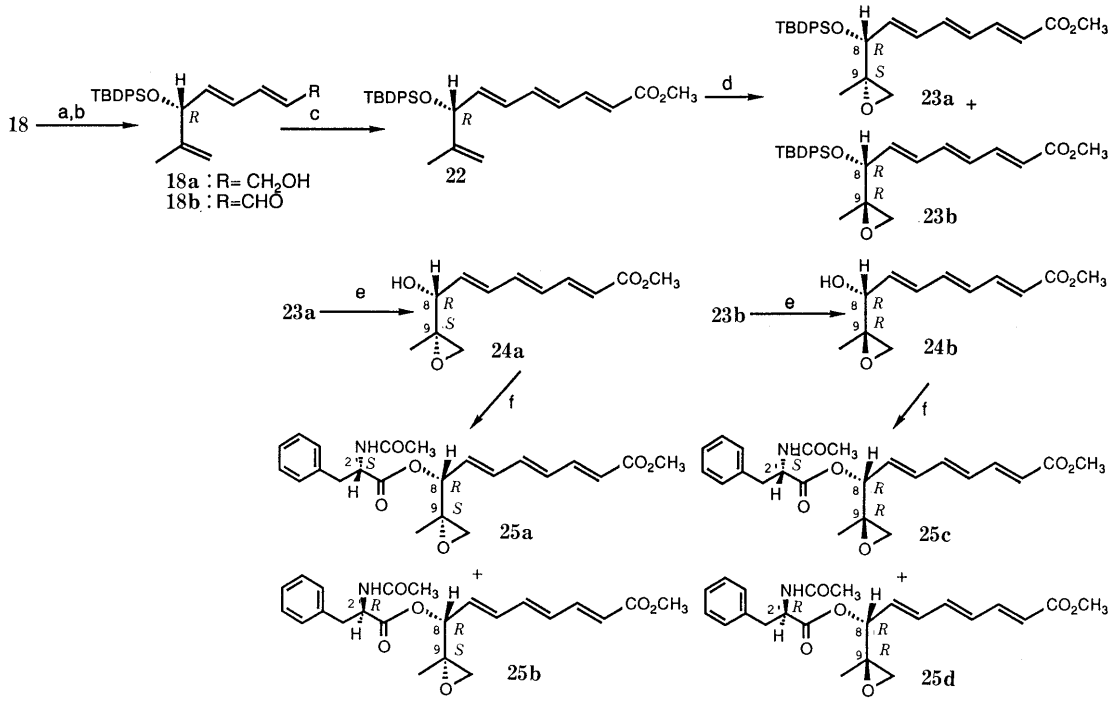
c) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, dry benzene; d) mCPBA, CH_2Cl_2

Chart 6



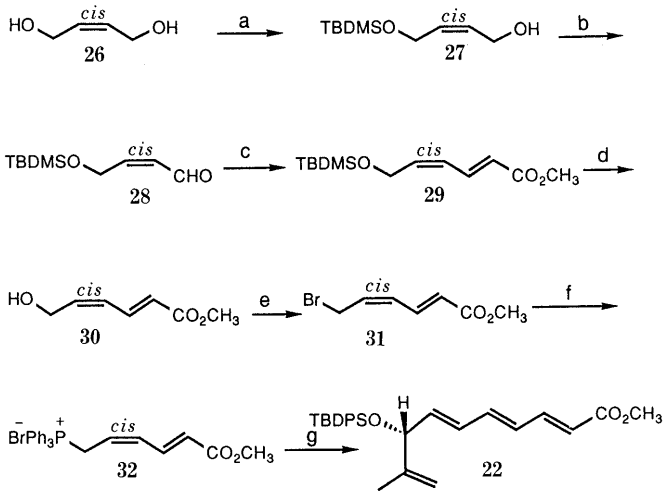
a) TBAF, THF; b) *N*-acetyl-L-phenylalanine, DCC, 4-pyrrolidinopyridine

Chart 7



a) DIBAL-H, dry CH_2Cl_2; b) active, MnO_2, CH_2Cl_2; c) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, dry benzen
d) mCPBA, CH_2Cl_2; e)TBAF, THF; f)*N*-acetyl-L-phenylalanine, DCC, 4-pyrrolidinopyridine

Chart 8



a) TBDMS-Cl, imidazole, dry DMF; b) active MnO_2, CH_2Cl_2;
c) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, benzene; d) TBAF, THF;
e) CBr_4, Ph_3P, CH_2Cl_2; f) Ph_3P, benzene; g) 10, NaOH, benzene

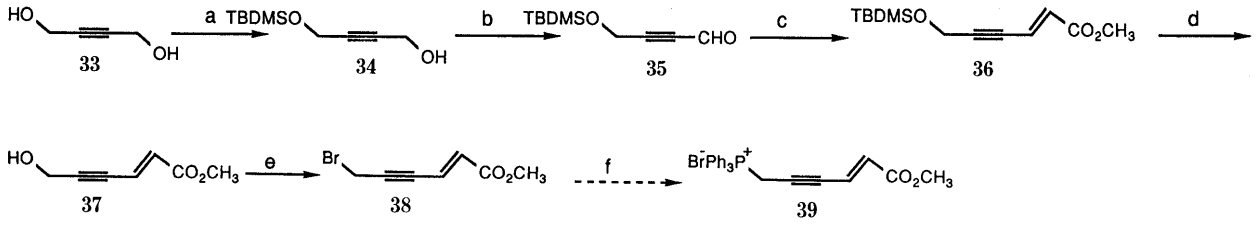
Chart 9

reaction of the aldehyde (**10**) with the Wittig reagent in aqueous sodium hydroxide unexpectedly gave the all-*trans* triene-ester (**22**) in low yield. The structure of the product was confirmed by direct comparison of the spectroscopic properties with those of a synthetic sample obtained by a stepwise elongation reaction as mentioned above.

Next, monosilylation of butyne-1,4-diol (**33**) with TBDMS-chloride gave the monosilyl ether (**34**) which was subjected to the same reaction sequence to give the ene-yne ester (**36**) in acceptable yield. The desilylated alcohol (**37**) was transformed to the bromide (**38**). An attempt to prepare the Wittig reagent by treatment of the bromide with triphenylphosphine was unsuccessful, resulting in an intractable tarry mixture.

On the other hand, condensation of the aldehyde (**17**) and methyl 4-dimethylphosphonocrotonate with sodium hydride as a base in dimethoxyethane (DME) gave the all-*trans* triene-ester (**22**) and the cyclic compound (**40**) in 14% and 40% yields, respectively. The structure of the latter (**40**) was proposed from its spectroscopic properties. Its mass spectrum (MS) showed the parent ion peak at *m/z* 466 corresponding to $C_{28}H_{34}O_3Si$ and its ^{1}H-NMR spectrum showed the signals due to three olefinic protons at δ 6.83 (d), 5.70 (m), and 5.25 (m) in addition to methylene protons. Its infrared (IR) spectrum ($CHCl_3$) exhibited a carbonyl band at 1715 cm^{-1}. Formation of the cyclic product is thought to be due to the participation of the conjugated double bonds at the elimination stage of methyl phosphonate, followed by a migration of the double bond to result in conjugation with the ester carbonyl group as depicted in Chart 11.

Eventually we found that the condensation of methyl 4-triphenylphosphoniumcrotonate and the aldehyde (**17**) using lithium methoxide in DME at 0°C furnished a mixture consisting of the all-*trans* trienoic ester (**22**) and the *trans*, *cis*, *trans*-trienoic ester (**41**) in 1 : 3 ratio in 73% total yield. When sodium hydride and potassium hydride were used as bases, the all-*trans* trienoic ester (**41**) was obtained as a major product. Furthermore, the higher the temperature, the lower the yield of the *trans*, *cis*, *trans*-trienoic ester (**41**). Epoxidation of the ester (**41**) gave two oxides (**42a** and **42b**) in 1 : 1 ratio in 87% total yield. Both oxides exhibited an AB-type quartet assigned to the methylene protons of the oxide moiety in their ^{1}H-NMR



a) TBDMS-Cl, imidazole, dry DMF; b) active MnO_2, CH_2Cl_2; c) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, benzene; d) TBAF, THF; e) CBr_4, Ph_3P, CH_2Cl_2; f) Ph_3P, benzene

Chart 10

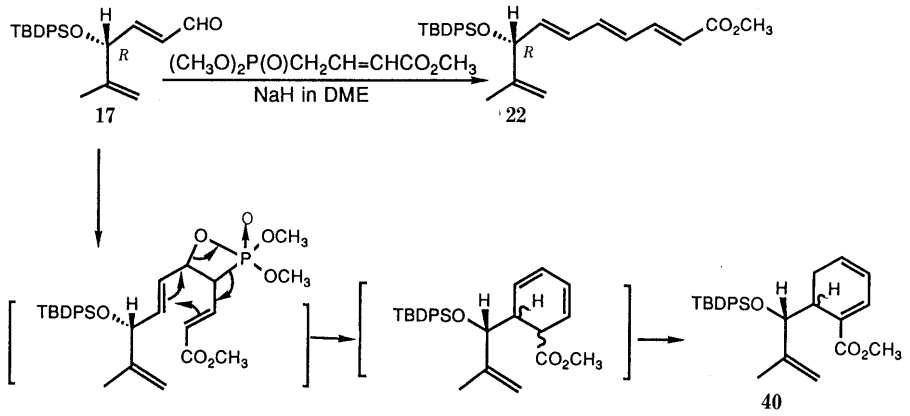


Chart 11

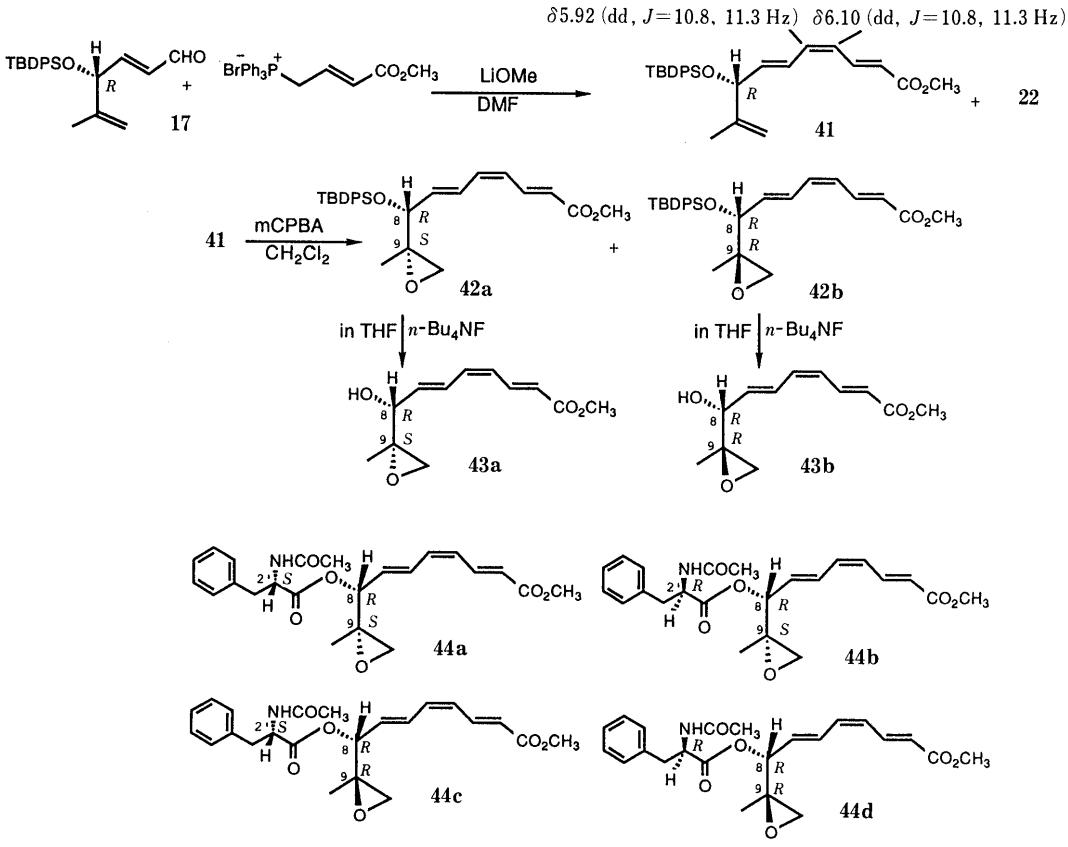
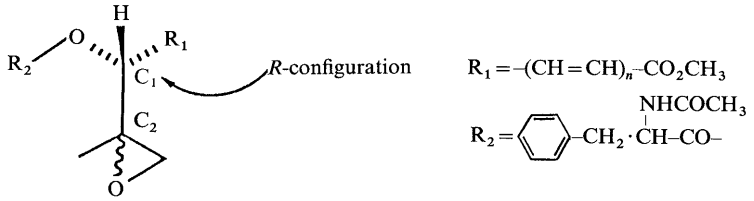


Chart 12

spectra, different from the previous case, but the structures of the two isomers were predicted to be **42a** ((*R*)-(*S*) configuration) and **42b** ((*R*)-(*R*) configuration): the former (**42a**) showed a larger difference between the chemical shifts of the AB-components (δ, 2.14 and 2.36 $J=4.3$ Hz), and the latter a smaller difference (δ, 2.57 and 2.68 $J=4.3$ Hz).

TABLE I. The Biological Test Data of Our Synthetic Compounds, AK-Toxin II Methyl Ester and Its Congeners



R_2	R_1	Configuration of C_2	$[\alpha]_D$ (in EtOH)	Toxicity to plant
TBDPS	–CH=CHCOOMe[a]	*S*	−13.1 (1.55)	+
TBDPS	–CH=CHCOOMe[a]	*R*	−22.9 (1.86)	−
TBDPS	–(CH=CH)$_2$COOMe[a]	*S*	−74.6 (1.06)	+
TBDPS	–(CH=CH)$_2$COOMe[a]	*R*	−81.4 (1.05)	−
TBDPS	–(CH=CH)$_3$COOMe[a]	*S*	−60.0 (1.00)	+
TBDPS	–(CH=CH)$_3$COOMe[a]	*R*	−59.9 (0.94)	−
H	–CH=CHCOOMe[a]	*S*	+68.2 (1.92)	+
H	–CH=CHCOOMe[a]	*R*	+61.9 (1.34)	−
H	–(CH=CH)$_2$COOMe[a]	*S*	+76.1 (1.00)	+
H	–(CH=CH)$_2$COOMe[a]	*R*	+64.4 (1.26)	−
H	–(CH=CH)$_3$COOMe[a]	*S*	+68.0 (1.00)	+
H	–(CH=CH)$_3$COOMe[a]	*R*	+68.3 (1.20)	−
Ac–L-Phe–	–CH=CHCOOMe[a]	*S*	+ 6.5 (0.28)	+
Ac–D-Phe–	–CH=CHCOOMe[a]	*S*	+27.2 (0.22)	+
Ac–L-Phe–	–CH=CHCOOMe[a]	*R*	+14.4 (0.54)	−
Ac–D-Phe–	–CH=CHCOOMe[a]	*R*	+35.5 (0.53)	−
Ac–L-Phe–	–(CH=CH)$_2$COOMe[a]	*S*	+15.0 (1.00)	+
Ac–D-Phe–	–(CH=CH)$_2$COOMe[a]	*S*	+13.4 (0.67)	+
Ac–L-Phe–	–(CH=CH)$_2$COOMe[a]	*R*	+13.2 (1.13)	−
Ac–D-Phe–	–(CH=CH)$_2$COOMe[a]	*R*	+21.9 (1.14)	−
Ac–L-Phe–	–(CH=CH)$_3$COOMe[a]	*S*	+22.8 (0.90)	++
Ac–D-Phe–	–(CH=CH)$_3$COOMe[a]	*S*	+16.3 (1.00)	++
Ac–L-Phe–	–(CH=CH)$_3$COOMe[a]	*R*	+22.8 (1.20)	−
Ac–D-Phe–	–(CH=CH)$_3$COOMe[a]	*R*	+21.0 (1.36)	−
Ac–L-Phe–	–(CH=CH)$_3$COOMe[b]	*S*	+79.8 (0.75)	++
Ac–D-Phe–	–(CH=CH)$_3$COOMe[b]	*S*	+83.1 (0.55)	++
Ac–L-Phe–	–(CH=CH)$_3$COOMe[b]	*R*	+92.7 (1.20)	−
Ac–D-Phe–	–(CH=CH)$_3$COOMe[b]	*R*	+71.3 (0.67)	−

a) *trans*, *trans-trans* and all-*trans* compounds. *b*) *trans cis trans* compounds.

The assignment was ultimately proved by our success in synthesizing AK-toxin II methyl ester.

Removal of the silyl group of **42a** followed by acylation with Ac–(L)-Phe–OH in the same manner gave two isomeric esters (**44a** and **44b**), the former of which exhibited an identical ^{1}H-NMR spectrum (400 MHz) with that of AK-toxin II methyl ester obtained from the natural source, indicating the successful accomplishment of the synthesis of AK-toxin II methyl ester.

The same reaction sequence on the oxide (**42b**) and separation of the products afforded stereoisomeric congeners (**44c** and **44d**) of AK-toxin II methyl ester. In this case, the configurations of the phenylalanine moieties of these esters were elucidated by the L-amino acid determination method.

The results of biological testing of our synthetic compounds, AK-toxin II methyl ester (**44a**) and its fifteen congeners, using leaves of Japanese white pear, revealed that the configurations at two asymmetric carbons in the epoxy-trienoic acid moiety have an essential role in the toxicity. Thus, all the compounds possessing *R* configuration at the carbon bearing a secondary hydroxyl group and *S* configuration at the quaternary carbon in the oxide ring show the host-specific toxicity to Japanese white pear. The toxicity increases with increasing length of the conjugated double bond system, though this system is not essential. The configuration at the amino acid moiety had no marked effect on the toxicity.

Experimental

Melting points were determined with a Yanagimoto micro-melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-408 spectrometer in chloroform. ^{1}H-NMR spectra were recorded on JEOL PMX-60, JEOL FX 90Q and JNM-GX 400 NMR spectrometer with tetramethylsilane as an internal standard, and chemical shifts are given in ppm. Optical rotations were measured with a JASCO DIP-181 digital polarimeter and high-resolution mass spectra (HR-MS) were taken with a JEOL JMS-DX303 instrument. Column chromatography was performed with Kieselgel 60 (70—230 mesh) and flash column chromatography was performed with Kieselgel 60G (Art 7731). Homogeneity of the compounds cited in this report was confirmed by examination of the ^{1}H-NMR spectra and thin layer chromatography (TLC).

Potassium 3,4-Isopropylidene-L-threonate (4) A solution of $KMnO_4$ (29.3 g, 0.18 mol) and K_2CO_3 (24.4 g, 0.18 mol) in water (600 ml) was added dropwise to a suspension of ascorbic acid acetonide (**3**) (30 g, 0.14 mol) in distilled water (600 ml) while CO_2 was introduced into the reaction mixture at 0°C and the whole was stirred at 0 °C for 30 min and heated at 50 °C for 2 h. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure (bath temperature 60 °C) to give a residue. EtOH (60 ml) was added to the residue and was evaporated *in vacuo*. The same procedure were repeated three times to remove water completely and then the residue was extracted with alcohol (100 ml) three times by refluxing for 30 min. The alcohol layer was combined and evaporated *in vacuo* to afford a residue. The residue was recrystallized from acetone–EtOH to

give the potassium salt (**4**) (25.3 g) (85%) as a pale brown crystalline solid. mp 154–157 °C (lit.[4] mp 155—157 °C), $[\alpha]_D^{15.8}$ +24.9 (c=1.53, water) (lit.[4] $[\alpha]_D^{22}$ +24.8 (c=2.58, water)). IR ($CHCl_3$): 3460, 1600—1690 cm^{-1}.

Methyl 3,4-Isopropylidene-L-threonate (5) A solution of hydrogen chloride (6.1 g, 0.17 mol) in anhydrous methanol (200 ml) was added dropwise to a suspension of **4** (32.6 g, 0.152 mol) in anhydrous methanol (100 ml). Excess diazomethane in ether was added to the solution under cooling (dry ice–acetone), then a few drops of acetic acid were added to the reaction mixture and the whole was evaporated *in vacuo*. The residue was extracted with ether (150 ml) three times and the combined ether layer was washed with 3% aqueous $NaHCO_3$ and water, dried with $MgSO_4$, and evaporated. The residue was chromatographed in chloroform over silica gel to afford **5** (18.2 g, 63%) as a colorless oil. IR ($CHCl_3$): 3540, 1740 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.22 and 1.28 (each 3H, s, CH_3), 3.02 (1H, d, J=7.2 Hz, >CHOH), 3.67 (3H, s, CO_2CH_3), 3.82—4.30 (4H, m, $-CH_2O-$, >CHO–, OH). $[\alpha]_D^{17}$ +21.0 (c=0.83, acetone), {lit.[4] $[\alpha]_D^{21}$ +21.3 (c=2.35, acetone)}.

Methyl 3,4-Isopropylidenedioxy-2-(*tert*-butyldiphenylsiloxy)butanoate (6) A solution of TBDPS chloride (11.7 g, 1.2 eq), imidazole (2.9 g, 1.2 eq), and the ester (**5**) (6.76 g, 35.6 mmol) in anhydrous pyridine (50 ml) was stirred at 70 °C for 2 d and then the reaction mixture was concentrated *in vacuo*. The residue was extracted with ether (150 ml three times) and the ether extract was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl and water, dried with $MgSO_4$, and evaporated. The residue was chromatographed in hexane–acetone (100 : 2) over silica gel to afford **6** (13.5 g, 89%) as a colorless oil. IR ($CHCl_3$): 1745 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.12 (9H, s, $C(CH_3)_3$), 1.33 (6H, s, >$C(CH_3)_2$), 3.45 (3H, s $COOCH_3$), 4.02 (2H, m, C_4-2H), 4.21—4.41 (2H, m, $C_{2,3}$-H), 7.30—7.81 (10H, m, aromatic H). $[\alpha]_D^{21}$ +27.1 (c=1.44, EtOH). HR-MS m/z: Calcd for $C_{24}H_{32}O_5Si$ (M^+): 428.2020. Found: 428.2014.

4,5-Isopropylidenedioxy-3-(*tert*-butyldiphenylsiloxy)-2-methylpentan-2-ol (7) A solution of the ester (**6**) (250 mg, 0.58 mol) in ether (5 ml) was added to a solution of methylmagnesium iodide prepared from magnesium (497 mg, 3.5 molar eq) and iodomethane (290 mg, 3.5 molar eq) in ether (5 ml) in the usual way and the whole was stirred at the same temperature for another 30 min. The reaction mixture was diluted with ether, washed with 3% aqueous NH_4Cl and water, dried with K_2CO_3 and evaporated *in vacuo* to leave a residue. The residue was chromatographed in chloroform over silica gel to give the glycol (**7**) (237 mg, 95%) as a colorless oil. IR ($CHCl_3$): 3570 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.07 (9H, s, $C(CH_3)_3$), 0.98 and 1.02 (each 3H, s, CH_3), 1.21 and 1.25 (each 3H, s, >CCH_3), 2.20 (1H, s, OH), 3.45—4.25 (4H, m, C_5-2H, $C_{3,4}$-H), 7.3—7.9 (10H, m, aromatic H). $[\alpha]_D^{22}$ −27.1 (c=1.81, EtOH). MS m/z: 428 (M^+).

4,5-Isopropylidenedioxy-3-(*tert*-butyldiphenylsiloxy)-2-methylpent-1-ene (8) Thionyl chloride (100 mg, 2.0 eq) was added to a solution of the alcohol (**7**) (175 mg, 0.41 mmol) in anhydrous pyridine (5 ml) at 0 °C and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated *in vacuo* and the residue was taken up in ether (30 ml). The ethereal solution was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl, and water, dried with $MgSO_4$ and evaporated *in vacuo*. The residue was chromatographed in hexane–acetone (100 : 4) over silica gel to give the olefin (**8**) (152 mg, 91%) as a colorless oil. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.08 (9H, s, $C(CH_3)_3$), 1.24 and 1.28 (each 3H, s, >CCH_3), 1.74 (3H, s, CH_3), 3.53—3.80 (2H, m), 4.05—4.30 (2H, m), 4.73 (2H, br s, $=CH_2$), 7.31—7.84 (10H, m, aromatic H). $[\alpha]_D^{19.8}$ −21.3 (c=0.95, EtOH). HR-MS m/z: Calcd for $C_{25}H_{34}O_3Si$ (M^+): 410.2278. Found: 410.2290.

3-(*tert*-Butyldiphenylsiloxy)-4-methyl-but-4-ene-1,2-diol (9) A solution of trifluroacetic acid (2.62 g, 23 mmol) and the olefin (**8**) (5.2 g, 13 mmol) in methanol (50 ml) was stirred at 70 °C for 2 h. After addition of sodium carbonate, the mixture was concentrated under reduced pressure to give a residue which was extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to afford the glycol (**9**) (4.3 g, 91%) as a slightly yellow oil. IR ($CHCl_3$): 3580 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.07 (9H, s, $C(CH_3)_3$), 1.66 (3H, s, C_4-CH_3), 3.13—3.80 (3H, m, C_1-2H, C_2-H), 4.13 (1H, d, J=6.0 Hz, C_3-H), 4.73 (2H, br s, $C=CH_2$), 7.30—7.78 (10H, m, aromatic H). $[\alpha]_D^{21}$ −18.6 (c=0.97, EtOH).

2-(*tert*-Butyldiphenylsiloxy)-3-methyl-but-3-enal (10) Periodic acid dihydrate (1.9 g, 8.3 mmol) was added to a solution of the α-glycol (**9**) (2.0 g, 5.4 mmol) in ether (20 ml) and the resulting mixture was stirred at room temperature for 4 h, and diluted with ether. The ethereal solution was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl and water, dried over $MgSO_4$ and evaporated *in vacuo* to give the aldehyde (**10**) (1.7 g, 94%) as a colorless oil. IR ($CHCl_3$): 1730 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.11 (9H, s, $C(CH_3)_3$), 1.66 (3H, s, C_3-CH_3), 4.36 (1H, d, J=1.8 Hz, C_2-H), 5.09 (1H, br s, C_4-H_a), 5.22 (1H, br s, C_4-H_b), 7.31—7.74 (10H, m, aromatic H), 9.36 (1H, d, J=1.8 Hz, CHO). MS m/z: 338 (M^+). The aldehyde was subjected to Wadsworth–Emmons reaction as mentioned below without further purification.

4-(*tert*-Butyldiphenylsiloxy)-5-methyl-hexa-2(*E*),5-dienoate (11a) and (11b) Sodium hydride (0.24 g, 1.5 eq, 60% in mineral oil) was placed in a three-necked flask, washed with anhydrous benzene (5 ml) three times, and then suspended in anhydrous benzene (20 ml). A solution of ethyl triethyl phosphonoacetate (1.4 g, 7.3 mmol) in benzene (6 ml) was added dropwise to the suspension and the mixture was stirred at room temperature for 30 min. To this mixture, a solution of the aldehyde (**10**) (1.7 g, 5 mmol) in anhydrous benzene (7 ml) was added dropwise, and the whole was stirred for another 30 min. The reaction mixture was diluted with ether, washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl, and water, dried with Na_2SO_4 and evaporated *in vacuo* to leave a residue. The residue was chromatographed in ether–hexane (2 : 100) over silica gel to give the ester (**11a**) (1.8 g, 90%) as a colorless oil.

By the same method as described above, the aldehyde (**10**) (2.23 g, 6.59 mmol) gave the methyl ester (**11b**) (2.29 g, 88%) using trimethyl phosphonoacetate in place of triethylphosphonoacetate.

The Ethyl Ester (**11a**): IR ($CHCl_3$): 1710, 1645 cm^{-1}. ^{1}H-NMR (60 Hz in $CDCl_3$): 1.10 (9H, s, $C(CH_3)_3$), 1.27 (3H, t, J=7.2 Hz, OCH_2CH_3), 1.64 (3H, s, C_5-CH_3), 4.18 (2H, q, J=7.2 Hz, OCH_2CH_3), 4.59—4.91 (3H, m, $=CH_2$, C_4-H), 5.94 (1H, dd, J=15.6, 0.6 Hz, =CH–), 6.81 (1H, dd, J=15.6, 4.2 Hz, –CH=), 7.30—7.72 (10H, m, aromatic H). $[\alpha]_D^{21.5}$ −28.95 (c=1.00, EtOH). MS m/z. 408 (M^+).

The Ethyl Ester (**11b**): IR ($CHCl_3$): 1720, 1660 cm^{-1}. ^{1}H-NMR (60 Hz in $CDCl_3$): 1.11 (9H, s, $C(CH_3)_3$), 1.62 (3H, s, C_5-CH_3), 3.70 (3H, s, $COOCH_3$), 4.67—7.84 (3H, m, C_4-H, C_6-2H), 5.98 (1H, dd, J=15.6, 1.3 Hz, =CH–), 6.81 (1H, dd, J=15.6, 5.4 Hz, –CH=), 7.25—7.75 (10H, m, aromatic H). $[\alpha]_D^{16}$ −24.7 (c=1.01, EtOH). HR-MS m/z: Calcd for $C_{24}H_{30}O_3Si$ (M^+): 394.1965. Found: 394.1973.

4(*R*)-(*tert*-Butyldiphenylsiloxy)-5,6-epoxy-5(*S*)-methyl-but-2(*E*)-enoate (12a, 12b and 12c, 12d) A solution of mCPBA (0.25 g, 1.4 mmol) and the ethyl ester (**11a**) (0.40, 1.0 mmol) in anhydrous methylene chloride (5 ml) was kept in the dark for 12 h. After adding 10% aqueous $NaHSO_3$, the mixture was diluted with chloroform. The solution was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl and water, dried with $MgSO_4$ and concentrated. The residue was chromatographed in ether–hexane (10 : 1) over silica gel to afford the oxide (**12a**) (0.16 g, 38%) as the faster running portion and the oxide (**12b**) (0.21 g, 51%) as the slower running one.

By use of the same method, the methyl ester (**11b**) (0.625 g, 1.59 mmol) gave the oxides (**12c**) (0.213 g, 33%) and (**12d**) (0.36 g, 58%).

The Oxide (**12a**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.10 (9H, s, $C(CH_3)_3$), 1.26 (3H, s, C_5-CH_3), 1.30 (3H, t, J=7.0 Hz, OCH_2CH_3), 1.86 (1H, d, J=4.90 Hz, C_6-H_a), 2.21 (1H, d, J=4.90 Hz, C_6-H_b), 3.86 (1H, dd, J=4.4, 1.5 Hz, C_4-H), 4.02 (2H, q, J=7.0 Hz, OCH_2CH_3), 6.14 (1H, dd, J=15.7, 1.5 Hz, =CH–), 6.95 (1H, dd, J=15.7, 4.4 Hz, –CH=), 7.30—7.72 (10H, m, aromatic H). $[\alpha]_D^{21.5}$ −26.7 (c=1.27, EtOH). MS m/z: 424 (M^+).

The Oxide (**12b**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.18 (9H, s, $C(CH_3)_3$), 1.35 (3H, s, C_5-CH_3), 1.26 (3H, t, J=7.3 Hz, OCH_2CH_3), 2.57 (2H, s, C_6-2H), 3.93 (1H, dd, J=5.3, 1.5 Hz, C_4-H), 4.14 (2H, q, J=7.3 Hz, OCH_2CH_3), 5.81 (1H, dd, J=15.7, 1.5 Hz, =CH–), 6.75 (1H, dd, J=15.7, 5.3 Hz, –CH=), 7.22—7.75 (10H, m, aromatic H). $[\alpha]_D^{21.5}$ −28.0 (c=1.22, EtOH). MS m/z: 424 (M^+).

The Oxide (**12c**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.09 (9H, s, $C(CH_3)_3$), 1.25 (3H, s, C_5-CH_3), 1.88 (1H, d, J=4.8 Hz, C_6-H_a), 2.22 (1H, d, J=4.8 Hz, C_6-H_b), 3.74 (3H, s, $COOCH_3$), 3.88 (1H, dd, J=4.2, 1.8 Hz, C_4-H), 6.14 (1H, dd, J=15.9, 1.8 Hz, =CH–), 7.01 (1H, dd, J=15.9, 4.2 Hz, –CH=), 7.25—7.77 (10H, m, aromatic H). $[\alpha]_D^{15}$ −13.1 (c=1.55, EtOH). MS m/z: 410 (M^+).

The Oxide (**12d**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.13 (9H, s, $C(CH_3)_3$), 1.35 (3H, s, C_5-CH_3), 2.56 (2H, s, C_6-2H), 3.69 (3H, s, $COOCH_3$), 3.97 (1H, dd, J=5.4, 1.8 Hz, C_4-H), 5.33 (1H, dd, J=15.9, 1.8 Hz, =CH–), 6.24 (1H, dd, J=15.9, 5.4 Hz, –CH=), 7.20—7.80 (10H, m, aromatic H). $[\alpha]_D^{15}$ −22.9 (c=1.86, EtOH). MS m/z: 410 (M^+).

Methyl 4(*R*)-Hydroxy-5,6-epoxy-5(*S*)-methylhex-2(*E*)-enoate (13a) and Its (5*R*)-Epimer (13b) A solution of TBAF (3 ml) (1 M in THF) and the epoxide (**12a**) (0.411 g, 1.0 mmol) in anhydrous THF (16 ml) was stirred at −20 °C and then at room temperature for 1 h. The reaction mixture was diluted with ether, washed with brine, dried with Na_2SO_4 and evaporated *in vacuo*. The residue was chromatographed in 2% hexane in chloroform over silica gel to afford the alcohol (**13a**) (0.117 g, 68%) as a colorless oil. A similar treatment of **12b** (450 mg, 1.1 mmol) gave the alcohol (**13b**)

(90 mg, 46%).

Compound **13a**: IR ($CHCl_3$): 1720, 3510 cm^{-1}. ^{1}H-NMR (60 MHz, in $CDCl_3$): 1.40 (3H, s, C_5-CH_3), 2.62 (1H, d, J=4.8 Hz, C_6-H_a), 2.87 (1H, d, J=4.8 Hz, C_6-H_b), 3.76 (3H, s, $COOCH_3$), 4.31 (1H, dd, J=4.8, 1.2 Hz, C_4-H), 6.16 (1H, dd, J=21.0, 1.2 Hz, =CH–), 6.95 (1H, dd, J=21.0, 4.8 Hz, –CH=), $[\alpha]_D^{15}$ +68.2 (c=1.92, EtOH). HR-MS m/z: Calcd for $c_8H_{12}O_4$ (M^+): 172.0735. Found: 172.0762.

Compound **13b**: IR ($CHCl_3$): 1720, 3510 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.32 (3h, s, C_5-CH_3), 2.69 (1H, d, J=4.8 Hz, C_6-H_a), 2.87 (1H, d, J=4.8 Hz, C_6-H_b), 3.75 (3H, s, $COOCH_3$), 4.10 (1H, dd, J=4.8, 1.2 Hz, C_4-H), 6.15 (1H, dd, J=21.0, 1.2 Hz, =CH–), 6.96 (1H, dd, J=21.0, 4.8 Hz, –CH=). $[\alpha]_D^{15}$ +61.9 (c=1.34, EtOH). HR-MS m/z: Calcd for $C_8H_{10}O_4$ (M^+): 172.0735. Found: 172.0704.

Methyl (4*R*,5*S*,2′*S*)-4-(*N*-Acetylphenylalanyloxy)-5,6-epoxy-5-methylhex-2(*E*)-enoate (14a), and Its Isomers (14b, 14c, and 14d) A solution of 1,3-dicyclohexyl-carbodiimide (DCC) (0.361 g, 1.74 mmol) and *N*-acetyl-L-phenylalanine (0.361 g, 1.74 mmol) in anhydrous ethyl acetate (10 ml) was stirred at room temperature for 1.5 h and filtered. The filtrate was added to a solution of the alcohol (**13a**) (100 mg, 0.58 mmol) and 4-pyrrolidinopyridine (0.04 g) in anhydrous ethyl acetate (5 ml) and the resulting mixture was stirred at room temperature for 24 h, then diluted with ether. The ethereal solution was washed with brine, dried with Na_2SO_4 and evaporated *in vacuo*. The residue was chromatographed in chloroform on silica gel to afford a mixture of the phenylalanyl esters (**14a** and **14b**). The mixture was separated by preparative TLC in chloroform : benzene : ether : acetone [5 : 2 : 1 : 0.5 (v/v)] to give **14a** (83 mg, 40%) and **14b** (52 mg, 25%) as colorless oils.

A similar treatment of **13b** (156 mg, 0.91 mmol) with *N*-acetyl-L-phenylalanine afforded **14c** (164 mg, 50.1%) and **14d** (121 mg, 37.1%).

Compound **14a**: IR ($CHCl_3$): 3450, 1740, 1725, 1670 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.28 (3H, s, C_5-CH_3), 1.99 (1H, s, $COCH_3$), 2.62 (1H, d, J=4.7 Hz, C_6-H_a), 2.77 (1H, d, J=4.7 Hz, C_6-H_b), 3.11 (2H, d, J=6.4 Hz, $C_{3'}$-2H), 3.77 (3H, s, $COOCH_3$), 4.92 (1H, dt, J=7.7, 6.4 Hz, $C_{2'}$-H), 5.16 (1H, dd, J=5.8, 1.5 Hz, C_4-H), 5.82 (1H, d, J=7.7 Hz, NH), 6.79 (1H, dd, J=15.8, 5.8 Hz, –CH=), 5.93 (1H, dd, J=15.8, 1.5 Hz, =CH–), 7.06—7.31 (5H, m, aromatic H). $[\alpha]_D^{21}$ +6.5 (c=0.28, EtOH). HR-MS m/z: Calcd for $C_{19}H_{23}NO_6$ (M^+): 361.1526. Found: 361.1521.

Compound **14b**: IR ($CHCl_3$): 3450, 1740, 1725, 1670 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.22 (3H, s, C_5-CH_3), 1.98 (1H, s, $COCH_3$), 2.57 (1H, d, J=4.7 Hz, C_6-H_a), 2.72 (1H, d, J=4.7 Hz, C_6-H_b), 3.11 (2H, d, J=6.5 Hz, $C_{3'}$-2H), 3.75 (3H, s, $COOCH_3$), 4.95 (1H, dt, J=7.7, 6.5 Hz, $C_{2'}$-H), 5.18 (1H, dd, J=5.3, 1.5 Hz, C_4-H), 5.80 (1H, d, J=7.7 Hz, NH), 6.03 (1H, dd, J=15.8, 1.5 Hz, =CH–), 6.48 (1H, dd, J=15.8, 5.3 Hz, –CH=), 7.11—7.33 (5H, m, aromatic H). $[\alpha]_D^{21}$ +27.2 (c=0.22, EtOH). HR-MS m/z: Calcd for $C_{19}H_{23}NO_6$ (M^+): 361.1526. Found: 361.1487.

Compound **14c**: IR ($CHCl_3$): 3450, 1740, 1725, 1670 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.30 (3H, s, C_5-CH_3), 1.99 (1H, s, $COCH_3$), 2.64 (1H, d, J=4.4 Hz, C_6-H_a), 2.78 (1H, d, J=4.4 Hz, C_6-H_b), 3.12 (2H, d, J=6.5 Hz, $C_{3'}$-2H), 3.77 (3H, s, $COOCH_3$), 4.91 (1H, dt, J=7.7, 6.5 Hz, $C_{2'}$-H), 5.24 (1H, dd, J=5.9, 1.4 Hz, C_4-H), 5.85 (1H, d, J=7.7 Hz, NH), 6.72 (1H, dd, J=15.8, 5.9 Hz, –CH=), 6.89 (1H, dd, J=15.8, 1.4 Hz, =CH–), 7.12—7.32 (5H, m, aromatic H). $[\alpha]_D^{21}$ +14.4 (c=0.54, EtOH). HR-MS m/z: Calcd for $C_{19}H_{23}NO_6$ (M^+): 361.1526. Found: 361.1490.

Compound **14d**: IR ($CHCl_3$): 3450, 1740, 1725, 1670 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.30 (3H, s, C_5-CH_3), 1.98 (1H, s, $COCH_3$), 2.68 (1H, d, J=4.5 Hz, C_6-H_a), 2.77 (1H, d, J=4.5 Hz, C_6-H_b), 3.17 (2H, d, J=6.0 Hz, $C_{3'}$-2H), 3.75 (3H, s, $COOCH_3$), 4.96 (1H, dt, J=7.7, 6.0 Hz, $C_{2'}$-H), 5.16 (1H, dd, J=5.0, 1.6 Hz, C_4-H), 5.91 (1H, d, J=7.7 Hz, NH), 6.00 (1H, dd, J=15.7, 1.6 Hz, =CH–), 6.80 (1H, dd, J=15.7, 5.0 Hz, –CH=), 7.13—7.32 (5H, m, aromatic H). $[\alpha]_D^{21}$ +35.5 (c=0.53, EtOH). HR-MS m/z: Calcd for $C_{19}H_{23}NO_6$ (M^+): 361.1526. Found: 361.1468.

4-(*tert*-Butyldiphenylsiloxy)-5-methylhexa-2(*E*),5-dien-1-ol (16) DIBAL-H (1.74 g, 7 ml of 25% in hexane, 2.1 eq) was added dropwise to the solution of **11** (2.3 g, 5.8 mmol) in methylene chloride (8 ml) under argon at −78 °C and the whole was stirred at the same temperature for 1 h. The reaction mixture was diluted with ice-cooled chloroform and brine, and filtered. The filtrate was washed with brine, dried with Na_2SO_4 and evaporated *in vacuo* to give a residue, which was chromatographed in benzene–methanol (100 : 1) on silica gel to afford the alcohol (**16**) (2.04 g, 95.5%) as a colorless oil. IR ($CHCl_3$): 3620 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.08 (9H, s, $C(CH_3)_3$), 1.65 (3H, br s, C_5-CH_3), 3.95 (2H, m, $\underline{CH_2}OH$), 4.58 (1H, m, C_4-H), 4.77 (1H, br s, C_6-H_a), 4.92 (1H, br s, C_6-H_b), 5.40—5.65 (2H, m, CH=CH), 7.22—7.80 (10H, m, aromatic H). $[\alpha]_D^{18}$ −28.1 (c=1.01, EtOH). MS m/z: 366 (M^+).

4-(*tert*-Butyldiphenylsiloxy)-5-methylhexa-2(*E*),5-dienal (17) A mixture of active MnO_2 (11 g) and the alcohol (**16**) (2.04 g, 5.57 mmol) in methylene chloride (100 ml) was stirred at room temperature for 30 min and filtered. The filtrate was concentrated to give the aldehyde (**17**) (1.87 g, 92%) as a slightly yellow oil. IR ($CHCl_3$): 1685 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.11 (9H, s, $C(CH_3)_3$), 1.66 (3H, br s, C_5-CH_3), 4.78—4.88 (3H, m, C_4-H, C_6-2H), 6.13 (1H, dd, J=16.2, 7.2 Hz, =CH–), 6.62 (1H, dd, J=16.2, 3.6 Hz, –CH=), 7.26—7.72 (10H, m, aromatic H), 9.47 (1H, d, J=7.2 Hz, CHO). MS m/z: 364 (M^+).

Methyl 6-(*tert*-Butyldiphenylsiloxy)-7-methylocta-2(*E*),4(*E*),7-trienoate (18) By use of the procedure described for the preparation of the ester (**11**) from the aldehyde (**10**), the aldehyde (**17**) (0.87 g, 2.4 mmol) gave the ester (**18**) (0.88 g, 85%) as a colorless oil. IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.09 (9H, s, $C(CH_3)_3$), 1.66 (3H, s, C_7-CH_3), 3.73 (3H, s, $COOCH_3$), 4.61 (1H, d, J=4.2 Hz, C_6-H), 4.76 (1H, br s, C_8-H_a), 4.86 (1H, br s, C_8-H_b), 5.74 (1H, d, J=14.8 Hz, =C_2H–), 5.91 (1H, dd, J=15.0, 4.2 Hz, –C_5H=), 6.13 (1H, dd, J=15.0, 9.0 Hz, =C_4H–), 7.16 (1H, dd, J=14.8, 9.0 Hz, –C_3H=), 7.22—7.70 (10H, m, aromatic H). $[\alpha]_D^{23}$ −105.8 (c=1.48, EtOH). HR-MS m/z: Calcd for $C_{26}H_{32}O_3Si$ (M^+): 420.2122. Found: 420.2118.

Oxidation of the Ester (18) By use of the method described for the preparation of the epoxides (**13a** and **13b**), the ester (**18**) (0.94 g, 2.2 mmol) gave the oxides (**19a**) (0.3 g, 31%) and (**19b**) (0.5 g, 51%) as colorless oils.

The Oxide (**19a**): IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.10 (9H, s, $C(CH_3)_3$), 1.28 (3H, s, C_7-CH_3), 2.00 (1H, d, J=4.8 Hz, C_8-H_a) 2.31 (1H, d, J=4.8 Hz, C_8-H_b), 3.75 (3H, s, $COOCH_3$), 3.85 (1H, d, J=4.2 Hz, C_6-H), 5.82 (1H, d, J=14.8 Hz, =C_2H–), 6.10—6.61 (2H, m, =C_5H– and =C_4H–), 7.26—7.74 (11H, m, –C_3H=, aromatic H). $[\alpha]_D^{23}$ −74.6 (c=1.05, EtOH). MS m/z: 436 (M^+).

The Oxide (**19b**): IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.11 (9H, s, $C(CH_3)_3$), 1.36 (3H, s, C_7-CH_3), 2.60 (2H, s, C_8-2H), 3.73 (3H, s, $COOCH_3$), 3.93 (1H, d, J=4.2 Hz, C_6-H), 5.67 (1H, d, J=15.4 Hz, =C_2H–), 5.73—6.04 (2H, m, =C_5H–, =C_4H–), 7.27—7.79 (11H, m, =C_3H–, and aromatic 10H). $[\alpha]_D^{23}$ −81.4 (c=1.05, EtOH). MS m/z: 436 (M^+).

Methyl 6(*R*)-Hydroxy-7,8-epoxy-7(*S*)-methylocta-2(*E*),4(*E*)-dienoate (20a), and Its 7*R*-Epimer (20b) By use of the method described for the preparation of **13a** and **13b**, **19a** (0.282 g, 0.65 mmol) and **19b** (0.212 g, 0.486 mmol) gave the alcohols (**20a**) (0.104 g, 81.2%) and (**20b**) (60 mg, 62%) respectively, as colorless oils.

The Alcohol (**20a**): IR ($CHCl_3$): 1700, 3550 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.36 (3H, s, C_7-CH_3), 2.62 (1H, d, J=4.8 Hz, C_8-H_a) 2.89 (1H, d, J=4.8 Hz, C_8-H_b), 3.75 (3H, s, $COOCH_3$), 4.22 (1H, d, J=6.0 Hz, C_6-H), 5.93 (1H, d, J=15.3 Hz, =C_2H–), 6.06 (1H, dd, J=14.7, 6.0 Hz, –C_5H=), 6.53 (1H, dd, J=14.7, 10.2 Hz, =C_4H–), 7.32 (1H, dd, J=15.3, 10.2 Hz, –C_3H=). $[\alpha]_D^{24}$ +76.1 (c=1.00, EtOH). HR-MS m/z: Calcd for $C_{10}H_{14}O_4$ (M^+): 198.0892. Found: 198.0876.

The Alcohol (**20b**): IR ($CHCl_3$): 1700, 3550 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 1.33 (3H, s, C_7-CH_3), 2.68 (1H, d, J=4.8 Hz, C_8-H_a), 2.87 (1H, d, J=4.8 Hz, C_8-H_b), 3.76 (3H, s, $COOCH_3$), 4.06 (1H, d, J=5.4 Hz, C_6-H), 5.93 (1H, d, J=15.0 Hz, =C_2H–), 6.07 (1H, dd, J=15.0, 5.4 Hz, –C_5H=), 6.49 (1H, dd, J=15.0, 10.2 Hz, =C_4H–), 7.32 (1H, dd, J=15.0, 10.2 Hz, –C_3H=). $[\alpha]_D^{24}$ +64.4 (c=1.26, EtOH). HR-MS m/z: Calcd for $C_{10}H_{14}O_4$ (M^+): 198.0892. Found: 198.0884.

Methyl (6*R*,7*S*,2′*S*)-4-(*N*-Acetylphenylalanyloxy)-7,8-epoxy-7-methylocta-2(*E*),4(*E*)-dienoate (21a), and Its Isomers (21b, 21c, 21d) By use of the procedure described for the preparation of **14a** and **14b**, the alcohol (**20a**) (0.104 g, 0.6 mmol) gave the phenylalanyl esters (**21a**) (120 mg, 59%) and (**21b**) (74 mg, 37%), and the alcohol (**20b**) (60 mg, 0.3 mmol) gave the phenylalanyl esters (**21c**) (55 mg, 47%) and (**21d**) (40 mg, 34%) respectively.

The Phenylalanyl Ester (**21a**): IR ($CHCl_3$): 3450, 1730, 1705, 1665 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.28 (3H, s, C_7-CH_3), 1.99 (3H, s, $COCH_3$), 2.60 (1H, d, J=4.7 Hz, C_8-H_a), 2.73 (1H, d, J=4.7 Hz, C_8-H_b), 3.09 (2H, d, J=6.4 Hz, $C_{3'}$-2H), 3.76 (3H, s, $COOCH_3$), 4.88 (1H, dt, J=7.5, 6.4 Hz, $C_{2'}$-H), 5.16 (1H, d, J=6.5 Hz, C_6-H), 5.86 (1H, dd, J=15.2, 6.5 Hz, –C_5H=), 5.92 (1H, d, J=15.4 Hz, =C_2H–), 6.07 (1H, d, J=7.5 Hz, NH), 6.30 (1H, dd, J=15.2, 10.2 Hz, =C_4H–), 7.02—7.37 (6H, m, –C_3H=, aromatic 5H). $[\alpha]_D^{24}$ +15.0 (c=0.67, EtOH). HR-MS m/z: Calcd for $C_{21}H_{25}NO_6$ (M^+): 387.1682. Found: 387.1632.

The Phenylalanyl Ester (**21b**): IR ($CHCl_3$): 3450, 1730, 1705, 1665 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.22 (3H, s, C_7-CH_3), 1.97 (3H, s, $COCH_3$), 2.57 (1H, d, J=4.7 Hz, C_8-H_a), 2.71 (1H, d, J=4.7 Hz, C_8-H_b), 3.11 (2H, d, J=6.4 Hz, $C_{3'}$-2H), 3.75 (3H, s, $COOCH_3$), 4.91 (1H, dt, J=7.9, 6.4 Hz, $C_{2'}$-H), 5.17 (1H, d, J=5.8 Hz, C_6-H), 5.96 (1H, dd, J=15.3, 5.8 Hz, –C_5H=), 5.94 (1H, d, J=15.9 Hz, =C_2H–), 6.04 (1H, d, J=7.9 Hz, NH), 6.40 (1H, dd, J=15.3, 10.5 Hz, =C_4H–), 7.09—7.38 (6H, m, –C_3H=,

aromatic 5H). $[\alpha]_D^{24}$ +13.4 (c=0.67, EtOH), HR-MS m/z: Calcd for $C_{21}H_{25}NO_6$ (M^+): 387.1682. Found: 387.1651.

The Phenylalanyl Ester (**21c**): IR ($CHCl_3$): 3450, 1730, 1705, 1665 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.30 (3H, s, C_7-CH_3), 1.99 (3H, s, $COCH_3$), 2.62 (1H, d, J=4.5 Hz, C_8-H_a), 2.79 (1H, d, J=4.5 Hz, C_8-H_b), 3.10 (2H, d, J=6.4 Hz, $C_{3'}$-2H), 3.76 (3H, s, $COOCH_3$), 4.89 (1H, dt, J=7.7, 6.4 Hz, $C_{2'}$-H), 5.19 (1H, d, J=6.9 Hz, C_6-H), 5.82 (1H, dd, J=15.3, 6.9 Hz, $-C_5H=$), 5.92 (1H, d, J=15.4 Hz, $=C_2H-$), 5.94 (1H, d, J=7.7 Hz, NH), 6.29 (1H, dd, J=15.3, 10.6 Hz, $=C_4H-$), 7.07—7.36 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{24}$ +13.2 (c=0.67, EtOH). HR-MS m/z: Calcd for $C_{21}H_{25}NO_6$ (M^+): 387.1682. Found: 387.1648.

The Phenylalanyl Ester (**21d**): IR ($CHCl_3$): 3450, 1730, 1705, 1665 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.30 (3H, s, C_7-CH_3), 1.97 (3H, s, OCH_3), 2.65 (1H, d, J=4.4 Hz, C_8-H_a), 2.74 (1H, d, J=4.4 Hz, C_8-H_b), 3.15 (2H, d, J=5.9 Hz, C_3-2H), 3.74 (3H, s, $COOCH_3$), 4.95 (1H, dt, J=7.9, 5.9 Hz, C_2-H), 5.12 (1H, d, J=5.7 Hz, C_6-H), 5.93 (1H, dd, J=15.3, 5.7 Hz, $-C_5H=$), 5.94 (1H, d, J=14.9 Hz, $=C_2H-$), 6.10 (1H, d, J=7.9 Hz, NH), 6.38 (1H, dd, J=15.3, 10.8 Hz, $=C_4H-$), 7.08—7.37 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{24}$ +21.9 (c=1.14, EtOH). HR-MS m/z: Calcd for $C_{21}H_{25}NO_6$ (M^+): 387.1682. Found: 387.1651.

Methyl 8-(*tert*-Butyldiphenylsiloxy)-9-methyldeca-2(*E*),4(*E*),6(*E*),9-tetraenoate (22) By use of the procedure described for the preparation of **18** from **11**, the diene-ester (**18**) (171 mg, 0.407 mmol) gave the triene-ester (**22**) (85 mg, 46.8% overall yield) as a colorless oil. IR ($CHCl_3$): 1700, 1620 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.08 (9H, s, $C(CH_3)_3$), 1.65 (3H, s, C_9-CH_3), 3.74 (3H, s, $COOCH_3$), 4.59 (1H, d, J=5.6 Hz, C_8-H), 4.74 (1H, br s, C_{10}-H_a), 4.86 (1H, br s, C_{10}-H_b), 5.75 (1H, dd, J=15.4, 5.6 Hz, $-C_7H=$), 5.84 (1H, d, J=14.9 Hz, $=C_2H-$), 6.11 (1H, dd, J=14.5, 10.5 Hz, $-C_5H=$), 6.19 (1H, dd, J=15.4, 10.5 Hz, $=C_6H-$), 6.47 (1H, dd, J=14.5, 10.0 Hz, $=C_4H-$), 7.13—7.69 (11H, m, $-C_3H=$, aromatic 10H). $[\alpha]_D^{15.5}$ −137.5 (c=0.91, EtOH). HR-MS m/z: Calcd for $C_{28}H_{34}O_3Si$ (M^+): 446.2278. Found: 446.2284.

Methyl 8(*R*)-(*tert*-Butyldiphenylsiloxy)-9,10-epoxy-9(*S*)-methyldeca-2(*E*),4(*E*),6(*E*)-trienoate (23a), and Its 9*R*-Epimer (23b) By use of the method described for the preparation of the epoxides (**12a**, **12b**), the triene-ester (**22**) (466 mg, 1.04 mmol) gave the epoxides (**23a**) (88 mg, 18%) and (**23b**) (135 mg, 28.1%) as colorless oils.

The Oxide (**23a**): IR ($CHCl_3$): 1710, 1620 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.09 (9H, s, $C(CH_3)_3$), 1.28 (3H, s, C_9-CH_3), 1.99 (1H, d, J=4.8 Hz, C_{10}-H_a), 2.28 (1H, d, J=4.8 Hz, C_{10}-H_b), 3.73 (3H, s, $COOCH_3$), 3.82 (1H, d, J=4.8 Hz, C_8-H), 5.87 (1H, d, J=15.4 Hz, $=C_2H-$), 5.92 (1H, dd, J=15.5, 4.8 Hz, $-C_7H=$), 6.06—6.68 (3H, m, $C_{4,5,6}$-H), 7.15—7.76 (11H, m, $-C_3H=$, aromatic 10H). $[\alpha]_D^{17}$ −60.0 (c=1.00, EtOH). MS m/z: 462 (M^+).

The Oxide (**23b**): IR ($CHCl_3$): 1710, 1620 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.10 (9H, s, $C(CH_3)_3$), 1.36 (3H, s, C_9-CH_3), 2.56 (1H, d, J=4.8 Hz, C_{10}-H_a), 2.63 (1H, d, J=4.8 Hz, C_{10}-H_b), 3.74 (3H, s, $COOCH_3$), 3.90 (1H, d, J=5.5 Hz, C_8-H), 5.83 (1H, d, J=15.2 Hz, $=C_2H-$), 5.72 (1H, dd, J=14.5, 5.5 Hz, $-C_7H=$), 5.84—6.62 (3H, m, $C_{4,5,6}$-H), 7.10—7.74 (11H, m, $-C_3H=$, aromatic 10H). $[\alpha]_D^{17}$ −60.0 (c=1.00, EtOH). MS m/z: 462 (M^+).

Methyl 8(*R*)-Hydroxy-9,10-epoxy-9(*S*)-methyl-deca-2(*E*),4(*E*),6(*E*)-trienoate (24a), and Its 9*R* Epimer (24b) By use of the procedure described for the preparation of **13a** and **13b**, the oxide (**23a**) (430 mg, 0.95 mmol) and its epimer (**23b**) (713 mg, 1.58 mmol) gave the alcohol (**24a**) (132 mg, 63.1%) and (**24b**) (270 mg, 78.1%) respectively as colorless oils.

The Alcohol (**24a**): IR ($CHCl_3$): 1710, 1620, 3540 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.37 (3H, s, C_9-CH_3), 2.53 (1H, s, OH), 2.62 (1H, d, J=4.6 Hz, C_{10}-H_a), 2.91 (1H, d, J=4.6 Hz, C_{10}-H_b), 3.75 (3H, s, $COOCH_3$), 4.21 (1H, d, J=6.5 Hz, C_8-H), 5.82 (1H, dd, J=14.5, 6.5 Hz, $-C_7H=$), 5.90 (1H, d, J=15.4 Hz, $=C_2H-$), 6.17—6.70 (3H, m, $C_{4,5,6}$-H), 7.31 (1H, dd, J=15.4, 10.5 Hz, $C_3H=$). $[\alpha]_D^{24}$ +68.0 (c=1.00, EtOH). HR-MS m/z: Calcd for $C_{12}H_{16}O_4$ (M^+): 224.1049. Found: 224.1023.

The Alcohol (**24b**): IR ($CHCl_3$): 1710, 1620, 3540 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.33 (3H, s, C_9-CH_3), 2.86 (1H, s, OH), 2.67 (1H, d, J=4.6 Hz, C_{10}-H_a), 2.87 (1H, d, J=4.6 Hz, C_{10}-H_b), 3.74 (3H, s, $COOCH_3$), 4.02 (1H, d, J=5.7 Hz, C_8-H), 5.65 (1H, d, J=15.2 Hz, $=C_2H-$), 5.85 (1H, dd, J=15.5, 5.7 Hz, $-C_7H=$), 6.15—6.73 (3H, m, $C_{4,5,6}$-H), 7.31 (1H, dd, J=15.2, 10.7 Hz, $C_3H=$). $[\alpha]_D^{24}$ +68.3 (c=1.20, EtOH). HR-MS m/z: Calcd for $C_{12}H_{16}O_4$ (M^+): 224.1049. Found: 224.1040.

Methyl 8(*R*)-(*N*-Acetylphenylalanyloxy)-9,10-epoxy-9(*S*)-methyldeca-2(*E*),4(*E*),6(*E*)-trienoate (25a), and Its Stereoisomers (25b, 25c, and 25d) By use of the procedure described for the preparation of **14a** and **14b**, the alcohol (**24a**) (63 mg, 0.28 mmol) gave the phenylalanyl esters (**25a**) (36 mg, 31%) and (**25b**) (52 mg, 49%), and the alcohol (**24b**) (75 mg, 0.33 mmol) gave the phenylalanyl esters (**25c**) (50 mg, 36.5%) and (**25d**) (55 mg, 44.8%) as oils.

The Phenylalanyl Ester (**25a**): IR ($CHCl_3$): 3450, 1640—1730 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.29 (3H, s, C_9-CH_3), 1.99 (3H, s, $COCH_3$), 2.57 (1H, d, J=4.8 Hz, C_{10}-H_a), 2.73 (1H, d, J=4.8 Hz, C_{10}-H_b), 3.10 (2H, d, J=6.2 Hz, $C_{3'}$-2H), 3.75 (3H, s, $COOCH_3$), 4.89 (1H, dt, J=7.7, 6.2 Hz, $C_{2'}$-H), 5.20 (1H, d, J=7.3 Hz, C_8-H), 5.69 (1H, dd, J=14.7, 7.3 Hz, $-C_7H=$), 5.94 (1H, d, J=15.2 Hz, $=C_2H-$), 6.06 (1H, d, J=7.7 Hz, NH), 6.21—6.69 (3H, m, $C_{4,5,6}$-H), 7.02—7.46 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{25}$ +22.8 (c=0.90, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$ (M^+): 413.1839. Found: 413.1813.

The Phenylalanyl Ester (**25b**): IR ($CHCl_3$): 3450, 1640—1730 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.23 (3H, s, C_9-CH_3), 1.97 (3H, s, $COCH_3$), 2.56 (1H, d, J=4.7 Hz, C_{10}-H_a), 2.71 (1H, d, J=4.7 Hz, C_{10}-H_b), 3.10 (2H, d, J=6.4 Hz, $C_{3'}$-2H), 3.74 (3H, s, $COOCH_3$), 4.91 (1H, dt, J=8.1, 6.4 Hz, $C_{2'}$-H), 5.18 (1H, d, J=6.8 Hz, C_8-H), 5.76 (1H, dd, J=14.8, 6.8 Hz, $-C_7H=$), 5.92 (1H, d, J=15.2 Hz, $=C_2H-$), 6.09 (1H, d, J=8.1 Hz, NH), 6.20—6.68 (3H, m, $C_{4,5,6}$-H), 7.11—7.41 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{25}$ +16.3 (c=0.90, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$ (M^+): 413.1839. Found: 413.1813.

The Phenylalanyl Ester (**25c**): IR ($CHCl_3$): 3450, 1640—1730 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.31 (3H, s, C_9-CH_3), 1.97 (3H, s, $COCH_3$), 2.62 (1H, d, J=4.7 Hz, C_{10}-H_a), 2.79 (1H, d, J=4.7 Hz, C_{10}-H_b), 3.10 (2H, d, J=6.3 Hz, $C_{3'}$-2H), 3.75 (3H, s, $COOCH_3$), 4.89 (1H, dt, J=7.7, 6.3 Hz, $C_{2'}$-H), 5.17 (1H, d, J=7.5 Hz, C_8-H), 5.75 (1H, dd, J=14.8, 7.5 Hz, $-C_7H=$), 5.93 (1H, d, J=15.4 Hz, $=C_2H-$), 6.09 (1H, d, J=7.7 Hz, NH), 6.20—6.61 (3H, m, $C_{4,5,6}$-H), 7.03—7.45 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{25}$ +22.8 (c=1.20 EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$ (M^+): 413.1839. Found: 413.1813.

The Phenylalanyl Ester (**25d**): IR ($CHCl_3$): 3450, 1640—1730 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.32 (3H, s, C_9-CH_3), 1.97 (3H, s, $COCH_3$), 2.65 (1H, d, J=4.5 Hz, C_{10}-H_a), 2.74 (1H, d, J=4.5 Hz, C_{10}-H_b), 3.15 (2H, d, J=5.9 Hz, $C_{3'}$-2H), 3.74 (3H, s, $COOCH_3$), 4.94 (1H, dt, J=7.9, 5.9 Hz, $C_{2'}$-H), 5.09 (1H, d, J=6.6 Hz, C_8-H), 5.75 (1H, dd, J=15.4, 6.6 Hz, $-C_7H=$), 5.92 (1H, d, J=15.2 Hz, $=C_2H-$), 6.08 (1H, d, J=7.9 Hz, NH), 6.20—6.60 (3H, m, $C_{4,5,6}$-H), 7.18—7.43 (6H, m, $-C_3H=$, aromatic 5H). $[\alpha]_D^{25}$ +21.0 (c=1.36, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$ (M^+): 413.1839. Found: 413.1813.

4-(*tert*-Butyldimethylsiloxy)-2(*Z*)-buten-1-ol (27) A solution of *cis*-2-butene-1,4-diol (0.88 mg, 10 mmol), imidazole (0.68 g, 10 mmol) and TBDMS chloride (1.5 g, 10 mmol) in anhydrous dimethylformamide (DMF) (20 ml) was stirred at room temperature for 8 h and concentrated under reduced pressure. The residue was dissolved in ether and the ether solution was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl and water, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed in hexane–acetone (100 : 5) on silica gel to give the mono-alcohol (**27**) (0.9 g, 45%) as a colorless oil. IR ($CHCl_3$): 3600 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 0.09 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 2.07 (1H, br s, OH), 4.17 (2H, d, J=3.5 Hz, $SiOCH_2$–), 4.27 (2H, d, J=3.5 Hz, –$\underline{CH_2}$OH), 5.55—5.58 (2H, m, CH=CH).

4-(*tert*-Butyldimethylsiloxy)-2(*Z*)-butenal (28) A mixture of active MnO_2 (4 g), the mono-alcohol (**27**) (0.72 g, 3.6 mmol) and methylene chloride (25 ml) was stirred at room temperature for 15 h. The reaction mixture was filtered and the filtrate was evaporated *in vacuo* to afford the aldehyde (**28**) (0.59 g, 83%) as an oil. IR ($CHCl_3$): 1680 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 0.10 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 4.67 (2H, dd, J=5.4, 2.7 Hz, $SiOCH_2$), 5.97 (1H, ddt, J=6.6, 10.8, 2.7 Hz, CH=$\underline{CH}$–CHO), 6.48 (1H, td, J=5.4, 10.8 Hz, $\underline{CH}$=CH–CHO), 10.1 (1H, d, J=6.6 Hz, CHO).

Methyl 6-(*tert*-Butyldimethylsiloxy)hexa-2(*E*),4(*Z*)-dienoate (29) By use of the method described for the preparation of **11** from **10**, the aldehyde (**28**) (500 mg, 1.5 mmol) gave the ester (**29**) (360 mg, 61%) as a colorless oil. IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 0.09 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 3.66 (3H, s, $COOCH_3$), 4.46 (2H, d, J=4.5 Hz, –OCH_2–), 5.87 (1H, d, J=14.5 Hz, $=C_2H-$), 5.92 (1H, dt, J=10.8, 4.5 Hz, $-C_5H=$), 6.14 (1H, dd, J=10.8, 10.8 Hz, $=C_4H-$), 7.60 (1H, dd, J=10.8, 14.5 Hz, $-C_3H=$). MS m/z: 256 (M^+).

Methyl 6-Hydroxyhexa-2(*E*),4(*Z*)-dienoate (30) A solution of TBAF (4.5 ml, 4.5 mmol) and the ester (**29**) (0.75 g, 2.9 mmol) in THF (30 ml) was stirred at −25 °C for 15 min. The reaction mixture was diluted with chloroform, and the solution was washed with 3% aqueous Na_2CO_3, 3% aqueous NH_4Cl, and water, dried with $MgSO_4$, and evaporated *in vacuo* to leave a residue which was chromatographed in chloroform on silica gel to give the alcohol (**30**) (380 mg, 91%) as a colorless oil. IR ($CHCl_3$):

3600, 1700 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 3.75 (3H, s, $COOCH_3$), 4.25 (2H, br d, J=3.6 Hz, OCH_2–), 5.85 (1H, d, J=15.0 Hz, =C_2H–), 6.05—6.45 (2H, m, =C_4H–, –C_5H=), 7.56 (1H, dd, J=15.0, 10.8 Hz, –C_3H=). MS m/z: 142 (M^+).

Methyl 6-Bromohexa-2(*E*),4(*Z*)-dienoate (31) Triphenyl phosphine (1.7 g, 6.5 mmol) was added portionwise to a solution of the alcohol (**30**) (0.62 g, 4.4 mmol) and carbon tetrabromide (1.8 g, 5.4 mmol) in methylene chloride (30 ml) and the whole was stirred at room temperature for 1 h. The reaction mixture was concentrated to leave a residue, which was chromatographed in chloroform on a silica gel. Elution with the same solvent gave the bromide (**31**) (0.89 g, 99%) as an oil. IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 3.78 (3H, s, $COOCH_3$), 4.18 (2H, d, J=8.0 Hz, $BrCH_2$–), 5.75—6.50 (3H, m, =C_2H–, =C_4H–, –C_5H=), 7.61 (1H, dd, J=15.0, 10.8 Hz, –C_3H=). MS m/z: 206 (M^+).

Methyl 6-Triphenylphosphonium-2(*E*),4(*Z*)-hexenoate (32) A solution of the bromide (**31**) (1.0 g, 4.9 mmol) and triphenylphosphine (1.3 g, 5.0 mmol) in benzene (20 ml) was refluxed for 12 h. The precipitate was collected by suction and the solid was recrystallized from acetonitrile–ether to afford the phosphonium salt (**32**) (2.1 g, 92%) as colorless crystals. mp 185.5—186.5 °C. *Anal.* Calcd for $C_{25}H_{24}BrO_2P \cdot 1/3H_2O$: C, 60.13; H, 5.22. Found: C, 59.93; H, 5.16. IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 3.69 (3H, s, $COOCH_3$), 5.15 (2H, dd, J=7.8, 16.8 Hz, PCH_2–), 5.61—6.15 (2H, m, $C_{2,4}$-H), 6.50—7.32 (2H, m, $C_{3,5}$-H), 7.50—8.10 (15H, m, aromatic H).

The Wittig Reaction of the Phosphonium Salt (32) with the Aldehyde (10) Aqueous 2% NaOH (10 ml) was added to the phosphonium salt (**32**) (0.8 g, 1.8 mmol) in water (50 ml) and the whole was stirred at room temperature for 2 h. Then a solution of the aldehyde (**10**) (0.51 g, 1.5 mmol) in benzene (10 ml) was added and the resulting mixture was refluxed for 3 h, diluted with benzene, washed with water, dried with $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed in hexane–ether (4 : 1) on silica gel to give the all-*trans* triene-ester (**22**) (0.21 g, 31%).

4-(*tert*-Butyldimethylsiloxy)-2-butyn-1-ol (34) By use of the method described for the preparation of the mono-alcohol (**27**), 2-butyne-1,4-diol (**33**) (0.5 g, 5.9 mmol) gave the mono-silyl alcohol (**34**) (0.48 g, 40%) as a colorless oil. IR ($CHCl_3$): 3560 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 0.09 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 4.26 (2H, s, $SiOCH_2$–), 4.28 (2H, br s, –CH_2OH), 4.33 (1H, br s, OH). MS m/z: 200 (M^+).

4-(*tert*-Butyldimethylsiloxy)-2-butynal (35) By the procedure described for the preparation of the aldehyde (**28**), the monosilyl alcohol (**34**) (0.5 g, 2.5 mmol) afforded the aldehyde (**35**) (0.4 g, 80%) as a colorless oil. IR ($CHCl_3$): 1680 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 0.09 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 4.48 (2H, br s, $SiOCH_2$–), 9.20 (1H, br s, CHO). MS m/z: 198 (M^+).

Methyl 6-(*tert*-Butyldimethylsiloxy)-hex-4-yn-2(*E*)-enoate (36) By the method described for the preparation of **29**, the aldehyde (**35**) (200 mg, 1.0 mmol) gave the ester (**36**) (180 mg, 70%) as a colorless oil. IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 0..09 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 3.70 (3H, s, $COOCH_3$), 4.41 (2H, s, $SiOCH_2$–), 6.15 (1H, d, J=15.0 Hz, CH=CH–$COOCH_3$), 6.75 (1H, d, J=15.0 Hz, CH=CH–$COOCH_3$). MS m/z: 256 (M^+).

Methyl 6-Hydroxyhex-4-yn-2(*E*)-enoate (37) By the procedure described for the synthesis of the alcohol (**30**), the ester (**36**) (2.60 g, 10 mmol) gave the alcohol (**37**) (0.93 g, 65%) as colorless prisms, mp 54.5—55.0 °C. *Anal.* Calcd for $C_7H_8O_3$: C, 59.99; H, 5.75. Found: C, 59.77; H, 5.83. IR ($CHCl_3$): 1710, 3600 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 3.75 (3H, s, $COOCH_3$), 4.40 (2H, br s, $HOCH_2$–), 6.21 (1H, d, J=17.0 Hz, CH=CH–$COOCH_3$), 6.75 (1H, d, J=17.0 Hz, CH=CH–$COOCH_3$).

Methyl 6-Bromo-hex-4-yn-2(*E*)-enoate (38) By the method described for the preparation of the bromide (**31**), the alcohol (**37**) (0.83 g, 5.9 mmol) gave the bromide (**38**) (1.2 g, 99%) as a slightly yellow oil. IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (60 MHz in $CDCl_3$): 3.75 (3H, s, $COOCH_3$), 4.05 (2H, d, J=2.0 Hz, $BrCH_2$–), 6.25 (1H, d, J=17.0 Hz, CH=CH–$COOCH_3$), 6.75 (1H, dt, J=17.0, 2.0 Hz, CH=CH–$COOCH_3$). MS m/z: 204 (M^+).

The Wadsworth–Emmons Reaction of the Aldehyde (17) with Methyl 4-Dimethylphosphonocrototonate A solution of methyl 4-dimethylphosphonocrotonate (0.686 g, 3.29 mmol) in DME (3 ml) was added to a solution of sodium hydride (0.079 g, 3.3 mmol) in DMF (2 ml) with stirring under argon at 0 °C for 5 min. To this mixture, a solution of the aldehyde (**17**) (0.6 g, 1.77 mmol) in dry DME (5 ml) was added. The whole was stirred at 0 °C for 1 h, then diluted with ether (30 ml) and the ether solution was washed with 3% aqueous NH_4Cl, 3% aqueous Na_2CO_3 and brine, dried with Na_2SO_4 and evaporated *in vacuo* to give a residue. The residue was chromatographed in ether–hexane (3 : 100) on a silica gel to give the all-*trans* compound (**22**) (0.105 g, 14.3%) and the cyclic compound (**40**) (0.340 g, 47.5%) as a colorless oil. IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.05 (9H, s, $C(CH_3)_3$), 1.74 (3H, s, $C_{2'}$-CH_3), 1.23—1.90 (1H, m, C_2-H), 2.08—3.00 (2H, m, C_3-2H), 3.63 (3H, s, $COOCH_3$), 4.15 (1H, d, J=8.6 Hz, $C_{1'}$-H), 4.50 (1H, br s, $C_{3'}$-H_a), 4.62 (1H, br s, $C_{3'}$-H_b), 5.25 (1H, m, C_4-H), 5.70 (1H, m, C_5-H), 6.83 (1H, d, J=5.3 Hz, C_6-H), 7.22—7.72 (10H, m, aromatic H). $[\alpha]_D^{22}$ +3.2 (c=1.06, EtOH). MS m/z: 446 (M^+).

Methyl 8(*R*)-(*tert*-Butyldiphenylsiloxy)-9(*S*)-methyldeca-2(*E*),4(*Z*),-6(*E*),9-tetraenoate (41) A methanolic solution of LiOMe (10 ml of 1 M solution in methanol) was added dropwise to a solution of the aldehyde (**17**) (2.6 g, 7.1 mmol) and methyl 4-triphenylphosphonium crotonate (4.71 g, 10.6 mmol) in anhydrous DME (30 ml) at −20 °C under argon and the resulting mixture was stirred at −4 °C for 24 h, and diluted with ether (50 ml). The ether solution was washed with 3% aqueous Na_2CO_3. 3% aqueous NH_4Cl and water, dried with $MgSO_4$, and evaporated *in vacuo* to give a residue. The residue was chromatographed in acetone–hexane (4 : 100) on silica gel to give a mixture of the *trans-cis-trans*-trienoic ester (**41**) and all-*trans*-trienoic ester (**22**). The mixture was separated by preparative TLC (chloroform : benzene : ether : acetone = 5 : 2 : 1 : 0.5) to give the *cis* compound (**41**) (1.65 g, 52%) and the all-*trans* compound (**22**) (0.55 g, 17%).

The *cis* Compound (**41**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (400 MHz in $CDCl_3$): 1.03 (9H, s, $C(CH_3)_3$), 1.60 (3H, s, C_9-CH_3), 3.70 (3H, s, $COOCH_3$), 4.52 (1H, d, J=6.2 Hz, C_8-H), 4.73 (1H, br s, C_{10}-H_a), 4.88 (1H, br s, C_{10}-H_b), 5.65 (1H, dd, J=6.2, 14.7 Hz, –C_7H=), 5.78 (1H, d, J=15.0 Hz, =C_2H–), 5.92 (1H, dd, J=11.3, 10.8 Hz, =C_5H–), 6.10 (1H, dd, J=11.3, 10.8 Hz, –C_4H=), 6.36 (1H, dd, J=11.3, 14.7 Hz, =C_6H–), 7.47 (1H, dd, J=11.3, 15.0 Hz, –C_3H=), 7.19—7.59 (10H, m, aromatic 10H). $[\alpha]_D^{24}$ −37.6 (c=1.00, EtOH). HR-MS m/z: Calcd for $C_{28}H_{34}O_3Si$ (M^+): 446.2278. Found: 446.2290.

Methyl 8(*R*)-(*tert*-Butyldiphenylsiloxy)-9,10-epoxy-9(*S*)-methyldeca-2(*E*),4(*Z*),6(*E*)-trienoate (42a), and Its Epimer (42b) By the procedure described for the preparation of the oxides (**12a** and **12b**), the *cis* compound (**41**) (250 mg, 0.56 mmol) afforded the oxides (**42a**) (104 mg, 42%) and (**42b**) (108 mg, 43%) as colorless oils.

The Epoxide (**42a**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.16 (9H, s, $C(CH_3)_3$), 1.30 (3H, s, C_9-CH_3), 2.14 (1H, d, J=4.3 Hz, C_{10}-H_a), 2.36 (1H, d, J=4.3 Hz, C_{10}-H_b), 3.76 (3H, s, $COOCH_3$), 3.86 (1H, d, J=6.5 Hz, C_8-H), 5.86 (1H, d, J=15.2 Hz, =C_2H–), 5.87 (1H, dd, J=6.5, 14.5 Hz, –C_7H=), 6.14 (1H, dd, J=11.0, 10.4 Hz, =C_5H–), 6.25 (1H, dd, J=11.0, 10.4 Hz, –C_4H=), 6.68 (1H, dd, J=10.4, 14.5 Hz, =C_6H–), 7.25—7.76 (11H, m, –C_3H=, aromatic 10H). $[\alpha]_D^{22}$ −36.6 (c=1.34, EtOH). HR-MS m/z: Calcd for $C_{28}H_{34}O_4Si$ (M^+): 462.2226. Found: 462.2226.

The Epoxide (**42b**): IR ($CHCl_3$): 1710 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.12 (9H, s, $C(CH_3)_3$), 1.36 (3H, s, C_9-CH_3), 2.57 (1H, d, J=4.3 Hz, C_{10}-H_a), 2.68 (1H, d, J=4.3 Hz, C_{10}-H_b), 3.77 (3H, s, $COOCH_3$), 3.92 (1H, d, J=6.1 Hz, C_8-H), 5.83 (1H, d, J=15.4 Hz, =C_2H–), 5.68 (1H, dd, J=7.2, 14.4 Hz, –C_7H=), 5.94—6.34 (3H, m, $C_{4,5,6}$-H), 7.24—7.75 (11H, m, –C_3H=, aromatic 10H). $[\alpha]_D^{22}$ −41.7 (c=1.34, EtOH). HR-MS m/z: Calcd for $C_{28}H_{34}O_4Si$ (M^+): 462.2226. Found: 462.2245.

Methyl 8(*R*)-Hydroxy-9,10-epoxy-9(*S*)-methyldeca-2(*E*),4(*Z*),6(*E*)-trienoate (43a) and Its 9*R*-Epimer (43b) By the method described for the preparation of **13a** and **13b**, the oxides (**42a**) (85 mg, 0.184 mmol) and (**42b**) (100 mg, 0.21 mmol) gave the alcohol (**43a**) (38 mg, 92%) and the alcohol (**43b**) (42 mg, 91%) respectively, as colorless oils.

The Alcohol (**43a**): IR ($CHCl_3$): 1700, 3600 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.38 (3H, s, C_9-CH_3), 2.54 (1H, br s, OH), 2.63 (1H, d, J=4.3 Hz, C_{10}-H_a), 2.92 (1H, d, J=4.3 Hz, C_{10}-H_b), 3.76 (3H, s, $COOCH_3$), 4.24 (1H, d, J=6.8 Hz, C_8-H), 5.93 (1H, d, J=15.4 Hz, =C_2H–), 5.83 (1H, dd, J=6.8, 15.2 Hz, –C_7H=), 6.22 (1H, dd, J=10.8, 10.8 Hz, =C_5H–), 6.33 (1H, dd, J=10.8, 10.8 Hz, –C_4H=), 6.95 (1H, dd, J=10.8, 15.2 Hz, =C_6H–), 7.75 (1H, dd, J=15.4, 10.8 Hz, –C_3H=). $[\alpha]_D^{25}$ +6.1 (c=1.15, CH_2Cl_2). HR-MS m/z: Calcd for $C_{12}H_{16}O_4$: 224.1049. Found: 224.1063.

The Alcohol (**43b**): IR ($CHCl_3$): 1700, 3600 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.35 (3H, s, C_9-CH_3), 2.55 (1H, br s, OH), 2.68 (1H, d, J=4.3 Hz, C_{10}-H_a), 2.89 (1H, d, J=4.3 Hz, C_{10}-H_b), 3.76 (3H, s, $COOCH_3$), 4.08 (1H, d, J=6.4 Hz, C_8-H), 5.91 (1H, d, J=15.4 Hz, =C_2H–), 5.81 (1H, dd, J=6.4, 14.5 Hz, –C_7H=), 6.22 (1H, dd, J=10.4, 10.4 Hz, =C_5H–), 6.33 (1H, dd, J=10.4, 10.8 Hz, –C_4H=), 6.92 (1H, dd, J=10.4, 14.5 Hz, =C_6H–), 7.75 (1H, dd, J=15.4, 10.8 Hz, –C_3H=). $[\alpha]_D^{25}$ +6.8 (c=1.13, CH_2Cl_2). HR-MS m/z: Calcd for $C_{12}H_{16}O_4$: 224.1049. Found: 224.1050.

Methyl 8(*R*)-(*N*-Acetyl-L-phenylalanyloxy)-9,10-epoxy-9(*S*)-methyldeca-(2*E*),(4*Z*),(6*E*)-trienoate (44a), and Its Epimers (44b, 44c, and 44d) By the method described for the preparation of the phenylalanyl esters (**14a** and **14b**), the *R-S* alcohol (**43a**) (109 mg, 0.473 mmol) gave the AK-toxin II methyl ester (**44a**) (60 mg, 31%) and D-phenylalanyl ester (**44b**) (80 mg, 41%) and the *R-R* alcohol (**43b**) (130 ml, 0.58 mmol) gave the L-phenylalanyl ester (**44c**) (70 mg, 30%) and the D-phenylalanyl ester (**44d**) (100 mg, 42%) as colorless oils.

AK-Toxin II Methyl Ester (**44a**): (Identical with AK-toxin II methyl ester obtained from AK-toxin II by treatment with diazomethane). IR ($CHCl_3$): 3480, 1730, 1700, 1670 cm^{-1}. ^{1}H-NMR (400 MHz in $CDCl_3$): 1.31 (3H, s, C_9-CH_3), 2.00 (3H, s, $COCH_3$), 2.62 (1H, d, J=4.7 Hz, C_{10}-H_a), 2.74 (1H, d, J=4.7 Hz, C_{10}-H_b), 3.12 (2H, d, J=6.2 Hz, $C_{3'}$-2H), 3.77 (3H, s, $COOCH_3$), 4.91 (1H, td, J=6.2, 7.5 Hz, $C_{2'}$-H), 5.27 (1H, d, J=7.9 Hz, C_8-H), 5.70 (1H, dd, J=7.9, 15.0 Hz, $-C_7H=$), 5.93 (1H, d, J=7.5 Hz, NH), 5.95 (1H, d, J=15.4 Hz, $=C_2H-$), 6.20 (1H, dd, J=11.4, 10.0 Hz, $-C_4H=$), 6.29 (1H, dd, J=11.3, 10.0 Hz, $=C_5H-$), 6.84 (1H, dd, J=11.3, 15.0 Hz, $=C_6H-$), 7.70 (1H, dd, J=15.4, 11.4 Hz, $-C_3H=$), 7.09—7.29 (5H, m, aromatic H). $[\alpha]_D^{15}$ +79.8 (c=0.75, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$: 413.1839. Found: 413.1818.

The Ester (**44b**): IR ($CHCl_3$): 3480, 1730, 1700, 1670 cm^{-1}. ^{1}H-NMR (400 MHz in $CDCl_3$): 1.25 (3H, s, C_9-CH_3), 1.97 (3H, s, $COCH_3$), 2.57 (1H, d, J=4.3 Hz, C_{10}-H_a), 2.73 (1H, d, J=4.3 Hz, C_{10}-H_b), 3.12 (2H, d, J=6.8 Hz, $C_{3'}$-2H), 3.76 (3H, s, $COOCH_3$), 4.91 (1H, td, J=6.8, 5.4 Hz, $C_{2'}$-H), 5.24 (1H, d, J=7.2 Hz, C_8-H), 5.72 (1H, dd, J=7.2, 14.5 Hz, $-C_7H=$), 6.02 (1H, d, J=5.4 Hz, NH), 5.92 (1H, d, J=14.8 Hz, $=C_2H-$), 6.12—6.45 (2H, m, $C_{4,5}$-H), 6.87 (1H, dd, J=10.8, 14.5 Hz, $=C_6H-$), 7.70 (1H, dd, J=14.8, 10.8 Hz, $-C_3H=$), 7.05—7.40 (5H, m, aromatic H). $[\alpha]_D^{15}$ +83.1 (c=0.55, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$: 413.1839. Found: 413.1797.

The Ester (**44c**): IR ($CHCl_3$): 3480, 1730, 1700, 1670 cm^{-1}. ^{1}H-NMR (400 MHz in $CDCl_3$): 1.32 (3H, s, C_9-CH_3), 1.99 (3H, s, $COCH_3$), 2.63 (1H, d, J=4.2 Hz, C_{10}-H_a), 2.81 (1H, d, J=4.2 Hz, C_{10}-H_b), 3.11 (2H, d, J=6.8 Hz, $C_{3'}$-2H), 3.76 (3H, s, $COOCH_3$), 4.89 (1H, td, J=6.8, 4.7 Hz, $C_{2'}$-H), 5.22 (1H, d, J=8.3 Hz, C_8-H), 5.64 (1H, dd, J=8.3, 14.5 Hz, $-C_7H=$), 5.94 (1H, d, J=4.7 Hz, NH), 5.93 (1H, d, J=15.1 Hz, $=C_2H-$), 6.15—6.42 (2H, m, $C_{4,5}$-H), 6.83 (1H, dd, J=14.5, 10.5 Hz, $=C_6H-$), 7.70 (1H, dd, J=15.1, 10.8 Hz, $-C_3H=$), 7.05—7.40 (5H, m, aromatic H). $[\alpha]_D^{15}$ +92.7 (c=1.20, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$: 413.1839. Found: 413.1805.

The Ester (**44d**): IR ($CHCl_3$): 3480, 1730, 1700, 1670 cm^{-1}. ^{1}H-NMR (90 MHz in $CDCl_3$): 1.34 (3H, s, C_9-CH_3), 1.98 (3H, s, $COCH_3$), 2.65 (1H, d, J=4.2 Hz, C_{10}-H_a), 2.71 (1H, d, J=4.2 Hz, C_{10}-H_b), 3.16 (2H, d, J=5.4 Hz, $C_{3'}$-2H), 3.76 (3H, s, $COOCH_3$), 4.95 (1H, td, J=5.4, 4.3 Hz, $C_{2'}$-H), 5.13 (1H, d, J=7.2 Hz, C_8-H), 5.75 (1H, dd, J=7.2, 14.5 Hz, $-C_7H=$), 5.96 (1H, d, J=4.3 Hz, NH), 5.94 (1H, d, J=14.8 Hz, $=C_2H-$), 6.15—6.47 (2H, m, $C_{4,5}$-H), 6.87 (1H, dd, J=14.5, 10.8 Hz, $=C_6H-$), 7.72 (1H, dd, J=14.8, 10.8 Hz, $-C_3H=$), 7.07—7.50 (5H, m, aromatic H). $[\alpha]_D^{15}$ +71.3 (c=0.67, EtOH). HR-MS m/z: Calcd for $C_{23}H_{27}NO_6$: 413.1839. Found: 413.1815.

Acknowledgement This study was supported in part by Grants-in-Aid for Scientific Research (No. 61571007 and 63303013) from the Ministry of Education, Science and Culture of Japan. We are indebted to Professor T. Ueno (Kyoto University) for his help in biological testing of our synthetic samples.

References

1) S. Tanaka, *Mem. Coll. Agr. Kyoto Univ.*, **28** (Phytopath. Series No. 6), 1 (1933).
2) T. Nakashima, T. Ueno, and H. Fukami, *Tetrahedron Lett.*, **23**, 4469 (1982); T. Nakashima, T. Ueno, H. Fukami, T. Taga, H. Masuda, K. Osaki, H Otani, K. Kohmoto, and S. Nishimura, *Agric. Biol. Chem.*, **49**, 807 (1985).
3) Preliminary report, H. Irie, K. Matsumoto, T. Kitagawa, Y. Zhang, T. Ueno, T. Nakashima, and H. Fukami, *Chem. Pharm. Bull.*, **35**, 2598 (1987).
4) T. Reichstein, A. Grussner, and W. Bosshard, *Helv. Chim. Acta*, **18**, 602 (1935).
5) A. Hassner and V. Alexanian, *Tetrahedron Lett.*, **1987**, 4475.
6) W. H. P. Lewis and H. Harris, *Nature* (London), **215**, 351 (1967).
7) T. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969).
8) J. F. Carvalho and G. D. Prestwich, *J. Org. Chem.*, **49**, 1251 (1984).