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Absolute Configuration of Main Chain of AAL-toxins.

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Key Words: AAL-toxin; *Alternaria alternata*; absolute configuration

Abstract: AAL-toxins TA_1 **1** and TA_2 **2**, host-specific toxins produced by *Alternaria alternata*, were degraded to 2-methylbutanol, 3-methylnonan-1,9-diol and *N*-protected 4-aminobutan-1,3-diol, which were further converted to (*R*)-MTPA esters. These esters were correlated with synthetic samples by comparison of their 500 MHz ^{1}H-NMR spectra. The remaining stereocenters were determined by the comparison of ^{1}H-NMR spectra of **6a** and **7** derived from **1** and **2** with those of synthetic model compounds. These data conclude that AAL-toxins possess 2*S*, 4*S*, 5*R*, 11*S*, 13*S*, 14*R* and 15*R* configurations.

Host-specific toxins (HST)[1] in plant diseases are interesting topics for studying host-parasite interaction. AAL-toxins TA_1 **1** and TA_2 **2**[2] (Figure 1), HST produced by *Alternaria alternata* f. sp. *lycopersici*, a causal fungus of tomato stem canker reproduce similar symptoms to those of the disease for susceptible genotype of tomato leaf in concentrations less than 10 ng/ml.[2,3] From genetic analysis, Gilchrist *et al.* proposed that a single gene (*asc*) controls sensitivity to the toxin and susceptibility to the fungus.[4] Although the same group suggested that the target of AAL-toxins is aspartate carbamoyl transferase (ACTase),[4] recent studies on the *asc* locus using RFLP analysis in tomato concluded that the locus does not encode ACTase.[5] Recently, mycotoxin fumonisins **3a**

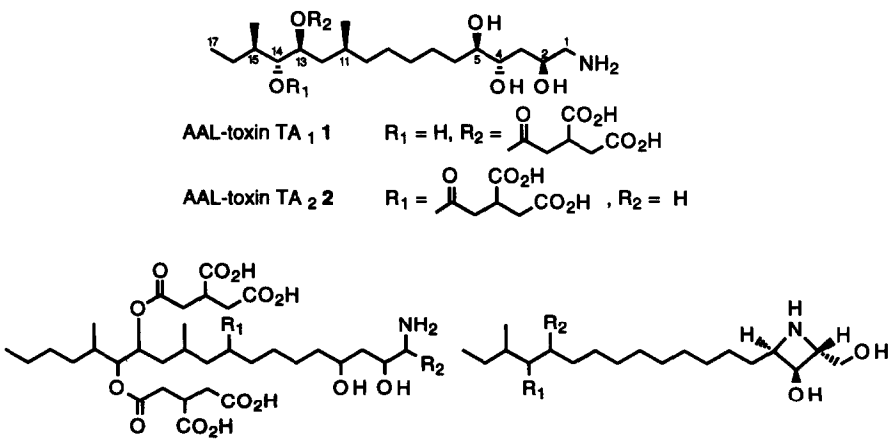


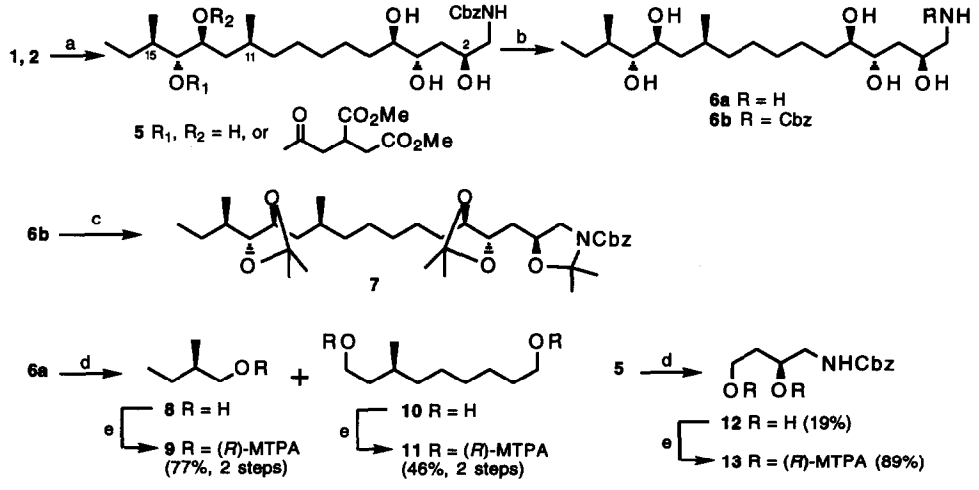
Figure 1

- **3c**,[6] structurally related to AAL-toxins, were found to be a tumor promotor[7] and an inhibitor of sphingolipid biosynthesis.[8] Both AAL-toxins and fumonisins exhibited similar biological activities in cytotoxicity to mammalian cell and phytotoxicity to susceptible tomato cell.[9] Based on structural similarity, Shier proposed to classify AAL-toxins and fumonisins including penaresidines,[10] **4a** and **4b** as a sphingosine analog toxin.[11]

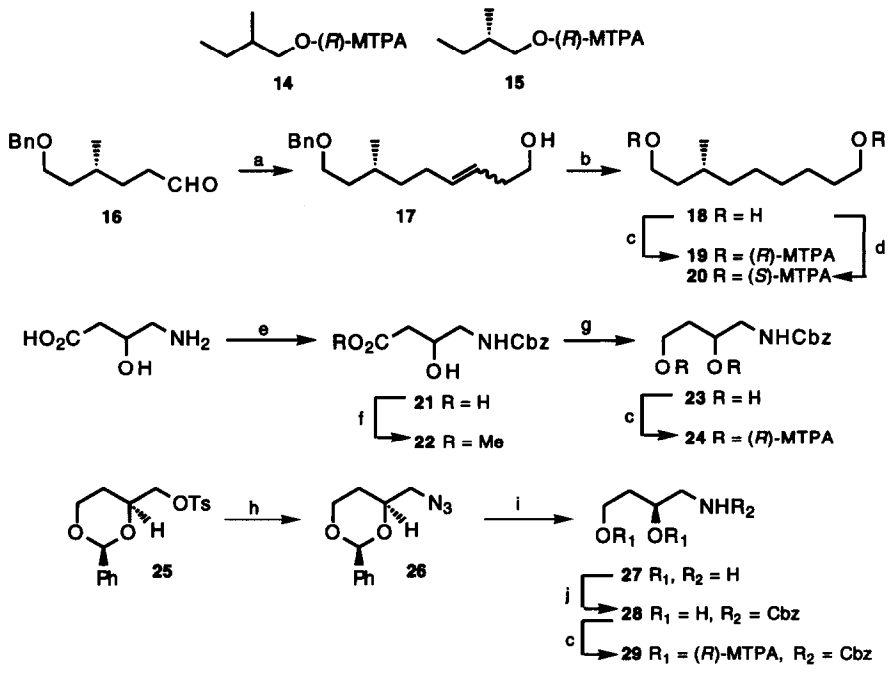
Although Bottini *et al.* determined the gross structure of **1** and **2** by the extensive analysis of MS, ^{1}H- and ^{13}C-NMR spectra,[2b,2c] relative and absolute stereochemistry of **1** and **2** remained to be solved. For understanding the mechanism of the host-specificity of AAL-toxins at the molecular level, the elucidation of stereostructure and synthetic studies are essential. Recently, we reported the absolute configuration of aminopentol part of **1** and **2**.[12,13] Kishi *et al.* independently reached the same conclusion using different approach synthesizing a number of possible isomers.[14] In this report, we describe a full account of our work on the absolute configuration of AAL-toxins TA_1 **1** and TA_2 **2**.

At first, we decided to degrade AAL-toxins to three fragments **8**, **10**, and **12** by oxidative scission of two vicinal diol moieties in **1** and **2** in order to establish the absolute configuration at C-2, C-11 and C-15. In principle, those configurations can be determined by direct comparison of optical rotation of the degradation products with that of synthetic materials. We, however, expected that this was impractical due to the small quantities of degradation products and the low values of their optical rotations. Hence, the degradation products **8**, **10**, and **12** were converted to (*R*)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) esters **9**, **11**, and **13**, which were compared with synthetic samples by reasonably sensitive high-field ^{1}H-NMR spectroscopy.

For degradative study, AAL-toxins **1** and **2** were isolated from the cultures of *Alternaria alternata* tomato pathotype (*A. alternata* f. sp. *lycopersici*) O-227.[3] Degradation of **1** and **2** was carried out in two different ways as shown in Scheme 1. At first, aminopentol **6a**[2b] was degraded by oxidative cleavage with $NaIO_4$. The resultant mixture of aldehydes was reduced with $NaBH_4$ to yield two alcohols **8** and **10**, which were directly submitted to esterification with (*R*)-MTPA to afford esters **9** and **11**. To obtain the stereochemical information at C-2, the other degradation was carried out. After methylation of a mixture of **1** and **2**, the amino group was protected by carbobenzyloxy (Cbz) group which also served as a chromophore in HPLC separation to yield **5**. Oxidative cleavage of **5** between C-4 and C-5, following reduction and HPLC separation gave diol **12**, which was further converted to bis-(*R*)-MTPA ester **13**. From aminopentol analog **6b**, acetonide **7** was prepared for the elucidation of relative stereochemistry of the left part of **1** and **2**.



Scheme 1 (a) CH_2N_2, MeOH; CbzCl, $NaHCO_3$, H_2O, quant.; (b) K_2CO_3, MeOH; (c) 2,2-dimethoxypropane, p-TsOH, 39% (2 steps); (d) $NaIO_4$, THF-H_2O (1:1), then $NaBH_4$; (e) (*R*)-(+)-MTPA, DCC, DMAP, CH_2Cl_2.



Scheme 2 (a) $HO(CH_2)_3PPh_3^+Br^-$, ^nBuLi, THF, rt, 53%; (b) H_2, $Pd(OH)_2$, EtOH, 49%; (c) (*R*)-MTPA, DCC, DMAP, CH_2Cl_2; (d) (*S*)-MTPA, DCC, DMAP, CH_2Cl_2; (e) CbzCl, Na_2CO_3, H_2O, 57%; (f) CH_2N_2, THF, quant.; (g) $LiAlH_4$, THF, 40%; (h) NaN_3, DMF, 100°C, 99%; (i) H_2, Pd/C, 1M HCl-MeOH, quant.; (j) CbzCl, $NaHCO_3$, H_2O, 98 %.

For comparison with the naturally derived substances, authentic samples of MTPA esters **14**, **15**, **19**, **20**, **24** and **29** were synthesized as shown in Scheme 2. Both esters **14** and **15** were prepared by the condensation of (*RS*)- and (*S*)-2-methylbutanol with (*R*)-MTPA. The preparation of (*R*)-diol **18** began with the aldehyde **16**[15] derived from (*R*)-citronellal. Wittig reaction of the ylide from 3-hydroxypropylphosphonium bromide with the aldehyde gave an isomeric mixture of alkenol **17**. Without separation, **17** was subjected to hydrogenation and concomitant debenzylation to afford diol **18** in 23% overall yield. The esterification of diol (*R*)-**18** with (*R*)- and (*S*)-MTPA yielded diastereomers **19** and **20**, respectively. Racemic alcohol **23** was prepared from γ-amino-β-hydroxybutyric acid. Similar treatment in the case of **5** gave *N*-protected methyl ester **22**. Reduction with $LiAlH_4$ gave diol **23** which was condensed with (*R*)-MTPA to afford ester **24**. Starting from tosylate **25**[16] derived from L-malic acid, **29** was prepared in four steps as shown in Scheme 2. Treatment with sodium azide gave azide **26** which was catalytically hydrogenated to yield aminodiol **27**. Protection of the resulting amino group with Cbz and esterification gave bis-(*R*)-MTPA ester **29** in 67% overall yield.

With the synthetic esters in hand, their ^{1}H-NMR spectra were measured at 500 MHz in order to confirm whether pairs of diastereomers were distinguishable. As shown in Figures 2, 3 and 4, most signals originated from methylene groups adjacent to asymmetric centers were well separated. This allowed us unambiguous identification of the esters from degradations. Comparison of ^{1}H-NMR spectrum of degradation product **9** with those of synthetic samples **14** and **15** clearly shows that **9** is identical with 2*R*-isomer of **15** (Figure 2). Similarly, comparison of the spectrum of naturally derived substance **11** with that of synthetic **20** reveals their identity (Figure 3). This proves that **11** is an enantiomer of **20** and the configuration of **11** is *S*. Finally, the results in Figure 4 indicate that the ester **13** obtained from **1** and **2** is identical with synthetic **29**. Hence, the absolute stereochemistry at C-2 of **13** was determined as *S*. The determination of the absolute configuration of

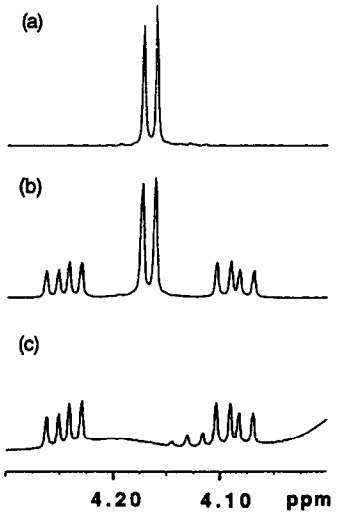


Figure 2 Parts of ^{1}H-NMR spectra (500 MHz) of: synthetic materials (a) **15**; (b) **14**; degradation product (c) **9**.

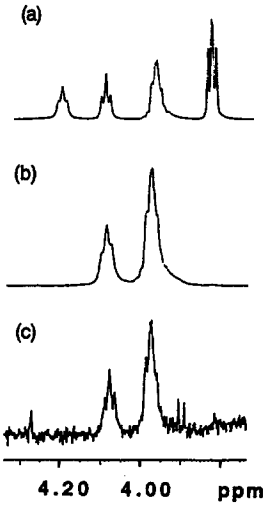


Figure 4 Parts of ^{1}H-NMR spectra (500 MHz) of: synthetic materials (a) **24**; (b) **29**; degradation product (c) **13**.

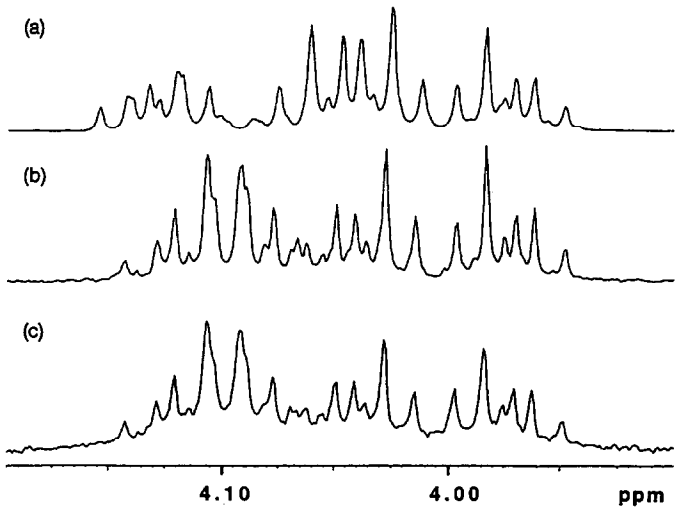
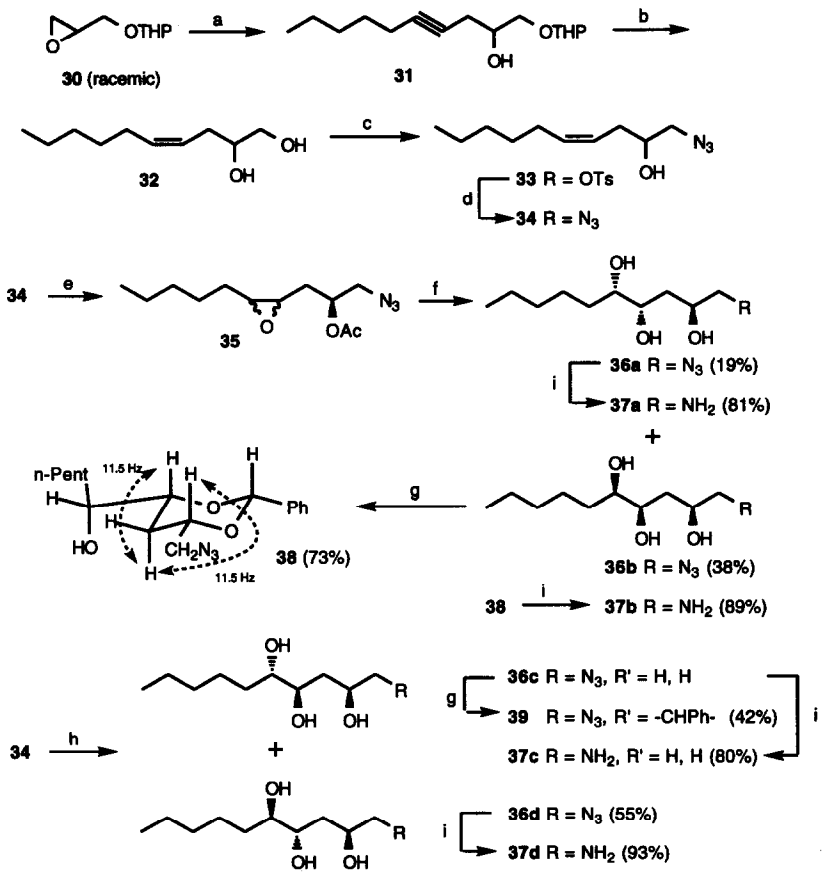


Figure 3 Parts of ^{1}H-NMR spectra (500 MHz) of: synthetic materials (a) **19**; (b) **20**; degradation product (c) **11**.

esters **9**, **11** and **13** specifies the absolute configuration of main chain of AAL-toxins as 2*S*, 11*S* and 15*R*.

It is reasonable to assume that molecule of AAL-toxins can be divided into two parts since the remote stereocenters are not affected each other in spectroscopic properties. This was ascertained by the following evidence; a structural difference of two components of AAL-toxins TA_1 **1** and TA_2 **2**, whose acyl group is substituted at C-13 and C-14, respectively, does not affect the NMR resonances of right half of **1**.[2c] Therefore, we expected that aminotriols **37a** - **37d** (Scheme 3), acetonides **44a** - **44d** (Scheme 4), and **53a**, **53b** (Scheme 5) are suitable model compounds for determining unsolved relative stereochemistries of **1** and **2**.

The synthetic pathway of four possible isomers **37a** - **37d** was shown in Scheme 3. The required carbon skeleton of the model triols was constructed by condensation of lithium acetylide derived from 1-heptyne with epoxide **30** in high yield. The coupling product **31** was hydrogenated to corresponding *cis*-olefin which was further converted to azide **34** by deprotection of THP group, tosylation of primary alcohol and azidation. From this homoallyl alcohol **34**, 4,5-*syn*- and 4,5-*anti*-diols were prepared by the following transformations. After acetylation, treatment of *O*-acetyl-**34** with m-chloroperbenzoic acid gave epoxide **35**[17] as a diastereomeric mixture. This was submitted to sequential hydrolysis with perchloric acid and aqueous KOH to afford a 1:2 mixture of two 4, 5-*syn*-triols **36a** and **36b**,[17] which were easily separated by SiO_2 chromatography. The major isomer



Scheme 3 (a) 1-heptyne, ^{n}BuLi, HMPA-THF (9:1), 0°C→rt, 82%; (b) H_2, Pd-$BaSO_4$, quinoline, MeOH; 1M HCl-MeOH, 94%; (c) TsCl, Py, CH_2Cl_2, 0°C, 70%; (d) NaN_3, DMF, 70°C, 47%; (e) Ac_2O, Py; mCPBA, CH_2Cl_2,quant.; (f) aq.7% $HClO_4$, dioxane, 60°C; 0.3M KOH, 60°C, 90% (2 steps); (g) PhCHO, $ZnCl_2$, C_6H_6; (h) OsO_4, NMO, MeCN-H_2O, 96%; (i) H_2, Pd-black, 0.1% HCl-MeOH.

36b was then converted to benzylidene acetal **38**, whose ^{1}H-NMR spectrum clearly shows 2,4-*syn* relationship (Scheme 3). Whereas catalytic dihydroxylation with OsO_4 of azide **34** gave hardly separable 4,5-*anti*-triols **36c** and **36d**. When this mixture was treated with benzaldehyde and $ZnCl_2$, 2,4-*syn* isomer **36c** predominantly yielded acetal **39** while unreacted 2,4-*anti*-isomer **36d** was recovered. The compounds **36a**, **36b**, **36d** and **39** were hydrogenated under acidic condition to afford the corresponding aminotriols **37a** - **37d** as hydrochloride salts. The stereospecific transformations from **34** to **37a** - **37d** and the NMR analysis of benzylidene acetals **38** and **39** enabled us to assign the relative stereocenters of aminotriols **37a** - **37d**.

In the ^{1}H-NMR spectra of AAL-toxins **1**, **2** and their deacylated analog **6a**, the right half in those compounds is indistinguishable.[2c] This means that **1** and **2** exist as the same conformation as that of **6a** in aqueous solution. In order to compare the ^{1}H-NMR spectrum of aminopentol **6a**,[2b] those of the synthesized aminotriols, **37a** - **37d** in D_2O were measured at 500 MHz (Table 1). Among the aminotriols, 2,4-*syn* isomers **37b** and **37c** were easily excluded by the comparison of the coupling constants (2-H and 4-H) in their ^{1}H-NMR spectra with those from **6a**. Although the NMR spectra of the remaining 2,4-*anti*-aminotriols **37a** and **37d** were very similar, inspection of both chemical shifts and *J*-values allowed us to determine that the relative stereochemistry of the right part of **6a** is the same as that of **37d** (2,4-*anti*-4,5-*anti*). In addition, ^{13}C-NMR data supported this conclusion; the resonances at 74.81 (C-5) and 35.88 ppm (C-3) in **37d** were nearly identical to those of **6a**[2b] while those signals in **37a** were observed at 75.54 and 37.31 ppm. Hence, the absolute configuration in right half of AAL-toxins **1** and **2** was elucidated as 2*S*, 4*S* and 5*R*. On the basis of *J*-values in the ^{1}H-NMR spectrum of **6a**, Bottini *et al.* proposed the relative stereochemistry at C-2, C-4 and C-5 as all-*S* or all-*R* (2,4-*anti*-4,5-*syn*).[2b,2c] Our data clearly indicate that 4,5-*syn* **37a** and 4,5-*anti* **37d** cannot be distinguished without comparing spectral data of the synthetic samples. Furthermore, the results of spectral analysis of the model aminotriol **37d** enabled us to conclude that the conformation of left part of **1** and **2** does not affect that of the right part in aqueous solution.

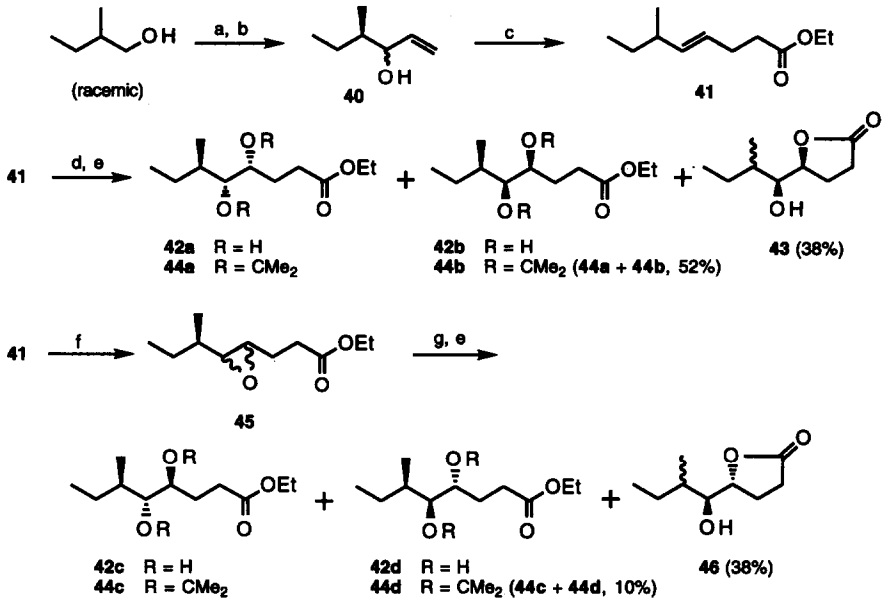
Table 1. ^{1}H-NMR data (500 MHz, D_2O) of aminotriols **37a** - **37d**, and aminopentol **6a** derived from AAL-toxins TA_1 **1**, and TA_2 **2**.

	δ (ppm)/J (Hz)				
	37a	**37b**	**37c**	**37d**	**6a**[a)]
1-H_A	3.15	3.19	3.19	*3.16*	*3.164*
	(3.3, 13.1)	(3.2, 13.1)	(3.0, 13.1)	*(2.9, 13.1)*	*(3.0, 13.1)*
1-H_B	2.93	2.96	2.96	*2.93*	*2.938*
	(9.6, 13.1)	(9.6, 13.1)	(9.6, 13.1)	*(9.9, 13.1)*	*(9.9, 13.1)*
2-H	4.06	4.07	4.09	*4.06*	*4.063*
	(3.3, 3.3,	(3.2, 6.4,	(3.0, 6.4,	*(2.9, 2.9,*	*(3.0, 3.0,*
	9.6, 9.6)	6.4, 9.6)	6.4, 9.6)	*9.9, 9.9)*	*9.9, 9.9)*
3-H_A	1.64	1.77	1.81	*1.67*	*1.650*
	(3.3, 9.6, 14.5)	(6.4, 6.4)	(3.3, 6.4, 14.6)	*(2.0, 9.9, 14.5)*	*(2.0, 9.9, 14.8)*
3-H_B	1.59	1.77	1.70	*1.54*	*1.533*
	(3.3, 9.6, 14.5)	(6.4, 6.4)	(6.4, 9.5, 14.6)	*(2.9, 10.8, 14.5)*	*(3.0, 10.8, 14.8)*
4-H	3.74	3.70	3.69	*3.76*	*3.739*
	(3.3, 4.1, 9.6)	(4.0, 6.4, 6.4)	(3.3, 4.6, 9.5)	*(2.0, 4.3, 10.8)*	*(2.0, 4.5, 10.8)*
5-H	3.49	3.53	3.56	*3.59*	*3.556*
	(4.1, 4.1, 8.2)	(4.0, 4.0, 8.5)	(3.4, 4.6, 9.1)	*(3.7, 4.3, 7.6)*	*(4.5, 6-8, 6-8)*

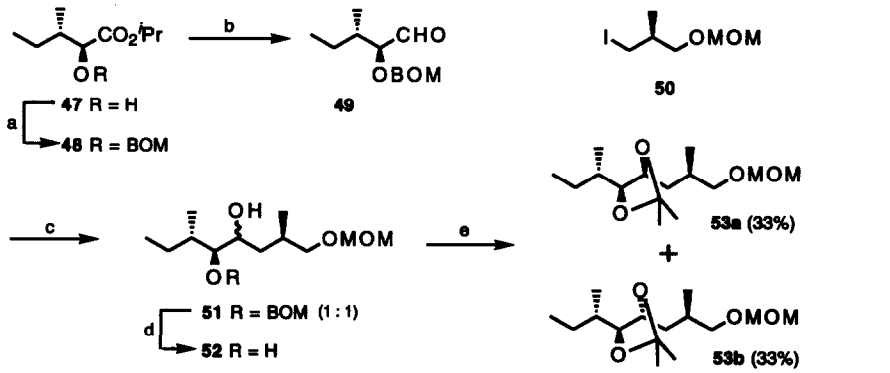
a) Data were taken from ref. 2b.

Next, we investigated three contiguous stereochemistries at C-13, C-14 and C-15 in AAL-toxins **1** and **2**. First, we synthesized four possible model acetonides **44a** - **44d** to compare **7** in NMR spectroscopy (Scheme 4). Swern oxidation of (*RS*)-2-methylbutanol, the coupling with vinylmagnesium bromide gave a diastereomeric

mixture of alcohol **40**, which, without separation, was submitted to orthoester Claisen rearrangement to yield γ,δ-unsaturated ester **41** in 36% overall yield. Oxidation of olefin **41** with OsO_4-*N*-methylmorpholine-*N*-oxide afforded *syn*-diols **42a** and **42b** which were further converted to *syn*-acetonides **44a** and **44b**. On the other hand, epoxidation of olefin **41** with m-chloroperbenzoic acid and following acid treatment gave *anti*-diols **42c** and **42d** which were transformed into *anti*-acetonides **44c** and **44d**. In these acetonide formations, concomitant lactonizations were occurred and considerable amounts of undesired lactones **43** and **46** were formed. Without separation, mixtures of these diastereomeric acetonides were submitted to ^{1}H-NMR measurement.



Scheme 4 (a) $(COCl)_2$, DMSO, CH_2Cl_2, -78°C; Et_3N; (b) CH_2=CHMgBr, THF, -78°C; (c) $CH_3C(OEt)_3$, propionic acid, 100°C, 36% (3 steps); (d) OsO_4, NMO, quant.; (e) 2,2-dimethoxypropane, p-TsOH; (f) mCPBA, CH_2Cl_2, 97%; (g) 3.5% $HClO_4$-THF.



Scheme 5 (a) BOMCl, ^{i}Pr$_2$NEt, CH_2Cl_2, 0°C→rt, 85 %; (b) DIBAH, Et_2O, -78°C, 78 %; (c) **50**, ^{t}BuLi, -78°C, 55 %; (d) H_2, Pd-black, EtOAc, quant.; (e) 2,2-dimethoxypropane, p-TsOH.

To obtain unambiguous information on the relative stereochemistry at C-13, C-14 and C-15, we synthesized stereochemically defined model compounds **53a** and **53b** as shown in Scheme 5. Protection of hydroxyester **47**[18] followed by reduction with DIBAH afforded aldehyde **49**. Alkyl lithium reagent derived from iodide **50**[19] was condensed with the aldehyde **49** to afford coupling product **51** which was obtained as nearly 1:1 epimeric mixture. After reductive deprotection of BOM ether, resultant diol **52** was converted to corresponding acetonides **53a** and **53b**, which were easily separated by SiO_2 chromatography.

The ^{1}H-NMR data of the synthetic acetonides **44a** - **44d**, **53a**, **53b** and the acetonide **7** derived from AAL-toxins were summarized in Table 2.[20] The assignment of each signal in ^{1}H-NMR spectra of these acetonides was performed by the analysis of COSY, HMQC and HMBC spectra, and by extensive decoupling experiments. Although partial structures between the acetonides **44a** - **44d** and chiral the acetonides **53a** and **53b** were fairly different, there were clear similarities in *anti*-acetonides and in *syn*-acetonides; the chemical shifts of acetonide methyls were very close to each other (Δ~0.01ppm) in the *syn*-acetonides **44a**, **44b** and **53a** but those in the *anti*-acetonides **44c**, **44d** and **53b** were clearly separated (Δ~0.1ppm). In addition, the chemical shifts of 13-H and 14-H in the *syn*-acetonides **44a**, **44b** and **53a** were markedly different from those in the *anti*-acetonides **44c**, **44d** and **53b** (*syn*; 13-H, ~3.8 ppm, 14-H, ~3.5 ppm: *anti*; 13-H, ~4.1 ppm, 14-H, ~3.8 ppm). The results indicate that the C(13)-C(17) moiety in the acetonides is independent from the partial structure away from C-11 in their ^{1}H-NMR spectra. Compared with the NMR data of the acetonide **7** and those of the synthetic acetonides, the relative stereochemistry at C-13 and C-14 in AAL-toxins was determined as *anti*.

Table 2. ^{1}H-NMR data (500 MHz, $CDCl_3$) of synthetic acetonides **44a** - **44d**, **53a**, **53b** and acetonide **7** derived from AAL-toxins TA_1 **1** and TA_2 **2**.[20]

	δ (ppm)/J (Hz)					
	13-H	14-H	15-CH_3	16-H (CH_2)	17-H (CH_3)	acetonide methyls
44a	3.8	3.50	0.91		0.92	1.360
	(m)	(7.0, 7.0)	(7.3)		(6.5)	1.369
44b	3.8	3.56	0.95		0.93	1.360
	(m)	(4.5, 7.8)	(6.6)		(7.4)	1.369
44c	*4.040*	*3.76*	*0.86*	*1.76*[b]	*0.91*	*1.32*
	(m)	*(5.2, 9.9)*	*(6.6)*	*1.20*[b]	*(7.4)*	*1.42*
44d	4.005	3.76	1.03	1.38[b]	0.93	1.32
	(m)	(5.2, 9.9)	(6.5)	1.08[b]	(7.4)	1.42
53a	3.88	3.45	0.90		0.91	1.363
	(2.8, 7.7, 9.9)	(6.3, 7.7)	(6.8)		(7.4)	1.377
53b	*4.12*	*3.76*	*0.83*	*1.75*	*0.91*	*1.33*
	(2.4, 5.2, 11.9)	*(5.2, 10.1)*	*(6.6)*	*1.20*	*(7.5)*	*1.43*
7	*4.08*[a]	*3.73*	*0.82*	*1.75*[b]	*0.91*	*1.33*
	(m)	*(5.2, 9.9)*	*(6.6)*	*1.18*[b]	*(7.3)*	*1.42*

a) The signal of 13-H was overlapped with that of 5-H.
b) The chemical shifts were obtained from COSY spectra.

The remaining relative stereochemistry for C-14 and C-15 was determined as follows. In the *anti*-acetonides **44c** and **44d**, the chemical shifts of 15-CH_3 and 16-H were markedly different; 0.86, 1.20 and 1.76 ppm in **44c**, 1.03, 1.08 and 1.38 ppm in **44d**. Since the stereochemically defined acetonide **53b** had nearly identical ^{1}H-NMR data for the C(13)-C(17) region with those of **44c** and **7**, the relative stereochemistry at C-14 and C-15 was established as *anti*. This result was supported by the following conformational analysis for **44c** and **44d**. From large coupling constants (9.9 Hz) in both acetonides, antiperiplanar relationship of 14-H and 15-H was

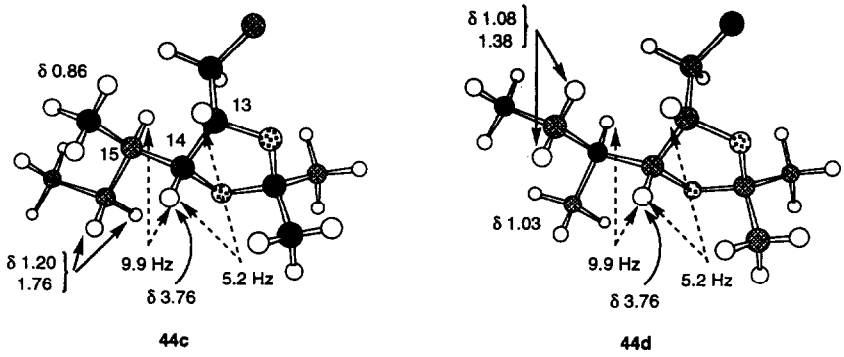


Figure 5 The proposed conformations of *anti*-acetonides **44c** and **44d**, with ester moieties omitted for clarity.

confirmed. In addition, nearly identical chemical shifts for 13-H, 14-H, and acetonide methyls suggested that both *anti*-acetonides exist as the virtually identical conformation except the location of 15-CH_3 and ethyl group (C-16, C-17). Based on these stereochemical data, MM2 calculations on **44c** and **44d** were performed and the results are shown in Figure 5. In these conformations, low-field shifts of 15-CH_3 in the ^{1}H-NMR spectrum of **44d** and of 16-H in that of **44c** can be explained by anisotropic effect of 14-oxygen. The established relative stereochemistry for C-13, C-14 and C-15 concludes absolute configurations of the left part of AAL-toxins as 13*S*, 14*R* and 15*R*, respectively. Thus, we determined the whole absolute stereochemistry of main chain of AAL-toxins TA_1 **1** and TA_2 **2** as depicted in Figure 1. Our empirical rule for the 1,2-acetonide with α-methyl group could be applied to the determination of the relative stereochemistry in left part of fumonisins.

With the absolute configuration of aminopentol part of **1** and **2** established, the conformation of the right half was examined next. From the calculated dihedral angles using Karplus equation and NOE studies for **37d**, the conformation of this part was proposed. MM2 calculation of this conformation, not global minimum search, was undertaken and the energy-minimized conformation is shown in Figure 6. This stereostructure indicated the hydrogen bonds to be between NH→2-O and 4-OH→5-O even in aqueous solution. Thus, in order to avoid steric hindrance between two pseudo-cyclic systems, the right part of **1** and **2** predominates the conformation as shown in Figure 6. Previous conformational studies of acyclic polyols[21] in D_2O showed that they exist as several energetically similar conformers. The conformation of aminotriol part in **1** and **2** is therefore a relatively unusual case in an acyclic system. The role of this conformer to biological activity is interesting.

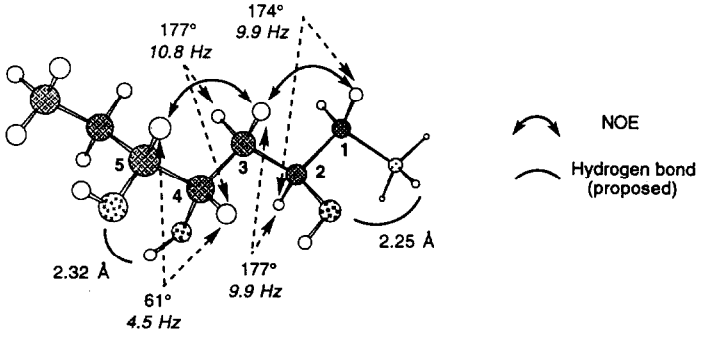


Figure 6 The proposed conformation of the right half of AAL-toxins **1** and **2**. The values were dihedral angles and distances in this conformation, and were coupling constants observed in ^{1}H-NMR spectrum of **1** and **2**.

In conclusion, the absolute configuration of AAL-toxins **1** and **2** except one at side chain has been established by degradation of **1** and **2**, and synthesizing model compounds. Currently, we are undertaking to determine the remaining absolute stereochemistry on the side chain of **1** and **2**, and to synthesize **1** and **2**.

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Experimental

Melting points were determined on Yanaco Micro-melting Point Apparatus MP-30 and were uncorrected, IR spectra on a Hitachi 285 and Perkin-Elmer 1720 spectrophotometer, ^{1}H- and ^{13}C-NMR spectra either on Bruker AM-500 or JEOL EX-270 spectrometers for solutions of $CDCl_3$, C_6D_6 or D_2O, mass spectra on JEOL DX-300 and 01SG-2 spectrometer, and optical rotation on a Jasco DIP-4 polarimeter. Column chromatography used Merck Kiesel gel 60 (0.04-0.063 mm) and Wakogel C-200 (0.075-0.15 mm) and TLC was performed on Merck Kiesel gel 60 F_{254}. HPLC was performed with Waters 600E and 741 data module and GL Science reversed phase column (Inertsil ODS-2, 5 μm, φ4.6 x 250 mm or φ6 x 250 mm). Solvents were dried by shortly before use from an appropriate drying agent. Anhydrous reactions were carried out under argon atmosphere. Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification.

Isolation of AAL-toxins TA_1 (1) and TA_2 (2). *Alternaria alternata* tomato pathotype (*A. alternata* f. sp. *lycopersici*) O-227 was inoculated to the cultures, in hundred twenty 500 ml flasks containing 150 ml of 2% potato-sucrose medium. The fermentation was carried out under fluorecent light at 22°C. After 18 days, the broth was filtrated and concentrated *in vacuo* to the volume 1.6 L. To this concentrate was added 400 ml of EtOH, and the resultant precipitate was removed by centrifugation. After evaporation of EtOH, aqueous layer was extracted with EtOAc (0.9 L x 3) and then n-BuOH (0.9 L x 5). The EtOAc extract was discarded. Concentration of the n-BuOH extract gave a residue (1.92 g) which was dissolved in H_2O and was applied to cation exchange column (Dowex 50 x 4, H^+ form, 30 ml). The column was washed with H_2O and eluted with 2M aqueous NH_4OH. Concentration gave a residue (227 mg) which was taken up to H_2O and purified with anion exchange chromatography (Dowex 1 x 4, AcO^- form, 30 ml) using 2M AcOH as eluent. The eluate was concentrated in vacuo to give a residue (85.1 mg) which was dissolved in MeOH and passed through SEP-PAK C18. The solution containing the toxin was further purified with reversed phase HPLC (Inertsil ODS, φ4.6 x 250 mm, MeOH/H_2O, 1:1-1:0, 0.5 ml/min, UV 210 nm, gradient time 60 min using gradient curve 10) to yield 1.9 mg of AAL-toxins TA_1 (**1**) and TA_2 (**2**) as a colorless caramel. Our sample was identical with the reported AAL-toxin TA in all spectroscopic analysis. $[\alpha]_{577}^{22}$ -23° (c 1.9, H_2O)^{22}; lit. $[\alpha]_{578}^{22}$ +22° (c 2.7, H_2O).[2c]

Degradation and derivatization of aminopentol (6a). To a solution of aminopentol **6a**[2b] (6.0 mg, 0.017 mmol) in 0.5 ml of THF-H_2O (1:1) was added sodium periodate (12.9 mg, 0.060 mmol). The mixture was stirred at room temperature for 3 h. The resultant yellow suspension was filtered through glass wool, and the residue was washed with 0.5 ml of THF-H_2O (1:1). Under ice-cooling, sodium borohydride (12.4 mg, 0.328 mmol) was added and stirred for 4 h at room temperature. The mixture was diluted with 2.5 ml of CH_2Cl_2, and acidified with 2M HCl. The organic phase was separated and washed with H_2O, and dried ($MgSO_4$). The extract was filtrated through glass wool, washed with 1.5 ml of CH_2Cl_2. To the filtrate was added 1,3-dicyclohexylcarbodiimide (DCC) (46.4 mg, 0.225 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (2.3 mg, 0.019 mmol), and (*R*)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) (52.6 mg, 0.225 mmol), and stirred for 17 h. After addition of DCC (50 mg, 0.242 mmol), stirring was continued for 3 h. Filtration and concentration gave an oil which was chromatographed (SiO_2, n-hexane/EtOAc, 85:15). The fraction containing esters **9** and **11** was concentrated and purified further (preparative SiO_2 TLC, n-hexane/EtOAc, 85:15) to afford 4.4 mg (77%) and 5.2 mg (46%) of **9** and **11**, respectively. These compounds are identical with material synthesized independently (vide infra).

***N*-(Benzyloxycarbonyl)-AAL toxin TA dimethyl ester (5).** The mixture of AAL-toxins TA_1 (**1**) and

TA_2 (**2**) (5.3 mg, 9.65 μmol) in 1 ml of MeOH was treated with excess CH_2N_2. Concentration gave an oil which was dissolved in 1 ml of MeOH. To the ice-cooled solution was added $NaHCO_3$ (3.2 mg, 0.038 mmol) and carbobenzyloxy chloride (2 μl, 0.014 mmol) and stirred at room temperature overnight. The mixture was quenched with 0.1 ml of concentrated ammonia, diluted with saturated $NaHCO_3$, and extracted with EtOAc. The extract was dried (Na_2SO_4) and concentrated to give an oil which was chromatographed (SiO_2, CH_2Cl_2/MeOH, 98:2-94:6) to afford 6.7 mg (quant.) of **5** as an oil. $[\alpha]_D^{23}$ -6.2° (c 0.49, $CHCl_3$). IR (NaCl): 3402, 2932, 2857, 1732, 1537, 1455, 1439, 1410, 1377, 1264, 1169, 1059, 1023, 839, 751, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.44-7.29 (5H, m, aromatic), 5.28 (1H, br.s, NH), 5.17 (0.5H, br.d, J = 11 Hz, 13-H), 5.11 (2H, s, benzylic), 4.82 (0.5H, dd, J = 8, 3.5 Hz, 14-H), 4.05 (1H, br.s, 2-H), 3.88 (0.5H, m, 14-H), 3.85 (1H, m, 4-H), 3.72 (1.5H, s, OCH_3), 3.70 (1.5H, s, OCH_3), 3.69 (3H, s, OCH_3), 3.64 (1H, m, 5-H), 3.43 (1H, m, 1-H_A), 3.39 (0.5H, m, 14-H), 3.30 (1H, m, 1-H_B), 3.25 (1H, m, 3'-H), 2.82 (0.5H, dd J = 16.5, 7.5 Hz, 2'-H or 4'-H), 2.78 (0.5H, dd, J = 16.5, 6.8 Hz, 2'-H or 4'-H), 2.75 (1H, dd, J = 17, 7 Hz, 2'-H or 4'-H), 2.68 (0.5H, dd, J = 17, 6 Hz, 2'-H or 4'-H), 2.67 (0.5H, dd, J = 16.5, 6.5 Hz, 2'-H or 4'-H), 2.60 (0.5H, dd, J = 16.5, 6.5 Hz, 2'-H or 4'-H), 2.58 (0.5H, dd, J = 16.5, 6.5 Hz, 2'-H or 4'-H), 1.80-0.95 (10H, m), 0.93 (1.5H, d, J = 7.0 Hz, 15-CH_3), 0.92-0.88 (7.5H, m, other CH_3). ^{13}C-NMR (67.5 MHz, $CDCl_3$): δ 174.1 (C), 172.7 (C), 172.0 (C), 171.9 (C), 170.8 (C), 157.4 (C), 135.7 (C), 128.5 (CH), 128.2 (CH), 128.1 (CH), 82.0 (CH), 76.5 (CH), 74.8 (CH), 74.4 (CH), 71.4 (CH), 71.1 (CH), 69.1 (CH), 69.0 (CH), 67.0 (CH_2), 52.5 (CH_3), 52.4 (CH_3), 52.1 (CH_3), 52.0 (CH_3), 47.0 (CH_2), 37.6 (CH), 37.4 (CH), 36.5 (CH), 35.8 (CH_2), 35.5 (CH_2), 35.1 (CH_2), 35.0 (CH_2), 34.8 (CH_2), 34.6 (CH_2), 34.5 (CH_2), 34.3 (CH_2), 31.9 (CH_2), 31.8 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.8 (CH), 28.7 (CH), 26.2 (CH_2), 25.37 (CH_2), 25.33 (CH_2), 25.1 (CH_2), 24.8 (CH_2), 20.8 (CH_3), 20.6 (CH_3), 15.2 (CH_3), 14.7 (CH_3), 10.9 (CH_3), 10.8 (CH_3). FIMS m/z: 684 (39), 683 (M^+, 76), 256 (72), 108 (30), 91 (12). FIHRMS m/z 683.3937 (M^+, $C_{35}H_{57}NO_{12}$ requires 683.3881).

Acetonide (7). To a solution of **5** (5.7 mg, 8.35 μmol) in 0.5 ml of MeOH-H_2O (4:1) was added K_2CO_3 (41.4 mg, 0.316 mmol). The mixture was stirred for 1 h, diluted with H_2O and extracted with EtOAc. The organic phase was washed with brine and dried (Na_2SO_4). Concentration of the extract gave an oil which was dissolved in 0.5 ml of 2,2-dimethoxypropane containing p-toluenesulfonic acid (0.5 mg, 2.63 μmol). The mixture was stirred for 40 min, quenched with saturated $NaHCO_3$, extracted with EtOAc, and dried (Na_2SO_4). Concentration yielded an oil which was chromatographed (preparative SiO_2 TLC, n-hexane/ether, 3:1) to afford 1.9 mg (39%) of acetonide **7** as an oil. $[\alpha]_D^{23}$ -4.8° (c 0.19, $CHCl_3$). IR (NaCl): 3456, 2931, 2857, 1711, 1462, 1411, 1378, 1355, 1240, 1217, 1111, 1059, 876, 701 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.5-7.3 (5H, m, aromatic), 5.2-5.1 (2H, m, benzylic), 4.27-4.17 (2H, m, 2-H and 4-H), 4.12-4.05 (2H, m, 5-H and 13-H), 3.82 (1H, m, 1-H_A), 3.73 (1H, dd, J = 5.2, 9.9 Hz, 14-H), 3.14 (1H, br.t, J = 10 Hz, 1-H_B), 1.80-1.65 (2H, m, 11-H and 16-H_A), 1.70-1.25 (14H, m), 1.61 (3H, s, acetonide CH_3), 1.54 (3H, s, acetonide CH_3), 1.420 (3H, s, acetonide CH_3), 1.414 (3H, s, acetonide CH_3), 1.330 (3H, s, acetonide CH_3), 1.325 (3H, s, acetonide CH_3), 1.25-1.15 (2H, m, 12-H_B and 16-H_B), 0.92 (3H, d, J = 6.7 Hz, 11-CH_3), 0.90 (3H, t, J = 7.4 Hz, 17-H), 0.82 (3H, d, J = 6.6 Hz, 15-CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 128.5 (CH), 128.3 (CH), 127.7 (CH), 107.7 (C), 107.3 (C), 82.4 (CH, C-14), 77.8 (CH, C-13), 75.9 (CH, C-5), 74.8 (CH, C-4), 72.0 (CH, C-2), 66.4 (CH_2, benzylic), 51.3 (CH_2, C-1), 36.8 (CH_2, C-12), 35.5 (CH_2, C-10), 34.2 (CH_2, C-3), 33.4 (CH, C-15), 30.2 (CH_2), 29.7 (CH_2), 29.1 (CH_3), 28.7 (CH, C-11), 28.6 (CH_3), 26.62 (CH_2), 26.42 (CH_2), 26.39 (CH_2), 26.31 (CH_3), 26.2 (CH_3), 25.9 (CH_3), 24.2 (CH_3), 21.0 (CH_3, 11-CH_3), 15.3 (CH_3, 15-CH_3), 10.4 (CH_3, C-17). EIMS m/z: 602 (M^+-CH_3, 0.9), 558 (4.4), 500 (2.2), 440 (1.2), 190 (2.4), 157 (1.9), 91 (100). EIHRMS m/z 602.4058 (M^+-CH_3, $C_{35}H_{56}NO_7$ requires 602.4057). The acetonide **7** existed as a mixture of rotamers.[23] This caused serious broardning of NMR signals around benzylic CH_2, C-1 and C-2, and quaternary carbon signals were missing.

Degradation and derivatization of 5. To a solution of **5** (3.0 mg, 4.39 μmol) in 0.4 ml of THF-H_2O (1:1)

was added sodium periodate (0.9 mg, 4.21 μmol) and stirred at room temperature. After 18 h, sodium borohydride (4.3 mg, 113 μmol) was added and stirred for further 2 h. The mixture was concentrated and the resultant residue was suspended in EtOAc. Filtration and concentration gave an oil which was purified with reversed phase HPLC (Inertsil ODS, φ6 x 250 mm, MeOH/H_2O, 1:1, 1.5 ml/min, UV 210 nm, R_t 7.4 min) to afford 0.2 mg (19%) of **12**. To a solution of **12** (0.2 mg, 0.83 μmol) in 0.2 ml of CH_2Cl_2 was added DCC (1.0 mg, 4.85 μmol), DMAP (0.1 mg, 0.855 μmol) and (*R*)-MTPA (1.0 mg, 4.27 μmol), and stirred for 18 h. The mixture was filtrated and concentrated to give an oil which was purified with reversed phase HPLC (Inertsil ODS, φ6 x 250 mm, MeOH/H_2O, 85:15, 1.5 ml/min, UV 254 nm, R_t 7.5 min) to afford 0.5 mg (89 %) of **13**, identical with material synthesized independently (vide infra).

(*R*)-MTPA ester (14). To a solution of (*RS*)-2-methylbutanol (1.21 μl, 9.41 μmol) in 0.5 ml of CH_2Cl_2 were added (*R*)-MTPA (2 mg, 8.55 μmol), DCC (1.94 mg, 9.41 μmol) and DMAP (0.1 mg, 0.855 μmol). The mixture was stirred for 30 h and was diluted with CH_2Cl_2. The organic phase was washed with water, 1M AcOH, saturated $NaHCO_3$ and brine, and dried (Na_2SO_4). Concentration gave a solid that was suspended with n-hexane and chromatographed (preparative SiO_2 TLC, n-hexane/EtOAc, 95:5) to afford 1.8 mg (72%) of **14** as an oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.53-7.51 (2H, m, aromatic), 7.41-7.39 (3H, m, aromatic), 4.24 (0.5H, dd, J = 10.7, 5.7 Hz, 1-H, 2*R*-isomer), 4.16 (1H, d, J = 6.1 Hz, 1-H, 2*S*-isomer), 4.08 (0.5H, dd, J = 10.7, 6.6 Hz, 1-H, 2*R*-isomer), 3.55 (3H, s, OCH_3), 1.82-1.73 (1H, m, 2-H), 1.45-1.35 (1H, m, 3-H_A), 1.25-1.15 (1H, m, 3-H_B), 0.92 (1.5H, d, J = 6.9 Hz, 2-CH_3, 2*S*-isomer), 0.91 (1.5H, d, J = 6.8 Hz, 2-CH_3, 2*R*-isomer), 0.90 (1.5H, t, J = 6.1 Hz, 4-H, 2*R*-isomer), 0.89 (1.5H, t, J = 7.6 Hz, 4-H, 2*S*-isomer).

(*R*)-MTPA ester (15). Starting from (*S*)-2-methylbutanol, **15** was synthesized in a similar way for **14**. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52 (2H, m, aromatic), 7.41-7.39 (3H, m, aromatic), 4.17 (2H, d, J = 6.1 Hz, 1-H), 3.55 (3H, s, OCH_3), 1.78 (1H, m, 2-H), 1.38 (1H, m, 3-H_A), 1.20 (1H, m, 3-H_B), 0.92 (3H, d, J = 6.9 Hz, 2-CH_3), 0.89 (3H, t, J = 7.4 Hz, 4-H).

(3*R*,5*EZ*)-1-Benzyloxy-3-methyl-6-nonen-9-ol (17). To a suspension of 3-hydroxypropyl-phosphonium bromide (250 mg, 0.623 mmol) in 5 ml of THF was added dropwise 0.76 ml of n-butyl lithium (1.6M in n-hexane, 1.22 mmol). After 1 h, a solution of aldehyde **16** (102.5 mg, 0.465 mmol) in THF was added dropwise, and was stirred for 45 min at room temperature. The mixture was quenched with saturated aqueous NH_4Cl, extracted with EtOAc, and dried (Na_2SO_4). Concentration and chromatography (SiO_2, n-hexane/EtOAc, 7:3) gave 64.3 mg (53%) of **17** (3:2 isomeric mixture) as oils. $[\alpha]_D^{23}$ 6.9° (c 0.49, $CHCl_3$). IR (NaCl): 3350, 2910, 2850, 1440, 1360, 1090, 1040, 730, 690 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.37-7.26 (5H, m, aromatic), 5.56-5.51 (1H, m, olefinic), 5.41-5.33 (1H, m, olefinic), 4.50 (2H, s, benzylic), 3.64-3.60 (2H, m, 9-H), 3.54-3.46 (2H, m, 1-H), 2.32 (1H, q, J = 6.8 Hz, 2-H), 2.25 (1H, q, J = 6.2 Hz, 2-H), 2.12-1.98 (2H, m), 1.45-1.34 (2H, m), 1.24-1.17 (1H, m), 0.89 (1.5H, d, J = 6.6 Hz, 3-CH_3), 0.88 (1.5H, d, J = 6.7 Hz, 3-CH_3). FIMS m/z: 264 (23), 263 (100), 262 (M^+, 97), 92 (12), 91(89). FIHRMS m/z 262.1927 (M^+, $C_{17}H_{26}O_2$ requires 262.1931).

(*R*)-3-Methylnonan-1,9-diol (18). To a solution of **17** (46.1 mg, 1.76 mmol) in 3 ml of EtOH was added $Pd(OH)_2$ on carbon (20% Pd, 9.4 mg). The mixture was stirred for 3.5 h under hydrogen atmosphere. The reaction mixture was filtrated through a pad of Celite. Concentration and chromatography (SiO_2, n-hexane/EtOAc, 4:1-0:100) afforded 15.0 mg (49%) of **18** as an oil. $[\alpha]_D^{24}$ 7.0° (c 0.31, $CHCl_3$). IR (NaCl): 3320, 2920, 2850, 1450, 1365, 1260, 1050, 725 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.72-3.63 (4H, m, 1-H and 9-H), 1.63-1.53 (4H, m), 1.45 (2H, br.s, OH), 1.41-1.24 (8H, m), 1.16 (1H, m), 0.89 (3H, d, J = 6.5 Hz, 3-CH_3). FIMS m/z: 176 (18), 175 (100), 174 (M^+, 13), 73 (37). FIHRMS m/z 174.1589 (M^+, $C_{10}H_{22}O_2$ requires 174.1617).

Bis-(*R*)-MTPA ester (19). The ester **19** was synthesized in a similar way as described for the compound **14**. ^{1}H-NMR (500 MHz, C_6D_6): δ 7.68 (4H, d, J = 7.7 Hz, aromatic), 7.12-7.05 (6H, m, aromatic), 4.15 (1H, ddd, J = 11.0, 7.1, 6.2 Hz, 1-H_A), 4.07 (1H, dt, J = 11.0, 7.1 Hz, 1-H_B), 4.06 (1H, dt, J = 10.8, 6.6 Hz, 9-H_A), 3.99 (1H, dt, J = 10.8, 6.7 Hz, 9-H_B), 3.43 (6H, s, OCH_3), 1.44 (1H, m, 3-H), 1.36-1.15 (5H, m), 1.06-0.91 (7H, m), 0.67 (3H, d, J = 6.5 Hz, 3-CH_3).

Bis-(*S*)-MTPA ester (20). The ester **20** was synthesized in a similar way as described for the compound **14**. ^{1}H-NMR (500 MHz, C_6D_6): δ 7.68 (4H, d, J = 7.7 Hz, aromatic), 7.12-7.05 (6H, m, aromatic), 4.13 (1H, dt, J = 10.9, 7.1 Hz, 1-H_A), 4.09 (1H, ddd, J = 10.9, 7.0, 6.1 Hz, 1-H_B), 4.05 (1H, dt, J = 10.8, 6.5 Hz, 9-H_A), 3.98 (1H, dt, J = 10.8, 6.7 Hz, 9-H_B), 3.43 (6H, s, OCH_3), 1.44 (1H, m, 3-H), 1.36-1.15 (5H, m), 1.06-0.91 (7H, m), 0.67 (3H, d, J = 6.5 Hz, 3-CH_3).

Methyl (*RS*)-[4-(Benzyloxycarbonyl)amino]-3-hydroxybutyrate (22). To a suspension of Na_2CO_3 (1.11g, 10.5 mmol) and 4-amino-3-hydroxybutyric acid (0.5 g, 4.02 mmol) was added dropwise carbobenzoxy chloride (0.659 ml, 4.62 mmol) over 10 min. The mixture was stirred vigorously at room temperature. After 1.5 h, ether was added and the organic phase was separated. The aqueous phase was acidified with 4M HCl under ice-cooling and extracted with EtOAc. The extracts were combined, washed with brine, and dried (Na_2SO_4). Concentration gave 610 mg (57%) of crude **21**. A solution of **21** (201 mg, 0.793 mmol) in 2.5 ml of THF was treated with excess CH_2N_2. Evaporation of the solvent and chromatography (SiO_2, n-hexane/EtOAc, 4:1) afforded 212 mg (quant.) of **22** as an oil. IR (NaCl): 3350, 3050, 2960, 1710, 1525, 1440, 1250, 1175, 1110, 1000, 750, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.38-7.30 (5H, m, aromatic), 5.21 (1H, br.s, NH), 5.10 (2H, s, benzylic), 4.13 (1H, m, 3-H), 3.71 (3H, s, OCH_3), 3.41 (1H, ddd, J = 14.0, 6.2, 3.1 Hz, 4-H_A), 3.39 (1H, br.s, OH), 3.19 (1H, dt, J = 14.0, 6.3 Hz, 4-H_B), 2.53 (1H, dd, J = 16.6, 4.5 Hz, 2-H_A), 2.48 (1H, dd, J = 16.6, 4.5 Hz, 2-H_B). EIMS m/z: 267 (M^+, 0.3), 108 (24), 107 (16), 104 (17), 92 (17), 91 (100). EIHRMS m/z 267.1095 (M^+, $C_{13}H_{17}NO_5$ requires 267.1107).

(*RS*)-[1-(Benzyloxycarbonyl)amino]-butan-2,4-diol (23). To a suspension of lithium aluminum hydride (14.8 mg, 0.39 mmol) was added dropwise a solution of ester **22** (70 mg, 0.26 mmol) in 0.5 ml of THF. The mixture was stirred for 4.5 h, quenched with 1M HCl and extracted with EtOAc. The extract was washed with brine and dried (Na_2SO_4). Concentration and chromatography (SiO_2, $CHCl_3$/MeOH, 95:5) afforded 24.8 mg (40%) of diol **23** as colorless crystals. mp 77-78°C (CH_2Cl_2-EtOAc). IR (KBr): 3280, 3090, 2930, 2780, 1685, 1565, 1445, 1415, 1330, 1310, 1270, 1230, 1155, 1110, 1070, 1050, 990, 875, 770, 720, 690 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.38-7.30 (5H, m, aromatic), 5.28 (1H, br.s, NH), 5.10 (2H, s, benzylic), 3.97 (1H, m, 3-H), 3.90-3.81 (2H, m, 1-H), 3.42 (1H, br.s, OH), 3.36 (1H, ddd, J = 13.4, 6.0, 3.1 Hz, 4-H_A), 3.17 (1H, dt, J = 13.4, 6.3 Hz, 4-H_B), 2.45 (1H, br.s, OH), 1.78-1.63 (2H, m, 2-H) . EIMS m/z: 239 (M^+, 0.1), 108 (36), 107 (26), 104 (44), 92 (22), 91 (100). EIHRMS m/z 239.1154 (M^+, $C_{12}H_{17}NO_4$ requires 239.1157).

Bis-(*R*)-MTPA ester (24). The ester **24** was synthesized in a similar way as described for the compound **14**. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.64-7.58 (4H, d, J = 7.7 Hz, aromatic), 7.21-7.01 (11H, m, aromatic), 5.08 (0.5H, m, NHCO), 5.07-4.92 (2.5H, m, benzylic and NHCO), 4.26 (0.5H, t, J = 5.8 Hz, 3-H, 3*R*-isomer), 4.13 (0.5H, t, J = 6.2 Hz, 3-H, 3*S*-isomer), 3.99 (1H, br.t, J = 6.3 Hz, 1-H, 3*S*-isomer), 3.82 (1H, dd, J = 6.9, 5.6 Hz, 1-H, 3*R*-isomer), 3.43 (1.5H, s, OCH_3, 3*S*-isomer), 3.38 (1.5H, s, OCH_3, 3*R*-isomer), 3.35 (1.5H, s, OCH_3, 3*R*-isomer), 3.34 (1.5H, s, OCH_3, 3*S*-isomer), 3.04-2.93 (1.5H, m, 4-CH_2 (3*R*-isomer) and 4-H_A (3*S*-isomer)), 2.78 (0.5H, dt, J = 14.7, 6.6 Hz, 4-H_B, 3*S*-isomer), 1.44-1.29 (2H, m, 3-H).

(*S*)-1-Azido-2,4-*O*-benzylidenebutane (26). To a solution of tosylate **25** (101.5 mg, 0.292 mmol) in 3 ml of DMF was added sodium azide (142.2 mg, 2.19 mmol) and heated at 100°C for 1.5 h. After cooling, the

mixture was diluted with ether, washed with water and dried (Na_2SO_4). Evaporation of the solvent gave 63.5 mg (99%) of azide **26** as an oil. $[\alpha]_D^{23}$ 6.4° (c 0.51, $CHCl_3$). IR (NaCl): 3050, 2970, 2930, 2870, 2100, 1455, 1400, 1365, 1315, 1275, 1245, 1220, 1140, 1110, 945, 885, 845, 755, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50 (2H, d, J = 8.6 Hz, aromatic), 7.38-7.31 (3H, m, aromatic), 5.55 (1H, s, benzylic), 4.30 (1H, ddd, J = 11.7, 5.0, 0.9 Hz, 4-H_A), 4.07 (1H, m, benzylic), 3.97 (1H, ddd, J = 12.0, 11.7, 2.5 Hz, 4-H_B), 3.41 (1H, dd, J = 13.0, 6.8 Hz, 2-H_A), 3.27 (1H, dd, J = 13.0, 3.8 Hz, 2-H_B), 1.91 (1H, m, 3-H_A), 1.50 (1H, m, 3-H_B). EIMS m/z: 218 (M^+, 5), 163 (45), 117 (15), 107 (26), 106 (42), 105 (100), 91 (35). EIHRMS m/z 218.0932 (M^+, $C_{11}H_{12}N_3O_2$ requires 218.0930). This was employed in the next step without further purification.

(*S*)-2,4-Dihydroxybutylamine hydrochloride (27). To a solution of azide **26** (100 mg, 0.469 mmol) in 4 ml of 1M HCl-MeOH was added Pd/C (10% Pd, 103 mg) The mixture was stirred for 3 h under hydrogen atmosphere. The reaction mixture was filtrated through a pad of Celite. Concentration afforded 71 mg (quant.) of **27** as a colorless caramel. $[\alpha]_D^{24}$ 0.27° (c 3.7, CH_3OH). IR (NaCl): 3420-2920, 1650, 1500, 1155, 1055 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.00 (1H, m, 2-H), 3.76-3.72 (2H, m, 4-H), 3.16 (1H, dd, J = 12.8, 2.9 Hz, 1-H_A), 2.94 (1H, dd, J = 12.8, 9.8 Hz, 1-H_B), 1.83-1.68 (2H, m, 3-H). EIMS m/z: 106 (MH^+, 1.5), 36 (100). EIHRMS m/z 106.0852 (M^+, $C_4H_{12}NO_2$ requires 106.0868). This was employed in the next step without further purification.

(*S*)-[1-(Benzyloxycarbonyl)amino]-butan-2,4-diol (28). To a solution of $NaHCO_3$ (92.8 mg, 0.868 mmol) and aminodiol **27** (35.1 mg, 0.248 mmol) in 4 ml of H_2O was added dropwise carbobenzyloxy chloride (0.039 ml, 0.273 mmol) over 10 min at 0°C. The mixture was stirred vigorously at room temperature. After 12 h, 0.1 ml of concentrated aqueous ammonia was added and diluted with saturated $NaHCO_3$. The mixture was extracted with EtOAc and dried (Na_2SO_4). Concentration and chromatography (SiO_2, $CHCl_3$/MeOH, 97:3) gave 52.7 mg (98%) of **28** as colorless crystals. mp 81.5-82.5°C (CH_2Cl_2-EtOAc). $[\alpha]_D^{24}$ -0.20° (c 3.0, CH_3OH). The spectral data of **28** were identical with those of **23**.

Bis-(*R*)-MTPA ester (29). The ester **29** was synthesized in a similar way as described for the compound **14**. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.63 (2H, d, J = 7.7 Hz, aromatic), 7.59 (2H, d, 7.7 Hz, aromatic), 7.32-7.00 (11H, m, aromatic), 5.06 (1H, m, NHCO), 5.01 (1H, d, J = 12.3 Hz, benzylic), 4.93 (1H, d, J = 12.3 Hz, benzylic), 4.09 (1H, br.t, J = 6.3 Hz, 2-H), 3.97 (1H, br.t, J = 6.3 Hz, 4-H), 3.43 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 2.98 (1H, dt, J = 14.5, 4.8 Hz, 1-H_A), 2.76 (1H, dt, J = 14.5, 6.3 Hz, 1-H_B), 1.42-1.38 (2H, m, 3-H).

(*RS*)-1-(Tetrahydropyran-2-yloxy)-4-decyne-2-ol (31). To a solution of HMPA (3.38 ml, 19.4 mmol) and 1-heptyne (1.87 g, 19.4 mmol) in 30 ml of THF at 0°C was added dropwise 12.1 ml of n-butyl lithium (1.6M solution in n-hexane, 19.4 mmol). The mixture was stirred for 1 h at room temperature. After cooling at 0°C, a solution of epoxide **30** (1.54 g, 9.71 mmol) was added. The mixture was allowed to warm to ambient temperature and stirred for 12 h. After addition of Na_2SO_4•H_2O, the mixture was decanted. Concentration and chromatography (SiO_2, n-hexane/EtOAc, 9:1-8:1) yielded 2.03 g (82%) of alkynol **31** as an oil. IR (NaCl): 3400, 2920, 2850, 1440, 1340, 1255, 1200, 1120, 1065, 1055, 1025, 970, 905, 870, 810 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.60-4.57 (1H, m, anomeric), 3.94-3.84 (2H, m, 2-H and OCH_2 (THP)), 3.84-3.75 (1H, m, 1-H_A), 3.67-3.55 (1H, m, 1-H_B), 3.58-3.49 (1H, m, OCH_2 (THP)), 2.48-2.33 (2H, m, 3-H), 2.15 (2H, m, 4-H), 1.87-1.73 (2H, m), 1.70-1.51 (6H, m), 1.38-1.27 (4H, m), 0.90 (3H, t, J = 7.1 Hz, 10-H). FIMS m/z: 256 (17), 255 (MH^+, 100), 145 (51), 91 (11), 85 (84). FIHRMS m/z 255.1971 (MH^+, $C_{15}H_{27}O_3$ requires 255.1960).

(2*RS*,4*Z*)-4-Decen-1,2-diol (32). To a solution of alkynol **31** (1.50 g, 5.90 mmol) and quinoline (1 ml,

8.46 mmol) in 25 ml of MeOH was added Pd-$BaSO_4$ (300 mg, 10% Pd, 0.283 mmol). The mixture was stirred for 14 h under hydrogen atmosphere. The reaction mixture was filtrated through a pad of Celite. To the filtrate, 10 ml of 1M HCl-MeOH was added and stirred for 30 min. The solution was diluted with EtOAc, washed with H_2O and brine, and dried (Na_2SO_4). Concentration and chromatography (SiO_2, n-hexane/EtOAc, 2:1) gave 951 mg (94%) of diol **32** as an oil. IR (NaCl): 3330, 2920, 2855, 1450, 1330, 1080, 1055, 900, 860, 720 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.57 (1H, m, olefinic), 5.39 (1H, m, olefinic), 3.75 (1H, m, 2-H), 3.68 (1H, dd, J = 11.1, 3.2 Hz, 1-H_A), 3.49 (1H, dd, J = 11.1, 7.2 Hz, 1-H_B), 2.30 (1H, m, 3-H_A), 2.22 (1H, m, 3-H_B), 2.05 (2H, dt, J = 6.9, 7.1 Hz, 6-H), 1.98 (2H, br.s, OH), 1.39-1.24 (6H, m), 0.89 (3H, t, J = 7.0 Hz, 10-H). EIMS m/z: 172 (M^+, 1.2), 123 (13), 110 (13), 97 (12), 84 (35), 83 (42), 81 (44), 79 (21), 70 (56), 69 (44), 68 (21), 67 (48), 61 (100). EIHRMS m/z 172.1478 (MH^+, $C_{10}H_{20}O_2$ requires 172.1463).

(2*RS*,4*Z*)-1-Tosyloxy-4-decen-2-ol (33). To a solution of diol **32** (940 mg, 5.46 mmol) in 45 ml of CH_2Cl_2 at -20°C was added p-toluenesulfonyl chloride (1.14 g, 6.00 mmol) and pyridine (6.62 ml, 8.18 mmol) in 10 ml of CH_2Cl_2. After 6 h, the mixture was allowed to warm to 0°C and stirred for 3 days, and then warmed to ambient temperature for a day. The mixture was diluted with ether and washed with saturated $CuSO_4$, saturated $NaHCO_3$, and brine, and dried (Na_2SO_4). Concentration and chromatography (n-hexane/EtOAc, 8:1-6:1) afforded 1.12 g (67%) of monotosylate **33** as an oil and 224 mg (24 %) of starting material. IR (NaCl): 3470, 2910, 2850, 1595, 1445, 1350, 1175, 1095, 975, 815, 805, 660 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.81 (2H, d, J = 8.2 Hz, aromatic), 7.36 (2H, d, J = 8.2 Hz, aromatic), 5.55 (1H, m, olefinic), 5.31 (1H, m, olefinic), 4.06 (1H, dd, J = 10.0, 3.3 Hz, 1-H_A), 3.93 (1H, dd, J = 10.0, 6.8 Hz, 1-H_B), 3.87 (1H, m, 2-H), 2.46 (3H, s, CH_3), 2.27 (1H, dd, J = 14.4, 7.0 Hz, 3-H_A), 2.22 (1H, dd, J = 14.4, 7.2 Hz, 3-H_B), 2.08 (1H, br.s, OH), 1.99 (2H, dt, J = 7.2, 7.0 Hz, 6-H), 1.41-1.21 (6H, m), 0.88 (3H, t, J = 7.0 Hz, 10-H). EIMS m/z: 327 (M^+, 0.1), 267 (2), 215 (24), 155 (100), 136 (28), 91 (81), 81 (21), 80 (18), 79 (26). EIHRMS m/z 327.1608 (MH^+, $C_{17}H_{23}O_4S$ requires 327.1630).

(2*RS*,4*Z*)-1-Azido-4-decen-2-ol (34). To a solution of tosylate **33** (1.04 g, 2.87 mmol) in 10 ml of DMF was added sodium azide (446 mg, 6.86 mmol). The mixture was heated at 70°C for 6 h and diluted with EtOAc. The organic phase was separated and washed with H_2O and brine, and dried (Na_2SO_4). Concentration and chromatography (SiO_2, n-hexane/EtOAc, 9:1) afforded 320 mg (47%) of azide **34** as an oil. IR (NaCl): 3340, 2930, 2870, 2105, 1680, 1445, 1275, 1080 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.60 (1H, m, olefinic), 5.36 (1H, m, olefinic), 3.81 (1H, m, 2-H), 3.38 (1H, dd, J = 12.4, 3.6 Hz, 1-H_A), 3.28 (1H, dd, J = 12.4, 7.0 Hz, 1-H_B), 2.35-2.23 (2H, m, 3-H), 2.05 (2H, q, J = 7.2 Hz, 6-H), 1.83 (1H, br.s, OH), 1.38-1.24 (6H, m), 0.89 (3H, t, J = 6.9 Hz, 10-H). EIMS m/z: 198 (M^+, 0.2), 126 (11), 112 (32), 83 (20), 82 (15), 81 (36), 69 (51), 55 (100). EIHRMS m/z 198.1570 (MH^+, $C_{10}H_{20}N_3O$ requires 198.1606).

(2*RS*,4*S,5*R**)-2-Acetoxy-1-azido-4,5-epoxydecane (35).** To a solution of azide **34** (23.1 mg, 0.12 mmol) in 0.5 ml of pyridine was added acetic anhydride (0.5 ml, 5.30 mmol). The solution was stirred for 17 h, diluted with ether, and washed with saturated $CuSO_4$, saturated $NaHCO_3$, and brine, and dried (Na_2SO_4). Concentration gave an oil which was dissolved in 1 ml of CH_2Cl_2 and treated with m-chloroperbenzoic acid (50.5 mg, ca 80%, 0.235 mmol) at 0°C. The mixture was stirred at room temperature for 4 h, and quenched by addition of saturated Na_2SO_3 and saturated $NaHCO_3$. After stirring for 30 min, the mixture was extracted with EtOAc, and dried (Na_2SO_4). Concentration gave 64.9 mg of crude epoxide **35** as an oil. IR (NaCl): 2925, 2850, 2100, 1740, 1440, 1365, 1280, 1225, 1045, 935, 820, 745 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.09 (0.5H, m, 2-H), 5.03 (0.5H, m, 2-H),# 3.02 (0.5H, dd, J = 13.3, 3.3 Hz, 1-H_A),# 2.95 (0.5H, dd, J = 13.3, 6.6 Hz, 1-H_B),# 2.86 (0.5H, dd, J = 13.3, 3.9 Hz, 1-H_A), 2.82 (0.5H, dd, J = 13.3, 6.0 Hz, 1-H_B), 2.68 (0.5H, dt, J = 8.0, 4.0 Hz, 4-H), 2.62-2.57 (1.5H, m, 5-H# and 4-H, 5-H), 1.75-1.65 (0.5H, m, 3-H_A), 1.72 (1.5H, s, OAc), 1.69 (1.5H, s, OAc),# 1.57 (0.5H, m, 3-H_B), 1.48-1.40 (1H, m, 3-H),# 1.33-1.19 (6H, m), 0.86 (3H, t, J = 7.1 Hz, 10-H). # major isomer. This was employed in the next step without further purification.

(2*S,4*S**,5*S**)-1-Azidodecan-2,4,5-triol (36a) and (2*S**,4*R**,5*R**)-1-Azidodecan-2,4,5-triol (36b).** To a solution of epoxide **35** (52.8 mg, 0.207 mmol) in 0.5 ml of dioxane was added 0.5 ml of 7% aqueous perchloric acid and heated at 60°C for 30 min. To the reaction mixture was added 4 ml of 0.3M KOH, and stirred for 30 min at 60 °C. The mixture was extracted with EtOAc, and dried (Na_2SO_4). Concentration and chromatography (SiO_2, $CHCl_3$/MeOH, 50:1) gave 6.0 mg (19%) and 18.4 mg (38%) of triols **36a** and **36b**, respectively.

36a: colorless needles. mp 90.5-91.5°C (n-hexane-acetone). IR (KBr): 3250, 2920, 2860, 2090, 1445, 1350, 1275, 1140, 1080, 1050, 940, 915, 885, 825, 725, 650 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.10 (1H, m, 2-H), 3.74 (1H, m, 4-H), 3.48 (1H, m, 5-H), 3.41 (1H, dd, J = 12.3, 4.0 Hz, 1-H_A), 3.35 (1H, dd, J = 12.3, 7.3 Hz, 1-H_B), 2.73 (1H, br.s, OH), 1.68 (2H, t, J = 6.0 Hz, 3-H), 1.55-1.26 (8H, m), 0.90 (3H, t, J = 6.5 Hz, 10-H). EIMS m/z: 232 (MH^+, 0.1), 157 (21), 113 (30), 95 (24), 84 (13), 83 (44), 69 (26), 59 (82), 55 (100). EIHRMS m/z 232.1662 (MH^+, $C_{10}H_{20}N_3O$ requires 232.1661).

36b: colorless needles. mp 34-35°C (benzene). IR (NaCl): 3350, 2930, 2860, 2100; 1660, 1440, 1275, 1070, 820, 735 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.07 (1H, m, 2-H), 3.72 (1H, m, 4-H), 3.43 (1H, m, 5-H), 3.38 (1H, dd, J = 12.5, 4.3 Hz, 1-H_A), 3.30 (1H, dd, J = 12.5, 6.5 Hz, 1-H_B), 2.20 (1H, br.s, OH), 1.73-1.62 (2H, t, J = 6.0 Hz, 3-H), 1.52-1.42 (2H, m), 1.39-1.26 (6H, m), 0.90 (3H, t, J = 6.8 Hz, 10-H). EIMS m/z: 232 (MH^+, 0.1), 157 (23), 151 (15), 139 (20), 113 (30), 99 (20), 95 (29), 86 (30), 83 (35), 81 (21), 69 (38), 55 (86), 43 (100). EIHRMS m/z 232.1663 (MH^+, $C_{10}H_{20}N_3O$ requires 232.1661).

(2*S,4*R**,5*R**)-1-Azido-2,4-*O*-benzylidenedecan-5-ol (38).** To a solution of benzaldehyde (40.3 mg, 0.38 mmol) and triol **36b** (8.8 mg, 0.038 mmol) in 0.4 ml of benzene was added $ZnCl_2$ (10.3 mg, 0.076 mmol). The mixture was stirred for 1.5 h at room temperature. Concentration gave an oil which was chromatographed (preparative SiO_2 TLC, n-hexane/EtOAc, 5:1, developed twice) afforded 8.8 mg (73%) of acetal **38** as an oil. IR (NaCl): 3425, 3040, 2920, 2860, 2100, 1450, 1400, 1375, 1340, 1280, 1215, 1150, 1115, 1060, 1020, 925, 905, 840, 760, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.50 (2H, m, aromatic), 7.41-7.34 (3H, m, aromatic), 5.60 (1H, s, benzylic), 4.09 (1H, dddd, J = 11.5, 6.6, 3.6, 2.8 Hz, 2-H), 3.77 (1H, ddd, J = 11.5, 6.0, 2.6 Hz, 4-H), 3.56 (1H, m, 5-H), 3.45 (1H, dd, J = 13.0, 6.6 Hz, 1-H_A), 3.33 (1H, dd, J = 13.0, 3.6 Hz, 1-H_B), 1.69 (1H, dt, J = 12.9, 11.5 Hz, 3-H_A), 1.56 (1H, ddd, J = 12.9, 2.8, 2.6 Hz, 3-H_B), 1.54-1.30 (8H, m), 0.90 (3H, t, J = 6.9 Hz, 10-H). EIMS m/z: 318 (M^+-H, 2.4), 190 (14), 157 (40), 107 (45), 105 (100), 83 (44), 79 (36), 77 (26). EIHRMS m/z 318.1817 (M^+-H, $C_{17}H_{24}N_3O_3$ requires 318.1818).

(2*S,4*S**,5*R**)-1-Azidodecan-2,4,5-triol (36d) and (2*S**,4*R**,5*S**)-1-Azido-2,4-*O*-benzylidenedecan-5-ol (39).** To a solution of *N*-methylmorpholine-*N*-oxide (118.8 mg, 1.01 mmol) and azide **34** (100 mg, 0.51 mmol) in 7.5 ml of CH_3CN-H_2O (2:1) was added 0.5 ml of OsO_4 (15.1 mM solution in H_2O, 7.57 mmol). The mixture was stirred at room temperature for 6 h, and saturated Na_2SO_3 was added. After stirring for 30 min, the mixture was extracted wit EtOAc, washed with 1M HCl and saturated Na_2CO_3, and dried (Na_2SO_4). Concentration gave an oil which was dissolved in 4 ml of benzene. To the solution was added benzaldehyde (0.5 ml, 4.92 mmol) and $ZnCl_2$ (127.2 mg, 0.90 mmol), and stirred at room temperature for 5 h. Concentration and chromatography (SiO_2, n-hexane/EtOAc, 8:1) afforded 65.0 mg (55%) triol **36d** and 68.3 mg (42%) of acetal **39**.

36d: colorless needles. mp 93-94°C (n-hexane-acetone). IR (KBr): 3320, 2925, 2870, 2140, 2005, 1450, 1300, 1060, 1035, 955, 915 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.13 (1H, ddt, J = 8.2, 7.4, 3.4 Hz, 2-H), 3.89 (1H, ddd, J = 9.8, 3.8, 3.0 Hz, 4-H), 3.68 (1H, ddd, J = 8.2, 4.1, 3.8 Hz, 5-H), 3.43 (1H, dd, J = 12.0, 3.4 Hz, 1-H_A), 3.36 (1H, dd, J = 12.0, 7.4 Hz, 1-H_B), 1.71 (1H, ddd, J = 14.4, 9.8, 3.4 Hz, 3-H_A), 1.61 (1H, ddd, J = 14.4, 8.2, 3.0 Hz, 3-H_B), 1.55-1.43 (2H, m), 1.34-1.25 (6H, m), 0.90 (3H, t, J = 6.8 Hz, 10-H). EIMS m/z: 232 (M^+-H, 0.1), 157 (22), 113 (30), 95 (26), 83 (45), 69 (26), 59 (78), 55 (100). EIHRMS m/z 232.1693 (M^+-H, $C_{17}H_{24}N_3O_3$ requires 232.1661).

39: an oil. IR (NaCl): 3425, 2920, 2860, 2100, 1710, 1450, 1400, 1380, 1340, 1280, 1220, 1115, 1015, 915, 840, 760, 700 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.55-7.50 (2H, m, aromatic), 7.40-7.30 (3H, m,

aromatic), 5.63 (1H, s, benzylic), 4.10 (1H, m, 2-H), 3.88-3.81 (2H, m, 4-H and 5-H), 3.48 (1H, dd, J = 13.0, 7.0 Hz, 1-H_A), 3.30 (1H, dd, J = 13.0, 3.8 Hz, 1-H_B), 1.81 (1H, dt, J = 12.8, 11.5 Hz, 3-H_A), 1.57 (1H, dt, J = 12.8, 2.3 Hz, 3-H_B), 1.51 (2H, m), 1.48-1.30 (6H, m), 0.90 (3H, t, J = 6.6 Hz, 10-H). EIMS m/z: 318 (M^+-H, 3.1), 157 (26), 107 (53), 106 (23), 105 (100), 79 (31), 77 (36). EIHRMS m/z 318.1820 (M^+-H, $C_{17}H_{24}N_3O_3$ requires 318.1818).

Hydrogenolysis of azides 36a, 36b, 36d and 39. To a solution of triol **36a** (5.1 mg, 0.022 mmol) in 1 ml of 0.1% HCl-MeOH was added Pd black (5 mg). The mixture was stirred under hydrogen atmosphere for 12 h. Filtration and concentration gave 4.3 mg (81%) of **37a**. Similarly, the azides **37b**, **37d** and **39** were converted to **37b** (89%), **37d** (93%) and **37c** (80%), respectively.
(2*S,4*S**,5*S**)-2,4,5-Trihydroxy-1-decylamine hydrochloride (37a):** a colorless caramel. IR (KBr): 3300, 2925, 2860, 1600, 1490, 1460, 1400, 1310, 1130, 1080, 1050, 1010, 960, 925, 840, 700. 3350, 2920, 1590, 1460, 1120, 1050 cm^{-1}. ^{1}H-NMR (500 MHz, D_2O): δ 4.06 (1H, dddd, J = 3.3, 3.3, 9.6, 9.6 Hz, 2-H), 3.74 (1H, ddd, J = 3.3, 4.1, 9.6 Hz, 4-H), 3.49 (1H, ddd, J = 4.1, 4.1, 8.2 Hz, 5-H), 3.15 (1H, dd, J = 3.3, 13.1 Hz, 1-H_A), 2.93 (1H, dd, J = 9.6, 13.1 Hz, 1-H_B), 1.64 (1H, ddd, J = 3.3, 9.6, 14.5 Hz, 3-H_A), 1.59 (1H, ddd, J = 3.3, 9.6, 14.5 Hz, 3-H_B), 1.57-1.22 (8H, m), 0.86 (3H, t, J = 6.8 Hz, 10-H). ^{13}C-NMR (67.5 MHz, D_2O) δ 75.54, 70.02, 65.02, 45.22, 37.31, 32.01, 31.20, 24.82, 22.11, 13.52. EIMS m/z: 206 (MH^+, 8.6), 157 (44), 113 (53), 105 (31), 104 (86), 95 (31), 86 (64), 69 (52), 60 (50), 36 (100). EIHRMS m/z 206.1748 (MH^+, $C_{10}H_{24}NO_3$ requires 206.1756).

(2*S,4*R**,5*R**)-2,4,5-Trihydroxy-1-decylamine hydrochloride (37b):** a colorless caramel. IR (KBr): 3350, 2920, 1590, 1460, 1120, 1050 cm^{-1}. ^{1}H-NMR (500 MHz, D_2O): δ 4.07 (1H, dddd, J = 3.2, 6.4, 6.4, 9.6 Hz, 2-H), 3.70 (1H, ddd, J = 4.0, 6.4, 6.4 Hz, 4-H), 3.53 (1H, ddd, J = 4.0, 4.0, 8.5 Hz, 5-H), 3.19 (1H, dd, J = 3.2, 13.1 Hz, 1-H_A), 2.96 (1H, dd, J = 9.6, 13.1 Hz, 1-H_B), 1.77 (2H, t, J = 6.4 Hz, 3-H), 1.58-1.22 (8H, m), 0.87 (3H, t, J = 6.7 Hz, 10-H). ^{13}C-NMR data (67.5 MHz, D_2O): δ 73.70, 71.00, 65.96, 44.48, 37.22, 32.10, 31.22, 24.93, 22.15, 13.54. EIMS m/z: 207 (21), 206 (MH^+, 8.6), 157 (44), 113 (53), 105 (31), 104 (86), 95 (31), 86 (64), 69 (52), 60 (50), 36 (100). EIHRMS m/z 206.1764 (MH^+, $C_{10}H_{24}NO_3$ requires 206.1756).

(2*S,4*R**,5*S**)-2,4,5-Trihydroxy-1-decylamine hydrochloride (37c):** a colorless caramel. IR (KBr): 3340-3300, 2910, 1590, 1460, 1300, 1150, 1125, 1070, 1020, 920, 850, 720 cm^{-1}. ^{1}H-NMR (500 MHz, D_2O): δ 4.09 (1H, dddd, J = 3.0, 6.4, 6.4, 9.6 Hz, 2-H), 3.69 (1H, ddd, J = 3.3, 4.6, 9.5 Hz, 4-H), 3.56 (1H, ddd, J = 3.4, 4.6, 9.1 Hz, 5-H), 3.19 (1H, dd, J = 3.0, 13.1 Hz, 1-H_A), 2.96 (1H, dd, J = 9.6, 13.1 Hz, 1-H_B), 1.81 (1H, ddd, J = 3.3, 6.4, 14.6 Hz, 3-H_A), 1.70 (1H, ddd, J = 6.4, 9.5, 14.6 Hz, 3-H_B), 1.58-1.22 (8H, m), 0.86 (3H, t, J = 6.7 Hz, 10-H). ^{13}C-NMR (67.5 MHz, D_2O): δ 74.60, 71.74, 66.24, 44.36, 36.18, 31.40, 31.20, 24.90, 22.11, 13.52. EIMS m/z: 206 (MH^+, 7.9), 157 (48), 113 (59), 105 (39), 104 (100), 95 (33), 87 (22), 86 (74), 69 (57), 61 (70), 36 (95). EIHRMS m/z 206.1765 (MH^+, $C_{10}H_{24}NO_3$ requires 206.1756).

(2*S,4*S**,5*R**)-2,4,5-Trihydroxy-1-decylamine hydrochloride (37d):** a colorless caramel. IR (KBr): 3300, 2920, 2490, 1590, 1460, 1070, 1020, 920, 840, 620 cm^{-1}. ^{1}H-NMR (500 MHz, D_2O): δ 4.06 (1H, dddd, J = 2.9, 2.9, 9.9, 9.9 Hz, 2-H), 3.76 (1H, ddd, J = 2.0, 4.3, 10.8 Hz, 4-H), 3.59 (1H, ddd, J = 3.7, 4.3, 7.6 Hz, 5-H), 3.16 (1H, dd, J = 2.9, 13.1 Hz, 1-H_A), 2.93 (1H, dd, J = 9.9, 13.1 Hz, 1-H_B), 1.67 (1H, ddd, J = 2.0, 9.9, 14.5 Hz, 3-H_A), 1.54 (1H, ddd, J = 2.9, 10.8, 14.5 Hz, 3-H_B), 1.58-1.22 (8H, m), 0.86 (3H, t, J = 6.5 Hz, 10-H). ^{13}C-NMR (67.5 MHz, D_2O): δ 74.81, 70.48, 65.00, 45.24, 35.88, 31.51, 31.19, 24.93, 22.09, 13.52. EIMS m/z: 206 (MH^+, 6.7), 157 (50), 113 (62), 105 (39), 104 (98), 95 (35), 87 (26), 86 (78), 69 (60), 61 (68), 36 (100). EIHRMS m/z 206.1755 (MH^+, $C_{10}H_{24}NO_3$ requires 206.1756).

Ethyl (4*E*,6*RS*)-6-methyl-4-octenoate (41). To a cooled solution of oxalyl chloride (1.83 ml, 20.94

mmol) in 48.8 ml of CH_2Cl_2 at -78°C was added dropwise dimethylsulfoxide (2.48 ml, 34.90 mmol) in 7.9 ml of CH_2Cl_2. After 10 min, (*RS*)-2-methylbutanol (1.536 g, 17.45 mmol) was added dropwise. The mixture was stirred for 1 h, and triethylamine (12.2 ml, 87.25 mmol) was added dropwise. The mixture was allowed to warm to temperature and stirred for 30 min. The solution was quenched with saturated NH_4Cl and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 and the combined extracts were washed with 1M HCl, saturated $NaHCO_3$ and H_2O and dried ($MgSO_4$). Removal of the solvent at atmospheric pressure gave crude aldehyde which was dissolved in 11 ml of THF. To a cooled solution of vinylmagnesium bromide (0.87M in THF, 30.1 ml, 26.18 mmol) in 5 ml of THF at -78°C was added dropwise the aldehyde solution shown above. After stirring for 1 h, the mixture was quenched with saturated aqueous NH_4Cl, and the resulting precipitate was dissolved with 1% HCl. The organic phase was separated and the aqueous phase was extracted with ether and the combined extracts were dried (Na_2SO_4). Removal of the solvent at atmospheric pressure gave a crude olefin **40**. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 5.87 (1H, ddd, J = 17.2, 10.6, 2.0 Hz, 2-H), 5.23 (1H, br.d, J = 17.2 Hz, 1-H_A), 5.16 (1H, br.d, J = 10.6 Hz, 1-H_B), 4.03-3.94 (1H, m, 3-H), 1.69-1.10 (3H, m, 4-H and 5-H), 0.93 (3H, d, J = 7.3 Hz, 4-CH_3), 0.89 (3H, t, J = 6.6 Hz, 6-H).

Propionic acid (0.065 ml, 0.87 mmol) and the olefin **40** was dissolved in triethylorthoacetic acid (32 ml, 175 mmol). The mixture was heated at 120°C and formed EtOH was continuously removed by distillation and stirred for 2 h. After cooling to room temperature, the mixture was diluted with ether and washed with 1M HCl, saturated $NaHCO_3$ and dried (Na_2SO_4). Concentration and chromatography (SiO_2, n-hexane/EtOAc, 9:1) afforded 1.16 g (36% in three steps) of ester **41** as an oil. IR (NaCl): 2962, 2930, 2875, 1739, 1456, 1372, 1346, 1176, 972 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 5.43-5.26 (2H, m, 4-H and 5-H), 4.12 (2H, q, J = 7.2 Hz, OCH_2), 2.40-2.26 (4H, m, 2-H and 3-H), 2.01-1.91 (1H, m, 6-H), 1.25 (3H, t, J = 7.2 Hz, OCH_2CH_3), 1.32-1.21 (2H, m, 7-H), 0.94 (3H, d, J = 6.6 Hz, 6-CH_3), 0.83 (3H, t, J = 7.2 Hz, 8-H). EIMS m/z: 184 (M^+, 1.1), 155 (4.5), 139 (6.7), 127 (5.6), 97 (25), 96 (91), 88 (21), 85 (17), 81 (100), 55 (84). EIHRMS m/z 184.1464 (M^+, $C_{11}H_{20}O_2$ requires 184.1453).

Ethyl (4*R,5*R**,6*R**)-4,5-*O*-Isopropylidene-6-methyloctanoate (44a) and Ethyl (4*S**,5*S**, 6*R**)-4,5-*O*-Isopropylidene-6-methyloctanoate (44b).** To a solution of ester **41** (30 mg, 0.163 mmol) in 8.5 ml of THF-acetone-H_2O (5:5:1) were added *N*-methylmorpholine-*N*-oxide (133.2 mg, 1.14 mmol) and OsO_4 (0.15M in H_2O, 0.193 ml, 0.029 mmol). The mixture was stirred at room temperature for 39 hr and diluted with CH_2Cl_2 and quenched with aqueous $NaHSO_3$. After stirring for 10 min, the mixture was extracted with CH_2Cl_2 and dried (Na_2SO_4). Concentration gave a crude diols **42a** and **42b** (36.1 mg). To the diols **42a** and **42b** (10 mg) was added 1 ml of 2,2-dimethoxypropane containing p-toluenesulfonic acid (0.44 mg, 2.3 μmol). The mixture was stirred at room temperature for 3.5 h. Concentration and chromatography (preparative SiO_2 TLC, $CHCl_3$/acetone, 9:1) afforded 6.2 mg (52%) of acetonides **44a** and **44b**, and 3.0 mg (38%) of lactone **43**.
43: an oil. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 4.67 (0.5H, dt, J = 3.3, 7.2 Hz, 4-H), 4.59 (0.5H, dt, J = 5.3, 7.2 Hz, 4-H), 3.45 (0.5 H, m, 5-H), 3.30 (0.5 H, m, 5-H), 2.71-2.45 (2H, m, 2-H), 2.31-2.01 (2H, m, 3-H), 1.74-1.12 (3H, m, 6-H and 7-H), 0.99-0.89 (6H, m, 8-H and 6-CH_3).
44a and **44b:** oils. IR (NaCl): 2965, 2934, 2878, 1737, 1462, 1378, 1246, 1165, 1064, 877 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.139 (1H, q, J = 7.2 Hz, OCH_2), 4.135 (1H, q, J = 7.2 Hz, OCH_2), 3.8 (1H, m, 4-H), 3.56 (0.5H, dd, J = 4.5, 7.8 Hz, 5-H, **44b**), 3.50 (0.5H, t, J = 7.0 Hz, 5-H, **44a**), 2.53 (1H, m, 2-H_A), 2.45 (1H, m, 2-H_B), 1.95 (1H, m, 3-H_A), 1.76 (1H, m, 3-H_B), 1.67-1.45 (2H, m, 6-H and 7-H_A), 1.360 (3H, s, acetonide CH_3), 1.369 (3H, s, acetonide CH_3), 1.26 (3H, t, J = 7.2 Hz, OCH_2CH_3), 1.20 (1H, m, 7-H_B), 0.95 (1.5H, d, J = 6.6 Hz, 6-CH_3, **44b**), 0.93 (1.5H, t, J = 7.4 Hz, 8-H, **44b**), 0.92 (1.5H, t, J = 6.5 Hz, 8-H, **44a**), 0.91 (1.5H, d, J = 6.3 Hz, 6-CH_3, **44a**). EIMS m/z: 243 (M^+-CH_3, 9.5), 183 (26), 155 (29), 143 (39), 137 (43), 115 (80), 109 (47), 99 (35), 95 (68), 87 (21), 85 (65), 59 (61), 43 (100). EIHRMS m/z 243.1606 (M^+-CH_3, $C_{13}H_{23}O_4$ requires 243.1597).

Ethyl (4*R,5*R**,6*RS*)-4,5-epoxy-6-methyloctanoate (45).** To a cooled solution of ester **41** (200 mg,

1.087 mmol) in 20 ml of CH_2Cl_2 at 0°C was added m-chloroperbenzoic acid (938 mg, ca 50%, 2.72 mmol). The mixture was stirred for 41 h and quenched with 10% $Na_2S_2O_3$. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous $NaHCO_3$, brine and dried (Na_2SO_4). Concentration gave 212 mg (97%) of epoxide **45**. This material was employed in next step without further purification. IR (NaCl):2965, 2929, 2877, 1738, 1463, 1374, 1350, 1248, 1180, 969, 895 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 4.19-4.10 (2H, q, J = 7.2 Hz, OCH_2), 2.83-2.72 (1H, m, 4-H), 2.54-2.40 (3H, m, 2-H and 5-H), 2.02-1.71(2H, m, 3-H), 1.59-1.53 (1H, m, 6-H), 1.46-1.12 (2H, m, 7-H), 1.26 (3H, t, J = 7.2 Hz, OCH_2CH_3), 0.99 (1.5H, d, J = 6.6 Hz, 6-CH_3), 0.96 (1.5H, d, J = 5.9 Hz, 6-CH_3), 0.92 (3H, t, J = 6.6 Hz, 8-H). EIMS m/z: 182 (M^+-H_2O, 5.0), 155 (4.9), 143 (7.7), 127 (3.8), 101 (9.3), 99 (8.0), 88 (8.5), 85 (100). EIHRMS m/z 182.1307 (M^+-H_2O, $C_{11}H_{18}O_2$ requires 182.1312).

Ethyl (4*S,5*R**,6*R**)-4,5-*O*-Isopropylidene-6-methyloctanoate (44c) and Ethyl (4*R**,5*S**, 6*R**)-4,5-*O*-Isopropylidene-6-methyloctanoate (44d).** To a cooled solution of epoxide **45** (25 mg, 0.125 mmol) in 1 ml of THF at 0°C was added 0.1 ml of 3.5% aqueous perchloric acid. The solution was stirred at room temperature for 9.5 h and quenched with saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2 and washed with brine and dried (Na_2SO_4). Concentration gave an oil which was dissolved in 1 ml of 2,2-dimethoxypropane containing p-toluenesulfonic acid (1.0 mg, 5.26 μmol). The mixture was stirred at room temperature for 1 h and quenched with saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2 washed with brine and dried (Na_2SO_4). Concentration and chromatography (preparative SiO_2 TLC, n-hexane/EtOAc, 88:12) yielded 3.0 mg (10%) of acetonides **44c** and **44d** as a mixture, 5.4 mg (38%) of lactone **46** and 8.9 mg (21%) of the starting material.

44c and **44d:** oils. IR (NaCl): 2965, 2935, 2878, 1739, 1733, 1464, 1456, 1379, 1369, 1242, 1220, 1165, 1132, 1066, 871 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.133 (1H, q, J = 7.2 Hz, OCH_2), 4.130 (1H, q, J = 7.0 Hz, OCH_2), 4.040 (0.5H, m, 4-H, **44c**), 4.005 (0.5H, m, 4-H, **44d**), 3.76 (1H, dd, J = 9.9, 5.2 Hz, 5-H, **44c** and **44d**), 2.53 (1H, m, 2-H_A), 2.40 (1H, m, 2-H_B), 1.76 (0.5H, m, 7-H_A, **44c**), 1.77-1.68 (2H, m, 3-H_A and 3-H_B), 1.67-1.60 (0.5H, m, 6-H, **44c**), 1.60-1.54 (0.5H, m, 6-H, **44d**), 1.42 (3H, s, acetonide CH_3), 1.38 (1H, m, 7-H_A, **44d**), 1.32 (3H, s, acetonide CH_3), 1.26 (3H, t, J = 7.2 Hz, OCH_2CH_3), 1.20 (0.5H, m, 7-H_B, **44c**), 1.08 (0.5H, m, 7-H_B, **44d**), 1.03 (1.5H, d, J = 6.5 Hz, 6-CH_3, **44d**), 0.93 (1.5H, t, J = 7.4 Hz, 8-H, **44d**), 0.91 (1.5H, t, J = 7.4 Hz, 8-H, **44c**), 0.86 (1.5H, d, J = 6.6 Hz, 6-CH_3, **44c**). The signals were assigned on the basis of COSY data. EIMS m/z: 243 (M^+-CH_3, 9.5), 183 (26), 155 (29), 143 (39), 137 (43), 115 (80), 109 (47), 99 (35), 95 (68), 87 (21), 85 (65), 59 (61), 43 (100). EIHRMS m/z 243.1606 (M^+-CH_3, $C_{13}H_{23}O_4$ requires 243.1597).

46: an oil. ^{1}H-NMR (270 MHz, $CDCl_3$): δ 4.64 (0.5H, dt, J = 3.3, 7.2 Hz, 4-H), 4.58 (0.5H, dt, J = 4.6, 7.2 Hz, 4-H), 3.70 (1H, m, 5-H), 2.68-2.45 (2H, m, 2-H), 2.37-2.07 (2H, m, 3-H), 1.97 (0.5H, d, J = 4.0 Hz, OH), 1.83 (0.5H, d, J = 4.6 Hz, OH), 1.79-1.14 (3H, m, 6-H and 7-H), 1.00-0.88 (6H, m, 8-H and 6-CH_3).

Isopropyl (2*S*,3*S*)-2-[(Benzyloxy)methoxy]-3-methylbutyrate (48). To a solution of ester **47** (1.0 g, 5.74 mmol) and *N*,*N*-diisopropylethylamine (2.0 ml, 11.5 mmol) in 15 ml of CH_2Cl_2 was added benzyl chloromethyl ether (1.2 ml, 8.61 mmol) at 0°C. The solution was stirred at room temperature for 21 h, and diluted with ether. The organic phase was separated and washed with 0.5M HCl, saturated $NaHCO_3$, and brine. The solution was dried (Na_2SO_4), concentrated, chromatographed (SiO_2, n-hexane/ether, 98:2), affording 1.37 g (85%) of BOM ether **48** as an oil. $[\alpha]_D^{24}$ -49.5° (c 10.0, $CHCl_3$). IR (NaCl): 2960, 2880, 1740, 1465, 1375, 1260, 1190, 1170, 1135, 1105, 1045, 965, 820, 735, 695 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.36-7.27 (5H, m, aromatic), 5.07 (1H, m, ^{i}Pr), 4.80 (2H, s, OCH_2O), 4.66 (1H, d, J = 11.8 HZ, benzylic), 4.62 (1H, d, J = 11.8 HZ, benzylic), 3.99 (1H, d, J = 5.7 Hz, 2-H), 1.89 (1H, m, 3-H), 1.57 (1H, m, 4-H_A), 1.3-1.2 (1H, m, 4-H_B), 1.24 (3H, d, J = 6.3 Hz, ^{i}Pr), 1.22 (3H, d, J = 6.3 Hz, ^{i}Pr), 0.98 (3H, d, J = 6.9 Hz, 3-CH_3), 0.91 (3H, d, J = 7.5 Hz, 5-H). EIMS m/z: 207 (M^+-$CO_2{}^i$Pr, 0.8), 92 (20), 91 (100), 42 (17). EIHRMS m/z 207.1384 (M^+-$CO_2{}^i$Pr, $C_{13}H_{19}O_2$ requires 207.1400).

(2*S*,3*S*)-2-[(Benzyloxy)methoxy]-3-methylbutan-1-al (49). To a solution of **48** (800 mg, 2.85 mmol) in 15 ml of ether at -78°C was added 2.1 ml of diisobutylaluminum hydride (1.5M in toluene, 3.14 mmol). After stirring this solution at -78°C for 1 h, 2 ml of MeOH and Celite were added. The mixture was allowed to warm to room temperature, and was stirred for 1 hr. Filtration and concentration gave an oil which was chromatographed (SiO_2, n-hexane/ether, 9:1) to afford 493 mg (78%) of aldehyde **49**. IR (NaCl): 2960, 2880, 1735, 1455, 1370, 1110, 1135, 1045, 735, 690 cm^{-1}. ^1H-NMR (500 MHz, $CDCl_3$): δ 9.68 (1H, d, J = 2.2 Hz, 1-H), 7.40-7.28 (5H, m, aromatic), 4.86 (1H, d, J = 7.0 Hz, OCH_2O), 4.80 (1H, d, J = 7.0 Hz, OCH_2O), 4.68 (1H, d, J = 11.8 Hz, benzylic), 4.64 (1H, d, J = 11.8 HZ, benzylic), 3.83 (1H, dd, J = 5.4, 2.2 Hz, 2-H), 1.91 (1H, m, 3-H), 1.56 (1H, m, 4-H_A), 1.30 (1H, m, 4-H_B), 1.00 (3H, d, J = 6.9 Hz, 3-CH_3), 0.92 (3H, d, J = 6.2 Hz, 5-H). FIMS m/z: 236 (M^+, 7), 207 (M^+-CHO, 25), 206 (100). EIMS m/z: 207 (M^+-CHO, 0.8), 92 (20), 91 (100), 42 (17). EIHRMS m/z 207.1385 (M^+-CHO, $C_{13}H_{19}O_2$ requires 207.1345).

(2*R*,4*RS*,5*S*,6*S*)-5-[(Benzyloxy)methoxy]-4-hydroxy-1-methoxymethoxy-2,6-dimethyloctane (51). To a solution of 3-(methoxy)methoxy-1-iodo-2-methylpropane **50** (101.5 mg, 0.452 mmol) in 1.5 ml of THF at -78°C was added 0.31 ml of tert-butyl lithium (1.49M in n-pentane, 0.458 mmol). After 10 min, a solution of aldehyde **49** (66.0 mg, 0.279 mmol) was added dropwise at -78°C. The mixture was allowed to warm to room temperature, and was stirred for 3 h. To the mixture was added $Na_2SO_4 \cdot H_2O$, and was stirred. Filtration and concentration gave an oil which was chromatographed (SiO_2, n-hexane/EtOAc, 2:1) to afford 54.5 mg (55%) of **51** as nearly 1:1 mixture. $[\alpha]_D^{23}$ 18.3° (c 0.19, $CHCl_3$). IR (NaCl): 3249, 2910, 2860, 1715, 1440, 1365, 1140, 1090, 1030, 910, 725, 685 cm^{-1}. ^1H-NMR (500 MHz, $CDCl_3$): δ 7.39-7.28 (5H, m, aromatic), 4.96 (0.5H, d, J = 6.9 Hz), 4.89 (0.5H, d, J = 6.9 Hz), 4.793 (0.5H, d, J = 6.8 Hz), 4.792 (0.5H, d, J = 11.6 Hz), 4.71 (0.5H, d, J = 11.8 Hz), 4.70 (0.5H, d, J = 11.8 Hz), 4.65 (0.5H, d, J = 11.8 Hz), 4.610 (1H, s, OCH_2O), 4.606 (1H, s, OCH_2O), 4.58 (0.5H, d, J = 11.6 Hz), 3.81-3.74 (1H, m, 5-H), 3.56 (0.5H, br.d, J = 9.3 Hz), 3.46-3.38 (2H, m, 1-H), 3.350 (1.5H, s, OCH_3), 3.349 (1.5H, s, OCH_3), 3.33 (0.5H, m), 3.22 (0.5H, t, J = 4.6 Hz), 2.91 (0.5H, br.d, J = 5 Hz), 2.11-2.01 (1H, m), 1.76-1.45 (3H, m), 1.39 (0.5H, m), 1.27-1.10 (1.5H, m), 1.00 (1.5H, d, J = 6.8 Hz), 0.97 (1.5H, d, J = 6.7 Hz), 0.91-0.86 (6H, m). EIMS m/z: 215 (M^+-BOMOH-H, 1.6), 207 (0.9), 205 (1.5), 177 (4.7), 155 (4.7), 147 (11), 115 (14), 91 (83), 85 (100). EIHRMS m/z 215.1668 (M^+-BOMOH-H, $C_{12}H_{23}O_3$ requires 215.1647).

(2*R*,4*S*,5*S*,6*S*)-4,5-*O*-Isopropylidene-1-methoxymethoxy-2,6-dimethyloctane (53a) and (2*R*, 4*R*,5*S*,6*S*)-4,5-*O*-Isopropylidene-1-methoxymethoxy-2,6-dimethyloctane (53b). To a solution of BOM ether **51** (11.1 mg, 0.031 mmol) in 1 ml of EtOAc was added Pd-black (10.9 mg). The mixture was stirred for 5.5 h under hydrogen atmosphere. The reaction mixture was filtrated through a pad of Celite. Concentration afforded an oil which was dissolved in 0.5 ml of 2,2-dimethoxypropane containing catalytic amount (0.6 mg, 3.15 μmol) of p-toluenesulfonic acid. The solution was stirred for an hour, and was diluted with CH_2Cl_2. The organic phase was washed with saturated $NaHCO_3$, and brine, dried (Na_2SO_4). Concentration and chromatography (preparative SiO_2 TLC, n-hexane/EtOAc, 9:1, developed twice) gave 2.8 mg (33%) of **53a** and 2.9 mg (33%) of **53b**.

53a: an oil. $[\alpha]_D^{23}$ -30.6° (c 0.23, $CHCl_3$). IR (NaCl): 2963, 2934, 2879, 1463, 1378, 1241, 1214, 1152, 1111, 1048, 995, 923, 892 cm^{-1}. ^1H-NMR (500 MHz, $CDCl_3$): δ 4.62 (2H, s, OCH_2O), 3.88 (1H, ddd, J = 9.9, 7.7, 2.8 Hz, 4-H), 3.45 (1H, dd, J = 7.7, 6.3 Hz, 5-H), 3.44 (1H, dd, J = 9.6, 5.5 Hz, 1-H_A), 3.42 (1H, dd, J = 9.6, 5.9 Hz, 1-H_B), 3.36 (3H, s, OCH_3), 1.99 (1H, m, 2-H), 1.70 (1H, m, 3-H_A), 1.65-1.50 (2H, m, 7-H_A and 6-H), 1.42 (1H, m, 3-H_B), 1.377 (3H, s, acetonide Me), 1.363 (3H, s, acetonide Me), 1.19 (1H, m, 7-H_B), 1.02 (3H, d, J = 6.8 Hz, 2-Me), 0.91 (3H, t, J = 7.4 Hz, 8-H), 0.90 (3H, d, J = 6.8 Hz, 6-Me). EIMS m/z: 259 (M^+-CH_3, 1.2), 187 (0.3), 155 (4.2), 154 (5.2), 125 (23), 85 (29), 83 (27), 69 (46), 55 (44), 43 (100). EIHRMS m/z 259.1919 (M^+-CH_3, $C_{14}H_{27}O_4$ requires 259.1908).

53b: an oil. $[\alpha]_D^{23}$ 66.6° (c 0.29, $CHCl_3$). IR (NaCl): 2962, 2934, 2878, 1463, 1379, 1368, 1240, 1219, 1153, 1111, 1048, 1008, 979, 965, 943, 921, 877 cm^{-1}. ^1H-NMR (500 MHz, $CDCl_3$): δ 4.62 (2H, s, OCH_2O),

4.12 (1H, ddd, J = 11.9, 5.2, 2.4 Hz, 4-H), 3.76 (1H, dd, J = 10.1, 5.2 Hz, 5-H), 3.39 (2H, d, J = 6.2 Hz, 1-H), 3.36 (3H, s, OCH_3), 2.05 (1H, m, 2-H), 1.75 (1H, m, 7-H_A), 1.70 (1H, m, 3-H_A), 1.58 (1H, m, 6-H), 1.43 (3H, s, acetonide Me), 1.33 (3H, s, acetonide Me), 1.20 (1H, m, 7-H_B), 1.05 (1H, ddd, J = 13.2, 10,6, 2.4 Hz, 3-H_B), 0.97 (3H, d, J = 6.7 Hz, 2-Me), 0.91 (3H, t, J = 7.5 Hz, 8-H), 0.83 (3H, d, J = 6.6 Hz, 6-Me). EIMS m/z: 259 (M^+-CH_3, 0.3), 187 (0.2), 185 (0.2), 171 (0.2), 155 (8.8), 125 (23), 85 (38), 83 (24), 69 (43), 55 (50), 45 (44), 43 (100). EIHRMS m/z 259.1906 (M^+-CH_3, $C_{14}H_{27}O_4$ requires 259.1908).

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17. For non protected epoxide *O*-deacetyl-**35**, the epoxide opening was attempted under acidic and basic conditions. In both cases, unidentified by-products were predominated. Since the epoxidation of *O*-acetyl-

34 gave nearly 1:1 diastereomer mixture, predominant formation of 2,4-*syn*-diol **36b** could be explained by acyl group assisted epoxide opening.

18. The ester **47** was prepared from L-isoleucine in two steps (i. $NaNO_2$, AcOH; ii. 0.45M HCl-^{i}PrOH, 70% overall).
19. The iodide **50** was derived from methyl (*S*)-3-hydroxy-2-methylpropionate in four steps (i. MOMCl, $^i Pr_2NEt$, DMAP, CH_2Cl_2; ii. $LiAlH_4$, ether; iii. TsCl, DMAP, Py; iv. NaI, acetone, 71% overall).
20. The numbering of all synthetic acetonides corresponds to those of AAL-toxins.
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22. The sign of optical rotation in our sample was opposite to that of the literature.[2c] In ORD spectrum of our sample, the sign of optical rotation was negative in the range of 230 and 590 nm. Hence, the reason for the disagreement is possibly due to the different ratio of the compounds **1** and **2** or simply error of depiction in ref. 2c. This was further comfirmed by the comparison of optical rotation of **6a**; $[\alpha]_{577}^{23}$ -17.5° (c 3.2, H_2O); lit. $[\alpha]_{578}^{22}$ -15° (c 2.7, H_2O).[2c]
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