Dehydrooligopeptides. XVI. Convenient Syntheses of Two Kinds of Antrimycins Av and Dv Containing Dehydrovaline Residues[1)]

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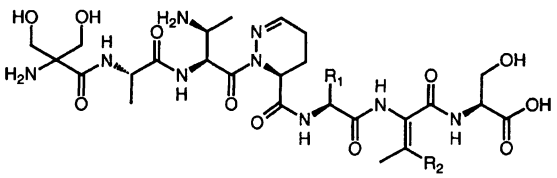
Eight kinds of peptide antibiotics, antrimycins (**1**), consist of four sorts of unusual α-amino acids, that is, hydroxymethylserine, (2*S*,3*S*)-2,3-diaminobutanoic acid, (*S*)-2,3,4,5-tetrahydro-3-pyridazinecarboxylic acid, and dehydrovaline (ΔVal) or (*E*)-dehydroisoleucine (ΔIle) from the N-terminus of **1**. The practical syntheses of the three segments containing these four acids, and all of the protected **1** by the usual fragment condensations of the three segments were accomplished. Moreover, after mild deprotection of the protecting groups, the two kinds of **1**, antrimycins Av and Dv comprising Ala^5–ΔVal^6 and Leu^5–ΔVal^6 segments respectively, were synthesized.

Peptide antibiotics, antrimycins (**1**),[2)] produced by *Streptomyces* (*St.*) *xanthocidicus MG-125-CF1*, are unique linear heptapeptides composed of a common N-terminal tetrapeptide and eight kinds of C-terminal tripeptide segments, and are similar to cirratiomycins,[3)] produced by *St. cirratus 248-Sq2*, as illustrated in Fig. 1. As can be seen from the structures, despite the small dehydrooligopeptides, interestingly, the natural products (**1**) are composed of four kinds of unusual α-amino acid residues, hydroxymethylserine (HMSer), (2*S*,3*S*)-2,3-diaminobutanoic acid (Dab), (3*S*)-2,3,4,5-tetrahydro-3-pyridazinecarboxylic acid (Pya), and dehydrovaline (ΔVal) or (*E*)-dehydroisoleucine (ΔIle) from the N-terminus of **1**.

We have already reported briefly an easy syntheses of the C-terminal dehydrotripeptides[4)] by the one-pot condensation of *N*-α-carboxy-dehydrovaline or dehydroisoleucine anhydride (**2**: ΔVal·NCA or ΔIle·NCA) with amine (*N*-) and carboxyl (*C*-) component α-amino acids (ΔNCA method).[5,6)] In our preceding papers,[7,8)] the stereoselective syntheses of the Dab and Pya derivatives and the acids containing dehydrotri- and tetrapeptides have been also reported.



1: Antrimycins R_1=Me, Et, n-Pr, i-Bu, R_2=Me, Et

Compd. No.		R_1	R_2
1a	Av	Me	Me
1b	Bv	Et	Me
1c	Cv	n-Pr	Me
1d	Dv	i-Bu	Me
1e	A	Me	Et
1f	B	Et	Et
1g	C	n-Pr	Et
1h	D	i-Bu	Et

Fig. 1.

Although the total synthesis of antrimycin Dv (Leu^5–ΔVal^6) has been reported,[9,10)] we have also succeeded in the syntheses of antrimycins Dv and Av (Ala^5–ΔVal^6) by a different route.[11)] Here, we wish to report in detail on the syntheses of the above-mentioned four unusual α-amino acid derivatives, the acids containing three segments, and all of the protected **1** from different routes. Futhermore, the examination of the optimal conditions for the deprotection of the protected **1** and the syntheses of antrimycins Av and Dv are also described in detail.

Results and Discussion

Syntheses of Three Segments of 1. To synthesize the C-terminal tripeptide of **1**, the one-pot condensation of **2**[4)] with an appropriate *N*-*t*-butoxycarbonyl (Boc)-α-amino acid (AA: Ala, Abu, Nva, and Leu) (Abu=2-aminobutanoic acid; Nva=norvaline) and then H–Ser–OBzl (benzyl ester) in CH_2Cl_2 in the presence of 4-dimethylaminopyridine (DMAP) at 0 °C gave Boc–AA–ΔVal (**3a—d**)- and ΔIle–Ser–OBzl (**3e—h**) (Scheme 1). Although the yields of **3a—h** were comparatively low and, similarly in the cases of **2e—h**, the geometries of the obtained products (**3e—h**) remained unchanged as a mixture of (*E*)- and (*Z*)-isomers in a 3:2 ratio, and this direct coupling method has been found to be superior to the usual stepwise elongation. Furthermore, to examine the deprotection conditions, variously protected similar dehydrotripeptides (**3i—k**) were also synthesized.

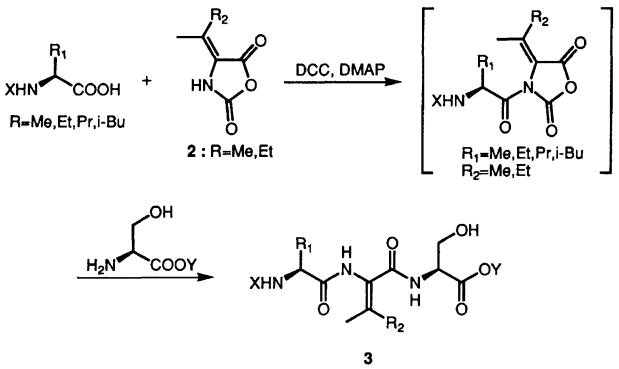
The yields, melting points, and physical constants (IR, ^{1}H NMR, and specific rotation) of **3a—k** are summarized in Tables 1 and 2.

The obtained **3a—h** were then condensed with the *C*-component dipeptide, Boc–Dab(Cbz)–Pya–OH (**14**) (Cbz=benzyloxycarbonyl), which was prepared

Table 1. The Yields and Melting Points of X–AA–ΔVal– and ΔIle–Ser–Y (**3**)

Compound No.	Yield %	Mp[b] θ_m/°C	Formula	Found (Calcd)/% C	H	N
3a	62	97—98	$C_{23}H_{33}N_2O_7$	59.23 (59.60	6.83 7.18	9.09 9.07)
3b	58	150—151	$C_{24}H_{35}N_3O_7$	60.08 (60.36	7.35 7.39	8.70 8.80)
3c	53	145—147	$C_{25}H_{37}N_3O_7$	60.71 (61.08	8.05 7.59	8.48 8.55)
3d	57	158—159	$C_{26}H_{39}N_3O_7$	61.86 (61.76	7.76 7.76	8.31 8.31)
3e	59[a]	107—108	$C_{24}H_{35}N_3O_7$	59.60 (60.36	7.31 7.31	8.59 8.59)
3f	54[a]	141—143	$C_{25}H_{37}N_3O_7$	60.75 (61.08	7.34 7.59	8.17 8.55)
3g	55[a]	146—148	$C_{26}H_{39}N_3O_7$	61.75 (61.76	7.71 7.76	8.34 8.31)
3h	54[a]	146—147	$C_{27}H_{41}N_3O_7$	62.35 (62.41	7.90 7.95	8.15 8.09)
3i	55	158—159	$C_{20}H_{27}N_3O_7$	56.92 (57.00	6.60 6.46	9.65 9.97)
3j	56	139—141	$C_{26}H_{31}N_3O_7$	62.44 (62.77	6.11 6.28	8.20 8.45)
3k	58	150—152	$C_{27}H_{33}N_3O_7$	63.40 (63.56	6.50 6.51	8.21 8.27)

a) Mixture of *E*- and *Z*-isomers. b) Colorless needles from EtOAc or hexane–EtOAc.



Compd. No.	X	Y	R_1	R_2
3a	Boc	Bzl	Me	Me
b	Boc	Bzl	Et	Me
c	Boc	Bzl	n-Pr	Me
d	Boc	Bzl	i-Bu	Me
e	Boc	Bzl	Me	Et
f	Boc	Bzl	Et	Et
g	Boc	Bzl	n-Pr	Et
h	Boc	Bzl	i-Bu	Et
i	Cbz	Me	Me	Me
j	Cbz	Bzl	Me	Me
k	Cbz	Bzl	Me	Et

Scheme 1.

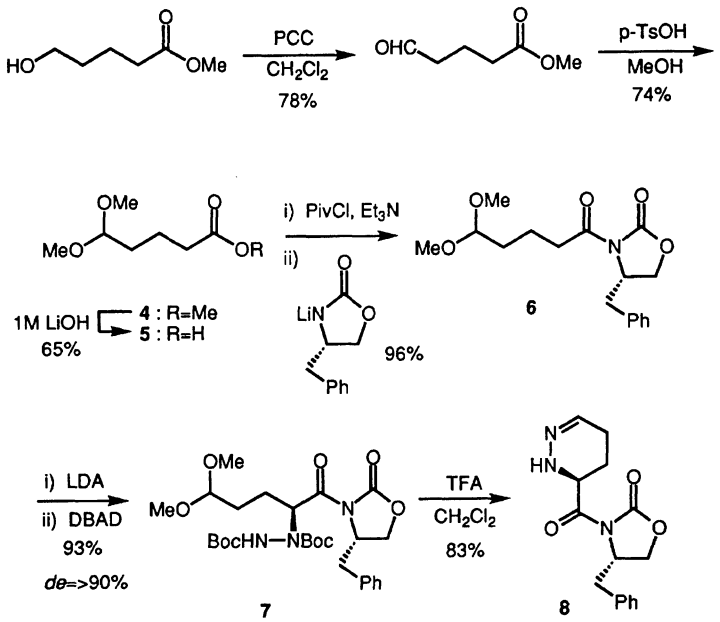
by the coupling of Boc–Dab(Cbz)–OH[8] with the Pya derivative synthesized below. As shown in Scheme 2, the starting methyl 5-oxopentanoate, derived by the oxidation of methyl 5-hydroxypentanoate with $C_5H_5NH^+ \cdot ClCrO_3^-$ (PCC) in CH_2Cl_2,[12,13] was treated with MeOH in the presence of *p*-toluenesulfonic acid (*p*-TsOH) to give the corresponding acetal ester (**4**). After ester hydrolysis of **4** with 1 M LiOH (1 M=1 mol dm^{-3}), the condensation of the obtained acetal acid (**5**) with pivaloyl chloride (Piv–Cl) in the presence of Et_3N in THF at −78 °C and then *N*-lithium (*S*)-4-benzyl-2-oxazolidinone[14] gave the corresponding *N*-acyl-2-oxazolidinone (**6**). The compound **6** was treated successively with butyllithium (BuLi) and di-*t*-butyl azodicarboxylate (DBAD) in THF at −78 °C to give the corresponding (*S*)-4-benzyl-3-[(*S*)-2-hydrazino]oxazolidinone derivative (**7**) in 93% yield with 90% de. Futhermore, intramolecular cyclization between the formyl and hydrazino groups by treatment of **7** with CF_3COOH (TFA) in CH_2Cl_2 took place smoothly to give the expected (*S*)-4-benzyl-3-[(*S*)-2,3,4,5-tetrahydro-3-pyridazinylcarbonyl]-2-oxazolidinone (**8**) in 83% yield.

On the other hand, the reaction of **7** with MeOMgI[15] in the mixture of CH_2Cl_2 and MeOH at 0 °C was done to remove oxazolidinone ring, giving the corresponding hydrazino methyl ester (**9**). Then, the ester **9** was cyclized with TFA in CH_2Cl_2 to give the desired 3-pyridazine-3-carboxylate (**10**) in 95% yield (Scheme 3).

The configurations of both **8** and **10** could be readily identified as *S* by comparison of the 2,4-dinitrophenyl derivative of the dihydro ester **11** with the authentic methyl (*R*)-1-(2,4-dinitrophenyl)-2,3,4,5-tetrahydro-3-pyridazinecarboxylate [(*R*)-**12**].[16] That is, the treatment of **10** with Na[BH_3CN] in MeOH and immediate arylation of the formed intermediate (**11**) with 2,4-dinitrophenyl fluoride (DNP-F) in EtOH was done to give the expected DNP-pyridazinecarboxylate (**12**).

Table 2. The IR, ^{1}H NMR Spectral Data and Specific Rotation of **3**

Compd.	IR, ν/cm^{-1} in KBr		^{1}H NMR, δ in $CDCl_3$				
			–NH– (J/Hz)		CH_3–	CH_3–	$[\alpha]_D^{25}$/°
No.	–NH–	–C=C–	br s	br d	($CH_3C\underline{H}_2$–)		(c 1.00, MeOH)
3a	3442	1656	7.80	6.99 (7.7) 5.02 (6.6)	2.06s	1.76s	−32.5
3b	3268	1644	7.82	7.03 (7.5) 5.07 (7.0)	2.05s	1.76s	−24.9
3c	3260	1650	7.82	7.04 (7.0) 5.09 (6.6)	2.20—1.10m		−20.8
3d	3260	1650	7.64	7.00 (7.5) 4.94 (7.3)	2.06s	1.76s	−22.6
3e	3466	1650	8.14	7.08 (7.7) 5.25 (6.6)	(E;2.39q)	1.72s	
				7.00 (7.7)	(Z;2.09q)	2.01s	
3f	3262	1647	7.85	7.00 (6.8) 5.09 (6.8)	(E;2.40q)	1.74s	
				6.95 (6.8)	(Z;2.12q)	2.01s	
3g	3448	1650	7.86	7.05 (7.7) 5.08 (6.8)	(E;2.45q)	1.74s	
				6.95 (7.7)	(Z;2.11q)	2.02s	
3h	3450	1650	7.75	6.97 (7.6) 4.97 (6.6)	(E;2.39q)	1.74s	
				6.94 (7.6)	(Z;2.11q)	2.02s	
3i	3436	1668	8.11	7.15 (6.2) 5.61 (6.2)	2.09q	1.72s	−32.4
3j	3334	1668	8.06	7.16 (8.0) 5.57 (6.4)	2.06q	1.72s	−31.0
3k	3380	1670	7.90	7.04 (7.0) 5.44 (5.9)	(E;2.42q)	2.04s	
				7.04 (7.0)	(Z;2.08q)	1.69s	

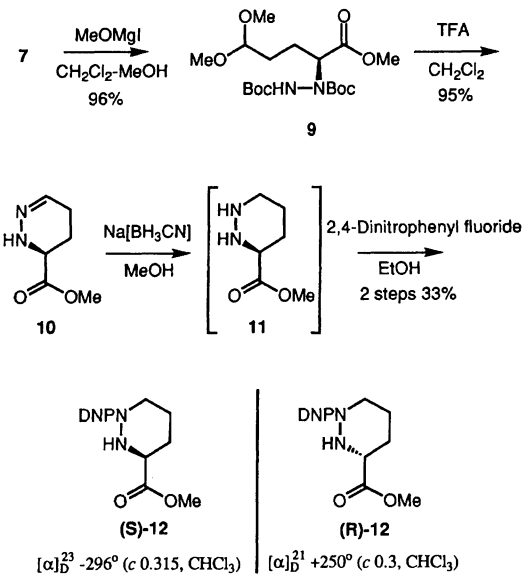


Scheme 2.

Since the specific rotation of the synthesized **12** showed the reverse sign and value to the (R)-isomer of **12**,[16] the configuration of the Pya derivatives, thus obtained, could be confirmed to be the (S)-isomer and was found to be identical with the Pya residue of **1**. Consequently, the stereoselective formation of the 2,3,4,5-tetrahydropyridazine ring was first successful.

Subsequently, the coupling of **8** with Boc–Dab(Cbz)–OH was done in CH_2Cl_2 in the presence of DMAP by the dicyclohexylcarbodiimide (DCC) method to give the expected dipeptide oxazolidinone amide (**13**) in 53% yield. Finally, the removal of the oxazolidinone ring of **13** by using LiOOH[17] gave **14** in 86% yield (Scheme 4).

On the other hand, the synthesis of an N-terminal dipeptide, Boc–HMSer(MOM)$_2$–Ala–OR (MOM= methoxymethyl, **18**; R=Bzl, **19**; R=H), was achieved from Boc–HMSer–OH (**15**) in four steps. The compound **15**, derived by the N-protection of H–HMSer–OH[18,19] with di-t-butyl dicarbonate (Boc_2O) in the presence of Et_3N in a mixture of H_2O and dioxane, was further protected with chloromethyl methyl ether (MOM-Cl) in the presence of diisopropylethylamine [(i-Pr)$_2$NEt] to give Boc–HMSer(MOM)$_2$–OMOM (**16**). The selective ester hydrolysis of **16** with 1 M LiOH in MeOH gave Boc–HMSer(MOM)$_2$–OH (**17**), which was then coupled with H–Ala–OBzl in the presence of diphenylphosphinic azide (DPPA) and Et_3N to give **18**. Finally, the catalytic hydrogenolysis of the Bzl group of **18** with 10% Pd/C in EtOH was done to give **19** in 91% yield (Scheme 5).



Scheme 3.

Consequently, all of the three partial skeletons **3**, **14**, and **19** of antrimycins (**1**) could be synthesized and used for the next fragment condensations.

Synthesis and Deprotection of the Protected 1. Deprotection of the Boc group of **3** with TFA in CH_2Cl_2 and then fragment condensation with **14** by using DPPA in the presence of Et_3N in DMF was done to give the expected Boc–Dab(Cbz)–Pya–AA–ΔVal (**20a**—**d**)- and ΔIle–Ser–OBzl (**20e**—**h**) in about 67% yields. Subsequently, final coupling of **19** with H–Dab(Cbz)–Pya–AA–ΔVal– or ΔIle–OBzl, formed by the deprotection of the Boc group of **20** by using TFA, was done in the presence of DPPA and Et_3N to give the protected **1**, Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–AA–ΔVal (**21a**—**d**) and ΔIle–Ser–OBzl (**21e**—**h**) in about 65% yields, according to Scheme 6.

Unfortunately, however, the protected **1** (**21a**—**h**) containing the ΔIle residue was obtained as a mixture of (*E*)- and (*Z*)-geometric isomers in about a 3:2 ratio, to the last. Accordingly, the deprotections of all the protecting groups of the obtained **21a** (Ala^5) and **21d** (Leu^5) containing a ΔVal residue, followed by the purification, gave antrimycins Av and Dv.

In order to deprotect under mild conditions, the catalytic hydrogenolysis of Cbz and Bzl groups with Pd/C and the hydrolytic deprotections of Boc and MOM groups with organic acid were studied extensively. Before the hydrogenolytic deprotection of the protected **1**, it was necessary to examine whether or not the carbon–carbon double bond of α-dehydroamino acid residue was hydrogenated. Accordingly, for example, five kinds of C-terminal dehydrotripeptide segments of **1** protected with different *N*- and *C*-protecting groups, that is, Boc–Ala–ΔAA–Ser–OBzl (**3a**: ΔVal, **3e**: ΔIle), Cbz–Ala–ΔVal–Ser–OMe (**3i**), and Cbz–Ala–ΔAA–Ser–OBzl (**3j**: ΔVal, **3k**: ΔIle) mentioned above, were submitted to the catalytic hydrogenation with 5% Pd/C in MeOH at room temperature. (Figs. 2, 3, and 4). In all cases, the Cbz and Bzl groups of the substrates were readily deprotected to give Boc–Ala–ΔAA–Ser–OH, H–Ala–ΔVal–Ser–OMe, and H–Ala–ΔAA–Ser–OH respectively almost quantitatively within only 20 min, without any hydrogenation to a C=C bond.

From the above results and the fact that the other protecting groups, MOM and Boc, are easily deprotected with acids such as TFA, the final deprotection of **21a** and **21d** with 5% Pd/C in MeOH–AcOH for 2 h and then with 70% TFA for 12 h at room temperature was done to give the deprotected product. The crude peptide thus obtained was purified on reversed-phase HPLC column using 15% CH_3CN–H_2O-0.05% TFA as the eluent to give antrimycins Av(**1a**) and Dv(**1d**) as TFA adducts in about 66% yields.

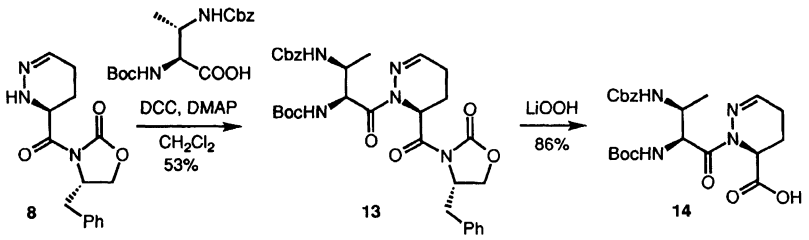
Consequently, all of the chemical and physical constants of thus obtained antrimycins Av and Dv were almost identical with those of the naturally occurring peptides,[20] as summarized in Table 3.

Experimental

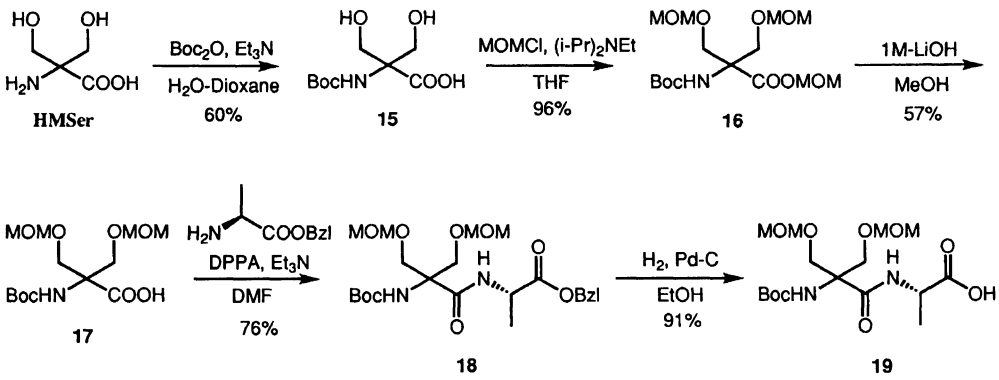
Melting points were measured with a Yamato Mp-21 micro-melting point apparatus, and uncorrected. The IR spectra were recorded with a Hitachi 270-30 spectrometer in KBr. The ^{1}H NMR and ^{13}C NMR spectra were measured with JEOL EX 90, FX 200, and JNE 500 spectrometers in $CDCl_3$, DMSO-d_6, C_6D_6, or CD_3OD solution with tetramethylsilane used as the internal standard. The specific rotations were measured in a 0.5 dm tube using a JASCO DIP-4 polarimeter in MeOH or H_2O. Thin-layer chromatography (TLC) was done with Merck silicagel 60F-254 plates and column chromatography was carried out with Merck silicagel 60 and Wakogel C-300. High-pressure liquid chromatography (HPLC) analyses and separations were done on the following columns using 15% CH_3CN–H_2O-0.05% TFA with a flow rate of 6.0 ml min^{-1} by detecting UV (215 nm) absorption: E. Merck Lichrosorb PR-18 (4ϕ×250 nm) and Tosoh gel ODS-120T (21.5 mmID×30 cm).

Boc–AA–ΔAA–Ser–OBzl (3a—h), Cbz–Ala–ΔVal–Ser–OMe (3i), Cbz–Ala–ΔAA–Ser–OBzl (3j, k). According to the method reported previously,[4] one-pot coupling of ΔAA·NCA (**2**) with X–AA–OH (X=Boc or Cbz) and then with H–Ser–OY (Y=Me or Bzl) in the presence of DCC and pyridine in CH_2Cl_2 gave the expected **3a**—**k** (Tables 1 and 2).

Methyl 5,5-Dimethoxypentanoate (4). A solution of methyl 5-oxopentanoate[12,13] (2.3 g, 18 mmol) in MeOH (30 ml) in the presence of *p*-TsOH·H_2O (0.10 g, 0.53 mmol) was stirred overnight at room temperature. The reaction mixture was neutralized with Et_3N and then concentrated in vacuo. The obtained residue was dissolved in EtOAc (50 ml) and washed twice with brine (15 ml) and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a residue, which was purified on a silica-gel column using hexane–EtOAc (1:1 v/v) to give **4** as a colorless oil. Yield 74%. IR (KBr) 1734 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ=1.57—1.76 (m, 4H), 2.26—2.44 (m, 2H), 3.26 (s, 6H), 3.61 (s, 3H), 4.34 (br t, 1H).



Scheme 4.



Scheme 5.

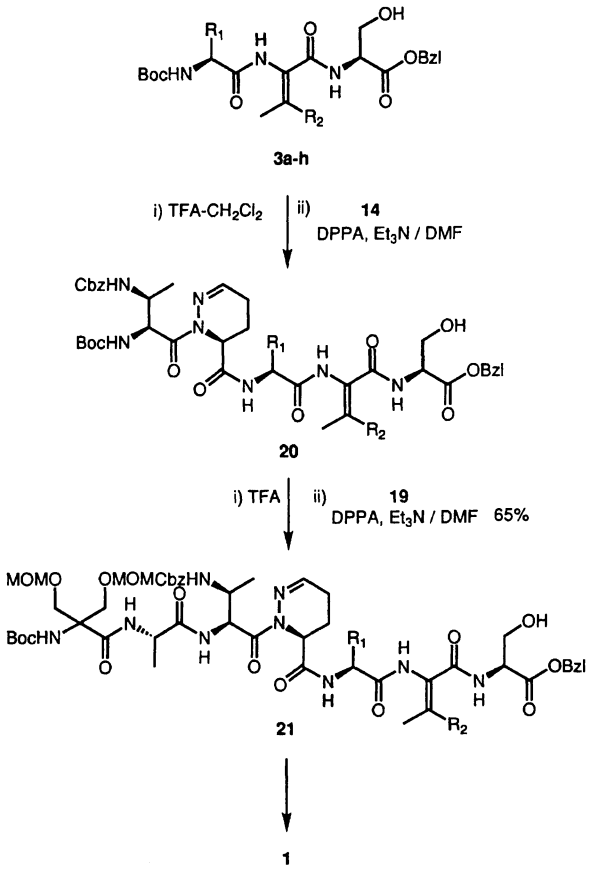
Table 3. The Chemical Data of Antrimycins Av and Dv

		Synthetic	Natural
Antrimycin Av	Mp/°C	173 (decomp)	178 (decomp)
(**1a**)	$[\alpha]_D$	−63.0°	−65.0°
	(H_2O)	(*c* 0.224)	(*c* 0.2)
	TLC(*Rf*)	0.12	0.12
Antrimycin Dv	Mp/°C	189 (decomp)	191 (decomp)
(**1d**)	$[\alpha]_D$	−64.7°	−74.0°
	(H_2O)	(*c* 0.118)	(*c* 0.1)
	TLC(*Rf*)	0.28	0.28

5,5-Dimethoxypentanoic Acid (5). A solution of **4** (5.00 g, 28.4 mmol) in MeOH (100 ml) in the presence of 1 M LiOH (42.6 ml, 42.6 mmol) was stirred for 2 h at room temperature. The reaction mixture was concentrated in vacuo to give a resulting aqueous solution, which was washed twice with diethyl ether (20 ml). The aqueous layer was adjusted to pH 3—4 with 10% citric acid and then extracted three times with EtOAc (30 ml). The combined extracts were washed with brine (20 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave **5** as a colorless oil, which was used to the next reaction without further purification. Yield 65%. IR (KBr) 3100, 1710 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.60—1.79 (m, 4H), 2.32—2.48 (m, 2H), 3.32 (s, 6H), 4.38 (br t, 1H), 9.23 (br s, 1H, COOH).

(*R*)-4-Benzyl-3-(5,5-dimethoxypentanoyl)-2-oxazolidinone (6). To a solution of **5** (0.65 g, 4.0 mmol) in THF (15 ml) in the presence of Et_3N (0.49 g, 4.8 mmol) under Ar gas at −78 °C was added Piv-Cl (0.51 g, 4.2 mmol). Colorless precipitates were deposited and the resulting mixture was stirred at −78 °C, and then treated with a solution of 5-lithium (*R*)-4-benzyl-2-oxazolidinone [made from (*R*)-4-benzyl-2-oxazolidinone (0.68 g, 3.8 mmol) in THF (10 ml) and BuLi (2.4 ml, 3.8 mmol, 1.6 M hexane solution at −78 °C]. After it was stirred at 0 °C for 30 min, the reaction mixture was further treated with saturated aqueous NH_4Cl solution (30 ml) and then the organic solvent was removed in vacuo. The residual aqueous solution was extracted three times with $CHCl_3$ (20 ml). The combined extracts were washed with saturated aqueous $NaHCO_3$ solution (10 ml) and brine (10 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a crude residue, which was purified on a silica-gel column using hexane–EtOAc (4 : 1 v/v) give **6** as a colorless syrup. Yield 96%. $[\alpha]_D^{26}$ +83.6° (*c* 1.11, MeOH). IR (KBr) 1782, 1704 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.68—1.87 (m, 4H), 2.75 (dd, 1H, *J*=9.2 and 13.2 Hz), 2.88—2.97 (m, 2H), 3.30 (dd, 1H), 3.33 (s, 6H), 4.18 (m, 2H), 4.41 (br t, 1H), 4.65 (m, 1H), 7.15—7.46 (m, 5H). Found: C, 63.28; H, 7.41; N, 4.49%. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36%.

(*S*)-4-Benzyl-3-[(*S*)-2-[1,2-bis(*t*-butoxycarbonyl)-hydrazino]-5,5-dimethoxypentanoyl]-2-oxazolidinone (7). To a solution diisopropylamine (70 mg, 0.69 mmol) in THF (2.2 ml) under Ar gas at −78 °C was added BuLi (0.27 ml, 0.67 mmol, 2.5 M hexane solution) dropwise for 20 min. A solution of **6** (0.20 g, 0.67 mmol) in THF (30 ml) was added slowly to the resulting solution. After this was



Scheme 6.

stirred for 30 min, a solution of DBAD (0.17 g, 0.75 mmol) in CH_2Cl_2 (4 ml) was added. After 3 min, acetic acid (90 μl, 1.6 mmol) and a saturated aqueous NH_4Cl solution (10 ml) were added at −78 °C for 30 min. The reaction mixture was concentrated in vacuo to give a residue, which was extracted three times with CH_2Cl_2 (10 ml). The combined extracts were washed with brine (10 ml) and dried over Na_2SO_4, and then concentrated in vacuo. The residue obtained was purified on a silica-gel column using hexane–EtOAc (4 : 1 v/v) to give **7** as colorless prisms. Yield 93%, mp 124—126 °C. $[\alpha]_D^{26}$ +52.1° (*c* 2.09, MeOH). IR (KBr) 3424, 1785, 1755, 1716, 1689 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.45 (s, 18H), 1.71—2.00 (m, 4H), 2.62—3.36 (m, 8H), 4.17 (m, 2H), 4.41 (m, 1H), 4.52 (m, 1H), 5.73 (m, 1H), 6.67 (s, 1H, NH), 7.14—7.36 (m, 5H). Found: C, 58.64; H, 7.63; N, 7.59%. Calcd for $C_{27}H_{41}N_3O_9$: C, 58.79; H, 7.49; N, 7.62%.

(*S*)-4-Benzyl-3-[(*S*)-2,3,4,5-tetrahydro-3-pyridazinyl]-2-oxazolidinone (8). A solution of **7** (0.10 g, 0.18 mmol) and TFA (0.5 ml) in CH_2Cl_2 (0.5 ml) was stirred at room temperature for 1 h and then concentrated in vacuo. The residue was dissolved in benzene (5 ml). Azeotropic distillation was done three times to give a residue, which was again dissolved in CH_2Cl_2 (10 ml). The resulting solution was washed with a saturated aqueous $NaHCO_3$ solution (5 ml) and the aqueous layer was extracted twice with $CHCl_3$ (5 ml). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The obtained residue was purified on a silica-gel column using hexane–EtOAc (1 : 2 v/v) to give crystals, which were recrystallized from hexane–

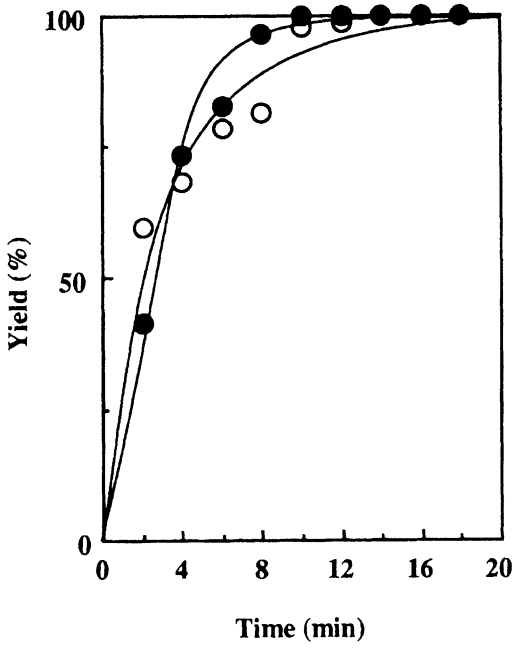


Fig. 2. Correlation between the yield and reaction time in the deprotection of Boc–Ala–ΔAA–Ser–OBzl (**3a** and **3e**) by the catalytic hydrogenolysis. ○: ΔVal, ●: ΔIle.

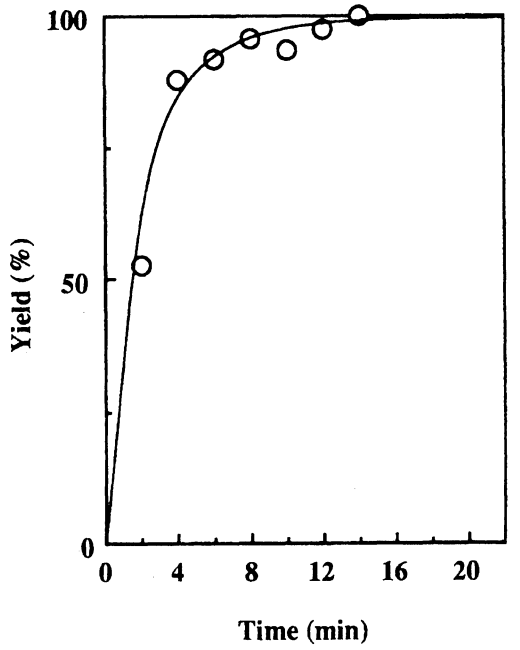


Fig. 3. Correlation between the yield and reaction time in the deprotection of Cbz–Ala–ΔVal–Ser–OMe (**3i**) by the catalytic hydrogenolysis.

EtOAc to give **8** as colorless prisms. Yield 83%, mp 116—117 °C. $[\alpha]_D^{26}$ +168° (*c* 1.09, MeOH). IR (KBr) 1785, 1778, 1698 cm^{-1}. ^1H NMR (C_6D_6) δ=1.69—2.28 (m, 4H), 2.45 (dd, 1H, *J*=7.1 and 13.6 Hz), 2.77 (dd, 1H, *J*=3.5 and 13.6 Hz), 3.32 (dd, 1H, *J*=9.0 Hz), 3.55 (dd, 1H, *J*=3.5 and 9.0 Hz), 4.16 (dddd, 1H), 4.50 (br t, 1H), 6.23 (br s, 2H), 6.82—7.31 (m, 5H). Found: C, 62.42; H, 5.84; N, 14.42%. Calcd

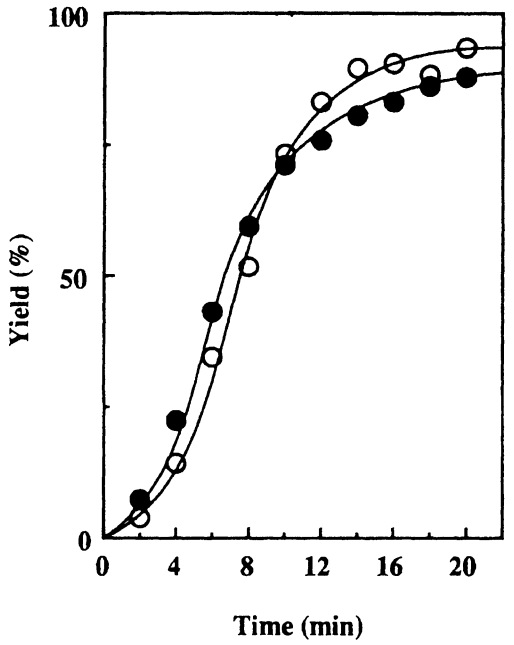


Fig. 4. Correlation between the yield and reaction time in the deprotection of Cbz–Ala–ΔAA–Ser–OBzl (**3j** and **3k**) by the catalytic hydrogenolysis. ○: ΔVal, ●: ΔIle.

for $C_{15}H_{17}N_3O_3$: C, 62.70; H, 5.96; N, 14.63%.

Methyl (*S*)-[1,2-Bis(*t*-butoxycarbonyl)hydrazino]-5,5-dimethoxypentanoate (9). To a suspension of **7** (0.30 g, 0.54 mmol) in MeOH (1.4 ml) and CH_2Cl_2 (1.4 ml) was added under stirring, a suspension of MeMgI [made from Mg (0.19 g, 7.8 mmol) and MeI (0.93 g, 6.51 mmol) in diethyl ether (10 ml) at −78 °C] in MeOH (1 ml). After this was stirred for 5 min at room temperature, a saturated aqueous NH_4Cl solution (10 ml) was added to the reaction mixture and then the organic solvent was evaporated. The residual aqueous solution was extracted three times with $CHCl_3$ (10 ml) and the combined extracts were washed with brine (10 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a residue, which was purified on a silica-gel column using hexane–EtOAc (2:1 v/v) to give **9** as a colorless syrup. Yield 96%. $[\alpha]_D^{26}$ −25.7° (*c* 1.11, MeOH). IR (KBr) 3316, 1746, 1713 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.47 (s, 18H), 1.53—2.13 (m, 4H), 3.31 and 3.32 (s, 6H), 3.72 (s, 3H), 4.36 (m, 1H), 4.76 (br s, 1H), 6.47 (br s, 1H, NH). Found: C, 52.85; H, 8.57; N, 6.87%. Calcd for $C_{18}H_{34}N_2O_8$: C, 53.19; H, 8.43; N, 6.89%.

Methyl (*S*)-2,3,4,5-Tetrahydro-3-pyridazinecarboxylate (10). A solution of **9** (0.21 g, 0.52 mmol) and TFA (2 ml) in CH_2Cl_2 (2 ml) was stirred at room temperature for 30 min and then concentrated in vacuo. The residue obtained was dissolved in benzene and then azeotropic distillation was done three times. The residue was dissolved in $CHCl_3$ (20 ml) and the solution was washed with a saturated aqueous $NaHCO_3$ solution (5 ml). The aqueous layer was extracted twice with $CHCl_3$ (5 ml), the combined extracts were washed with brine (5 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave **10** as a colorless syrup. Yield 95%. $[\alpha]_D^{26}$ +139° (*c* 0.831, MeOH). IR (KBr) 3318, 1740 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.76—2.34 (m, 4H), 3.66—3.86 (m, 4H), 5.20 (br s, 1H, NH), 6.73 (br s, 1H). Found: C, 46.36; H, 7.88; N, 21.63%. Calcd for $C_5H_{10}N_2O_2$: C, 46.14; H, 7.75; N, 21.53%.

Methyl (*S*)-1-(2,4-Dinitrophenyl)-3-pyridazinecarboxylate [(*S*)-12]. A solution of **10** (70 mg, 0.49 mmol) in MeOH (1 ml) was stirred with $Na[BH_3CN]$ (72 mg, 0.99 mmol) at room temperature overnight. The reaction mixture was concentrated in vacuo to give a residue, which was added to brine (5 ml). The resulting solution was extracted four times with $CHCl_3$ (5 ml), and the combined extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The obtained residue (**11**) was dissolved in EtOH (0.5 ml) and treated with excess 2,4-dinitrophenyl fluoride (DNP-F) (93 mg, 0.49 mmol). After this was stirred for 30 min, the reaction mixture was concentrated in vacuo to give a residue, which was purified on a silica-gel column using hexane–EtOAc (3:1 v/v). The obtained crystals were recrystallized from $CHCl_3$–hexane to give (*S*)-**12** as yellow needles. Yield 33%, mp 95—96 °C. $[\alpha]_D^{23}$ −296° (*c* 0.315, $CHCl_3$) Lit,[14] *R*-isomer: $[\alpha]_D^{21}$ +250° (*c* 0.3, $CHCl_3$). IR (KBr) 3250, 1750, 1608 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.59—2.23 (m, 4H), 3.17 (m, 1H), 3.55—3.89 (m, 6H), 7.00 (d, 1H, *J*=9.2 Hz), 8.18 (dd, 1H, *J*=2.6 and 9.2 Hz), 8.38 (d, 1H, *J*=2.6 Hz). Found: C, 46.64; H, 4.43; N, 17.98%. Calcd for $C_{12}H_{14}N_4O_6$: C, 46.45; H, 4.55; N, 18.06%.

(*S*)-4-Benzyl-3-[(*S*)-2-[(2*S*,3*S*)-3-(benzyloxycabonylamino-2-(*t*-butoxycarbonylamino)butanoyl]-2,3,4,5-tetrahydro-3-pyridazinylcarbonyl]-2-oxazolidinone (13). To a solution of Boc–Dab(Cbz)–OH (0.12 g, 0.35 mmol) in CH_2Cl_2 (2 ml) was added a solution of DCC (80 mg, 0.38 mmol) in CH_2Cl_2 (1 ml) at 0 °C. After this was stirred for 20 min, the resulting solution was further treated with **8** (0.10 g, 0.35 mmol) in the presence of DMAP (5 mg, 0.04 mmol) at 0 °C for 1 h and at room temperature for 5 h. The dicyclohexylurea deposited was filtered off and the filtrate was concentrated in vacuo. The obtained residue was purified on a silica-gel column using hexane–EtOAc (3:1 v/v) to give **13** as a colorless syrup. Yield 83%. $[\alpha]_D^{24}$ +131° (*c* 0.420, MeOH). IR (KBr) 3424, 1785, 1671, 1635, 1500 cm^{-1}. ^1H NMR (C_6D_6) δ=1.24 (d, 3H, *J*=6.8 Hz), 1.40 (s, 9H), 1.40—1.66 (m, 4H), 2.53 (dd, 1H, *J*=8.1 and 13.6 Hz), 2.92 (dd, 1H, *J*=3.3 and 13.6 Hz), 3.30 (dd, 11H, *J*=9.2 Hz), 3.55 (dd, 1H, *J*=3.1 and 9.2 Hz), 4.15 (dddd, 1H, *J*=3.1, 3.3, and 9.2 Hz), 4.75 (m, 1H), 5.09 (s, 2H), 5.75—6.20 (m, 4H), 6.43 (br s, 1H), 6.96—7.35 (m, 10H). Found: C, 61.74; H, 6.11; N, 11.19%. Calcd for $C_{32}H_{39}N_5O_5$: C, 61.82; H, 6.32; N, 11.27%.

(*S*)-2-[(2*S*,3*S*)-3-(Benzyloxycarbonylamino)-2-(*t*-butoxycarbonylamino)butanoyl]-2,3,4,5-tetrahydro-3-pyridazinecarboxylic Acid (14). To a solution of **13** (0.10 g, 0.16 mmol) in THF–water (2.8 ml, 3:1 v/v) was added 30% H_2O_2 (0.1 ml) and then 1 M LiOH (0.33 ml, 0.33 mmol) at 0 °C. After this was stirred at 0 °C for 3 h, the excess H_2O_2 was quenched by a saturated aqueous $Na_2S_2O_3$ solution and the resulting solution was added to a saturated aqueous $NaHCO_3$ solution (15 ml). Evaporation of THF gave an aqueous solution, which was washed three times with diethyl ether (10 ml) and then adjusted to pH 4 with citric acid. The aqueous solution was extracted three times with EtOAc (10 ml) and the combined extracts were washed three times with brine (5 ml) and dried over anhy-

drous Na_2O_4. Concentration in vacuo gave a residue, which was purified on a silica-gel column using hexane–EtOAc (1 : 1 v/v) to give **14** as a colorless syrup. Yield 89%. $[\alpha]_D^{24}$ +6.9° (*c* 0.67, MeOH). IR (KBr) 3364, 1725, 1677, 1632, 1515 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.08 (d, 3H, *J*=6.6 Hz), 1.41 (s, 9H), 1.70—2.50 (m, 4H), 4.24 (m, 1H), 5.09—5.90 (m, 6H), 6.98 (br s, 1H), 7.33 (s, 5H), 8.39 (br s, 1H, COOH). Found: C, 56.84; H, 6.21; N, 11.87%. Calcd for $C_{22}H_{30}N_4O_7$: C, 57.13; H, 6.54; N, 12.11%.

Boc–HMSer–OH (15). To a solution of H–HMSer–OH (13.5 g, 99.9 mmol) in water (100 ml) was added a solution of Boc_2O (26.2 g, 120 mmol) in dioxane (200 ml) and Et_3N (16.7 ml, 117 mmol) at room temperature. After this was stirred for 4 h, a dioxane solution (100 ml) of Boc_2O (26.2 g, 120 mmol) and Et_3N (16.7 ml, 117 mmol) was added three times to the prepared solution at 4-h intervals. After this was stirred for 2 h, the reaction mixture was poured into water (200 ml). The resulting solution was washed three times with diethyl ether (100 ml) and the aqueous layer was acidified to pH 2 with 1 M HCl and then extracted four times with EtOAc (200 ml). The combined extracts were washed three times with brine (80 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave crude crystals, which were recrystallized from EtOAc to give **15** as colorless prisms. Yield 60%, mp 135—137 °C. IR (KBr) 3436, 1734, 1692, 1548 cm^{-1}. ^1H NMR (DMSO-d_6) δ=1.37 (s, 9H), 3.32 (br s, 2H, OH), 3.64 (s, 4H), 6.28 (br s, 1H, NH), 11.00—13.00 (br s, 1H, COOH). Found: C, 46.03; H, 7.32; N, 5.89%. Calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.28; N, 5.96%.

Boc–HMSer(MOM)$_2$–OMOM (16). To a solution of **15** (0.30 g, 1.3 mmol) in THF (4 ml) was added three times a mixture of MOM-Cl (0.90 ml, 12 mmol) and (*i*-Pr)$_2$NEt (2.1 ml, 12 mmol) at 2-h intervals at room temperature. After this was stirred overnight, the reaction mixture was concentrated in vacuo to give a residue, which was dissolved in EtOAc (30 ml) and washed twice with brine (10 ml) and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a residue, which was purified on a silica-gel column using hexane–EtOAc (4 : 1 v/v) to give **16** as a colorless syrup. Yield 96%. IR (KBr) 3450, 1760, 1710, 1503 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.44 (s, 9H), 3.34 (s, 6H), 3.48 (s, 3H), 4.00 (ABq, 4H, *J*=9.9 Hz), 4.62 (s, 4H), 5.35 (s, 2H), 5.54 (br s, 1H, NH). Found: C, 49.28; H, 8.10; N, 3.81%. Calcd for $C_{15}H_{29}NO_9$: C, 49.04; H, 7.96; N, 3.81%.

Boc–HMSer(MOM)$_2$–OH (17). To a solution of **16** (0.20 g, 0.54 mmol) in MeOH (2 ml) was added 1 M LiOH (1.1 ml, 1.1 mmol) at room temperature. After it was stirred for 6 h, the reaction mixture was treated with a saturated aqueous $NaHCO_3$ solution (20 ml) and then MeOH was distilled away. The residual aqueous layer was washed twice with diethyl ether (10 ml) and acidified to pH 3—4 with citric acid, and then extracted three times with EtOAc (15 ml). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The obtained crystals were recrystallized from hexane-diisopropyl ether to give **17** as colorless prisms. Yield 57%, mp 79—80 °C. IR (KBr) 3348, 3364, 1722, 1503 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.44 (s, 9H), 3.45 (s, 6H), 3.98 (ABq, 4H, *J*=9.9 Hz), 4.63 (s, 4H), 5.73 (br s, 1H, NH), 7.24 (br s, 1H, COOH). Found: C, 48.29; H, 8.00; N, 4.29%. Calcd for $C_{13}H_{25}NO_8$: C, 48.29; H, 7.79; N, 4.33%.

Boc–HMSer(MOM)$_2$–Ala–OBzl (18). To a solution of **17** (1.0 g, 3.1 mmol) and *p*-TsOH·H–Ala–OBzl (1.1 g, 3.1 mmol) in DMF (15 ml) was added dropwise, with stirring, a solution of DPPA (0.80 ml, 3.7 mmol) in DMF (5 ml) and then a solution of (*i*-Pr)$_2$NEt (1.2 ml, 6.8 mmol) in DMF (5 ml) at 0 °C. After it was stirred at 0 °C for 30 min and at room temperature overnight, the reaction mixture was added to EtOAc (150 ml). The resulting solution was washed twice with 10% citric acid (30 ml), a saturated aqueous $NaHCO_3$ solution (30 ml), and brine (30 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a crude residue, which was purified on a silica-gel column using hexane–EtOAc (3 : 1 v/v) to give crystals of **18**. Recrystallization from hexane–diisopropyl ether gave **18** as colorless prisms. Yield 76%, mp 46—48 °C. $[\alpha]_D^{24}$ −10.3° (*c* 1.22, MeOH). IR (KBr) 3406, 3322, 1752, 1713, 1674, 1533 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.42 (d,3H, *J*=7.0 Hz), 1.43 (s, 9H), 3.34 (s, 6H), 3.98 (ABq, 2H, *J*=10.1 Hz), 3.99 (s, 2H), 4.62 (s, 4H), 4.65 (dq, 1H, *J*=6.2 Hz), 5.16 (s, 2H), 5.65 (br s, 1H, NH), 7.35 (s, 5H), 7.48 (br d, 1H, NH, *J*=7.0 Hz). Found: C, 56.98; H, 7.38; N, 5.68%. Calcd for $C_{23}H_{36}N_2O_9$: C, 57.01; H, 7.49; N, 5.78%.

Boc–HMSer(MOM)$_2$–Ala–OH (19). A suspension of **18** (868 mg, 1.79 mmol) in EtOH (8 ml) in the presence of 10% Pd/C (100 mg) was hydrogenated catalytically at room temperature for 1 h. After removal of Pd/C, the filtrate was concentrated in vacuo to give crystals, which were recrystallized from hexane–EtOAc to give **19** as colorless prisms. Yield 91%, mp 121—122 °C. $[\alpha]_D^{24}$ −2.6° (*c* 1.1, MeOH). IR (KBr) 3430, 3334, 1710, 1635, 1524 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.43 (s, 9H), 1.46 (s, 3H), 3.35 (s, 6H), 3.98 (s, 4H), 4.45—4.85 (m, 5H), 5.83 (br s, 1H, NH), 7.56 (br d, 1H, NH, *J*=6.6 Hz), 10.57 (br s, 1H, COOH). Found: C, 48.56; H, 7.50; N, 6.92%. Calcd for $C_{16}H_{30}N_2O_9$: C, 48.72; H, 7.67; N, 7.10%.

Protected C-Terminal Pentapeptides (20). Typical Procedure: A solution of an appropriate **3** (0.18 mmol) in a mixture of TFA and CH_2Cl_2 (1 ml, 1 : 1 v/v) was stirred at room temperature for 30 min and then concentrated in vacuo. The obtained residue was dissolved in a small amount of benzene and then azeotropic distillation was done three times. A solution of DPPA (47 μl, 0.22 mmol) in DMF (0.25 ml) and then a solution of Et_3N (56 μl, 0.43 mmol) in DMF (0.25 ml) was added slowly to a solution of the obtained residual TFA-salt and **14** (38 μl, 0.18 mmol) in DMF (0.5 ml) at 0 °C. After it was stirred at 0 °C for 2 h and at room temperature overnight, the reaction mixture was poured into EtOAc (30 ml) and washed with 10% citric acid (5 ml), a saturated aqueous $NaHCO_3$ solution (5 ml) and brine (5 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave a crude viscous syrup, which was purified on a silica-gel column using $CHCl_3$–MeOH (50 : 1—20 : 1 v/v) to give **20** as a colorless amorphous solid.

Boc–Dab(Cbz)–Pya–Ala–ΔVal–Ser–OBzl (20a). Yield 66%. $[\alpha]_D^{24}$ −17.8° (*c* 0.589, MeOH). IR (KBr) 3328, 1662, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=1.16 (d, 3H, *J*=6.7 Hz), 1.37 (d, 3H, *J*=7.3 Hz), 1.43 (s, 9H), 1.75—2.26 (m, 10H), 3.82 (br s, 1H), 3.97 (dd, 2H), 4.12 (dq, 1H), 4.23 (dt, 1H), 4.69 (dq, 1H), 4.93 (br s, 1H), 5.16 (s, 2H), 5.19 (s, 2H), 5.35 (br t, 1H), 5.52 (br d, 1H, *J*=9.1 Hz), 5.28 (br s, 1H), 6.98 (br s, 1H), 7.10 (br d, 1H, *J*=7.3 Hz), 7.19 (br s, 1H), 7.30—7.36 (m, 10H), 7.76 (br s, 1H). Found: C,

58.71; H, 6.54; N, 11.79%. Calcd for $C_{40}H_{53}N_7O_{11}\cdot 1/2H_2O$: C, 58.81; H, 6.66; N, 12.00%.

Boc–Dab(Cbz)–Pya–Abu–ΔVal–Ser–OBzl (20b). Yield 61%. $[\alpha]_D^{25}$ −11.5° (*c* 0.716, MeOH). IR (KBr) 3424, 2974, 2932, 1725, 1665, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.82 (t, 3H, *J*=7.7 Hz), 0.92 (d, 3H, *J*=7.6 Hz), 1.31 (s, 9H), 1.50—1.85 (m, 7H), 1.93 (s, 3H), 2.07—2.20 (m, 2H), 3.60—3.80 (m, 2H), 4.15—4.23 (m, 2H), 4.38 (m, 1H), 4.85 (t, 1H, *J*=6.1 Hz), 4.80—5.20 (m, 3H), 5.13 (ABq, 2H, *J*=12.8 Hz), 6.40 (br d, 1H, *J*=7.9 Hz), 6.80 (br d, 1H, *J*=7.2 Hz), 6.95 (br s, 1H), 7.30—7.36 (m, 10H), 7.64 (br d, 1H, *J*=7.0 Hz), 8.20 (br d, 1H, *J*=7.0 Hz), 9.15 (br s, 1H). Found: C, 59.06; H, 6.61; N, 11.82%. Calcd for $C_{41}H_{55}N_7O_{11}\cdot 1/2H_2O$: C, 59.27; H, 6.79; N, 11.80%.

Boc–Dab(Cbz)–Pya–Nva–ΔVal–Ser–OBzl (20c). Yield 77%. $[\alpha]_D^{25}$ −11.7° (*c* 0.522, MeOH). IR (KBr) 3364, 2974, 1662, 1524 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.86 (t, 3H, *J*=7.3 Hz), 0.91 (d, 3H, *J*=6.7 Hz), 1.25—1.36 (m, 2H), 1.37 (s, 9H), 1.70—1.48 (m, 7H), 1.72—1.85 (m, 2H), 1.93 (s, 3H), 2.08—2.20 (m, 2H), 3.60—3.80 (m, 2H), 4.15—4.28 (m, 2H), 4.37 (m, 1H), 4.85 (t, 1H, *J*=6.1 Hz), 4.96—5.07 (m, 3H), 5.13 (ABq, 2H, *J*=12.8 Hz), 6.40 (br d, 1H, *J*=8.5 Hz), 6.79 (br d, 1H, *J*=7.9 Hz), 6.95 (br s, 1H), 7.30—7.36 (m, 10 Hz), 7.63 (br d, 1H, *J*=7.9 Hz), 8.20 (br d, 1H, *J*=7.0 Hz), 9.15 (br s, 1H). Found: C, 59.44; H, 6.67; N, 11.60%. Calcd for $C_{42}H_{55}N_7O_{11}\cdot 1/2H_2O$: C, 59.27; H, 6.79; N, 11.80%.

Boc–Dab(Cbz)–Pya–Leu–ΔVal–Ser–OBzl (20d). Yield 63%. $[\alpha]_D^{25}$ −5.1° (*c* 0.53, MeOH). IR (KBr) 3430, 2962, 1719, 1665, 1589, 1515 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.84 and 0.90 (d, 6H, *J*=6.4 Hz), 0.90 (d, 3H, *J*=6.2 Hz), 1.37 (s, 9H), 1.47 (m, 2H), 1.62—1.90 (m, 6H), 1.93 (s, 3H), 2.08—2.18 (m, 2H), 3.62—3.79 (m, 2H), 4.12—4.40 (m, 3H), 4.86 (t, 1H, *J*=6.1 Hz), 4.94—5.13 (m, 6H), 6.78 (br d, 1H, *J*=8.6 Hz), 6.95 (br s, 1H), 7.30—7.36 (m, 10H), 7.61 (br d, 1H, *J*=7.0 Hz), 8.21 (br d, 1H, *J*=7.3 Hz), 9.17 (br s, 1H). Found: C, 59.83 H, 6.79; N, 11.41%. Calcd for $C_{43}H_{59}N_7O_{11}\cdot 1/2H_2O$: C; 60.13; H, 7.04; N, 11.41%.

Boc–Dab(Cbz)–Pya–Ala–ΔIle–Ser–OBzl (20e). Yield 64%. $[\alpha]_D^{25}$ −21.3° (*c* 0.627, MeOH). IR (KBr) 3424, 2938, 1668, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.91 and 0.95 (m, 9H), 1.26 (d, 3H, *J*=7.0 Hz), 1.37 (s, 9H), 1.70—1.85 (m, 2H), 1.64 and 1.95 (s, 3H), 2.08—2.25 (m, 2H), 2.02 and 2.35 (q, 2H, *J*=7.0 Hz), 3.60—3.80 (m, 2H), 4.20—4.40 (m, 3H), 4.86 (t, 1H, *J*=6.1 Hz), 4.94—5.16 (m, 6H), 6.39 (br d, 1H, *J*=8.6 Hz), 6.80 (br d, 1H, *J*=7.3 Hz), 6.95 (br s, 1H), 7.30—7.36 (m, 10 H), 7.50 and 7.53 (br d, 1H, *J*=7.0 Hz), 8.30 and 8.32 (br d, 1H), 9.10 and 9.12 (br s, 1H). Found: C, 59.37; H, 6.55; N, 11.89%. Calcd for $C_{41}H_{51}N_7O_{11}\cdot 1/2H_2O$: C, 59.27; H, 6.79; N, 11.80%.

Boc–Dab(Cbz)–Pya–Abu–ΔIle–Ser–OBzl (20f). Yield 58%. $[\alpha]_D^{25}$ −10.6° (*c* 0.619, MeOH). IR (KBr) 3346, 2974, 1662, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.88—0.95 (m, 6H), 1.37 (s, 9H), 1.51—1.90 (m, 4H), 1.64 and 1.92 (s, 3H), 2.08—2.20 (m, 2H), 2.03 and 2.20 (q, 2H, *J*=7.6 Hz), 3.62—3.78 (m, 2H), 4.08—4.42 (m, 3H), 4.85 and 4.87 (t, 1H, *J*=6.1 Hz), 4.95—5.16 (m, 6H), 6.39 (br d, 1H, *J*=7.9 Hz), 6.80 (br d, 1H, *J*=8.0 Hz), 6.95 (br s, 1H), 7.30—7.36 (m, 10 H), 7.55 and 7.59 (br d, 1H, *J*=7.3 Hz), 8.19 and 8.21 (br d, 1H), 9.12 and 9.14 (br s, 1H). Found: C, 59.18; H, 6.96; N, 11.62%. Calcd for $C_{42}H_{57}N_7O_{11}\cdot 1/2H_2O$: C, 59.07; H, 6.96; N, 11.48%.

Boc–Dab(Cbz)–Pya–Nva–ΔIle–Ser–OBzl (20g). Yield 72%. $[\alpha]_D^{25}$ −11.0° (*c* 0.634, MeOH). IR (KBr) 3442, 2932, 2872, 1665, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.82—1.00 (m, 6H), 1.20—2.40 (m, 16H), 3.50—3.80 (m, 2H), 4.10—4.46 (m, 3H), 4.80—5.10 (m, 5H), 5.12 (s, 2H), 6.40 (br d, 1H, *J*=8.3 Hz), 6.81 (br d, *J*=7.6 Hz), 6.95 (br s, 1H), 7.20—7.40 (m, 10H), 7.44—7.64 (m, 1H), 8.22 and 8.23 (br d, 1H, *J*=6.7 Hz), 9.15 (br s, 1H). Found: C, 60.13; H, 6.82; N, 11.47%. Calcd for $C_{43}H_{59}N_7O_{11}\cdot 1/2H_2O$: C, 60.13; H, 7.04; N, 11.41%.

Boc–Dab(Cbz)–Pya–Leu–ΔIle–Ser–OBzl (20h). Yield 60%. $[\alpha]_D^{25}$ −9.0° (*c* 0.616, MeOH). IR (KBr) 3424, 2962, 1665, 1521 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.80—1.00 (m, 9H), 1.20—2.40 (m, 17H), 3.50—3.80 (m, 2H), 4.00—4.50 (m, 3H), 4.80—5.20 (m, 7H), 6.42 (br d, 1H), 6.80 (br d, 1H), 6.95 (br s, 1H), 7.30—7.40 (m, 10H), 7.56 and 7.60 (br d, 1H), 8.26 (br d, 1H), 9.18 (br s, 1H). Found: C, 60.87; H, 7.10; N, 10.94%. Calcd for $C_{44}H_{61}N_7O_{11}\cdot 1/2H_2O$: C, 60.54; H, 7.16; N, 11.23%.

Protected Antrimycins (21). Typical Procedure: A solution of an appropriate protected pentapeptide (**20**) (0.12 mmol) in TFA and CH_2Cl_2 (1 ml, 1 : 1 v/v) was stirred at room temperature for 30 min. Concentration in vacuo, followed by the azeotropic distillation with benzene three times, gave a residual syrup, which was crystallized by trituration with diethyl ether. A solution of DPPA (30 μl, 0.14 mmol) in DMF (0.2 ml) and then a solution of Et_3N (38 μl, 0.29 mmol) in DMF (0.2 ml) was added to a solution of the obtained crystals and **19** (47 mg, 0.12 mmol) in DMF (0.5 ml) at 0 °C. After it was stirred for 1 h and left at room temperature overnight, the reaction mixture was diluted with EtOAc (30 ml) and washed twice with 10% citric acid (5 ml), a saturated aqueous $NaHCO_3$ solution (5 ml), and brine (5 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave crystals, which were purified on a silica-gel column using a mixture of $CHCl_3$—MeOH (20 : 1 v/v) to give **21** as colorless amorphous solid.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Ala–ΔVal–Ser–OBzl (21a). Yield 65%. $[\alpha]_D^{24}$ −30.2° (*c* 0.414, MeOH). IR (KBr) 3334, 2974, 2938, 1659, 1530 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.94 (d, 3H, *J*=6.7 Hz), 1.20 (d, 3H, *J*=6.7 Hz), 1.26 (d, 3H, *J*=7.0 Hz), 1.35 (s, 9H), 1.65 (s, 3H), 1.72—1.82 (m, 2H), 1.95 (s, 3H), 2.10—2.20 (m, 2H), 3.19 and 3.21 (s, 6H), 3.64—3.88 (m, 6H), 4.18—4.30 (m, 2H), 4.35—4.43 (m, 2H), 4.47—4.54 (m, 4H), 4.87 (t, 1H, *J*=6.1 Hz), 4.96 (m, 1H), 4.98 (ABq, 2H, *J*=13.1 Hz), 5.13 (ABq, 2H, *J*=12.8 Hz), 5.45 (dd, 1H), 6.62 (br d, 1H, *J*=8.2 Hz), 6.88 (br s, 1H), 6.98 (br s, 1H), 7.30—7.36 (m, 10H), 7.59 (br d, 1H, *J*=7.4 Hz), 7.65 (m, 10H), 7.77 (br d, 1H), 8.31 (br d, 1H, *J*=6.4 Hz), 9.11 (br s, 1H). Found: C, 55.31; H, 6.64; N, 11.33%. Calcd for $C_{51}H_{79}N_9O_{17}\cdot H_2O$: C, 55.58; H, 6.86; N, 11.44%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Abu–ΔVal–Ser–OBzl (21b). Yield 62%. $[\alpha]_D^{25}$ −20.2° (*c* 0.645, MeOH). IR (KBr) 3328, 2968, 2938, 1722, 1659, 1533 cm^{-1}. ^1H NMR (DMSO-d_6) δ=0.88 (t, 3H, *J*=7.3 Hz), 0.92 (d, 3H, *J*=6.7 Hz), 1.20 (d, 3H, *J*=6.7 Hz), 1.35 (s, 9H), 1.50—2.00 (m, 10H), 2.10—2.15 (m, 2H), 3.19 and 3.21 (s, 6H), 3.60—3.90 (m, 6H), 4.10—4.45 (m, 4H), 4.45—4.60 (m, 4H), 4.87 (t, 1H, *J*=6.1 Hz), 4.95—5.05 (m, 3H), 5.13 (s, 2H), 5.46 (br d, 1H), 6.62 (br d, 1H, *J*=8.2 Hz), 6.88 (br s, 1H), 6.98 (br s, 1H), 7.31—7.36 (m, 10 H), 7.65 (br

d, 1H, J=7.1 Hz), 7.79 (br d, 1H, J=7.2 Hz), 8.22 (br d, 1H, J=7.0 Hz), 9.15 (s, 1H). Found: C, 56.17; H, 6.81; N, 10.97%. Calcd for $C_{52}H_{75}N_9O_{17}\cdot H_2O$: C, 55.95; H, 6.95; N, 11.29%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Nva–ΔVal–Ser–OBzl (21c). Yield 70%. $[\alpha]_D^{25}$ −19.5° (c 0.611, MeOH). IR (KBr) 3322, 2938, 1719, 1659, 1555 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.86 (t, 3H, J=7.4 Hz), 0.94 (d, 3H, J=6.7 Hz), 1.20 (d, 3H, J=6.7 Hz), 1.25—1.85 (m, 18H), 1.93 (s, 3H), 2.05—2.20 (m, 2H), 3.19 and 3.21 (s, 6H), 3.60—3.90 (m, 6H), 4.15—4.45 (m, 4H), 4.48—4.54 (m, 4H), 4.86 (t, 1H, J=5.8 Hz), 4.95—5.12 (m, 3H), 5.13 (s, 2H), 5.48 (br d, 1H), 6.60 (br d, 1H, J=8.6 Hz), 6.90 (br s, 1H), 6.97 (br s, 1H), 7.30—7.36 (m, 10H), 7.64 (br d, 1H, J=7.4 Hz), 7.79 (br d, 1H, J=7.0 Hz), 8.22 (br d, J=7.4 Hz), 9.14 (br s, 1H). Found: C, 56.78; H, 7.01; N, 11.07%. Calcd for $C_{53}H_{77}N_9O_{17}\cdot 1/2H_2O$: C, 56.77; H, 7.01; N, 11.24%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Leu–ΔVal–Ser–OBzl (21d). Yield 55%. $[\alpha]_D^{25}$ −16.4° (c 0.534, MeOH). IR (KBr) 3334, 2956, 1656, 1524 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.83 and 0.88 (d, 6H, J=6.4 Hz), 0.91 (d, 3H, J=6.7 Hz), 1.20 (d, 3H, J=6.7 Hz), 1.40—1.95 (m, 11H), 1.93 (s, 3H), 2.05—2.20 (m, 2H), 3.19 and 3.21 (s, 6H), 3.60—3.90 (m, 6H), 4.15—4.45 (m, 4H), 4.48—4.58 (m, 4H), 4.87 (t, 1H, J=5.8 Hz), 4.95—5.06 (m, 3H), 5.13 (s, 2H), 5.50 (m, 1H), 6.59 (br d, 1H, J=8.6 Hz), 6.90 (br s, 1H), 6.97 (br s, 1H), 7.30—7.36 (m, 10H), 7.62 (br d, 1H, J=7.0 Hz), 7.80 (br d, 1H, J=7.0 Hz), 8.24 (br d, J=7.6 Hz), 9.17 (br s, 1H). Found: C, 56.92; H, 6.97; N, 10.85%. Calcd for $C_{54}H_{79}N_9O_{17}\cdot 1/2H_2O$: C, 57.13; H, 7.10; N, 11.10%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Ala–ΔIle–Ser–OBzl (21e). Yield 65%. $[\alpha]_D^{25}$ −35.8° (c 0.227, MeOH). IR (KBr) 3330, 1650, 1530 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.95 and 0.97 (t, 3H, J=5.8 Hz), 1.20 (d, 3H, J=7.0 Hz), 1.25 (d, 3H, J=5.8 Hz), 1.35 (s, 9H), 1.70—1.85 (m, 2H), 1.64 and 1.94 (s, 3H), 2.08—2.22 (m, 2H), 2.02 and 2.44 (q, 6H, J=5.8 Hz), 3.19 and 3.21 (s, 6H), 3.60—3.90 (m, 6H), 4.18—4.31 (m, 2H), 4.32—4.80 (m, 2H), 4.96 (m, 1H), 4.99 (ABq, 2H, J=12.8 Hz), 5.13 (ABq, 2H, J=13.4 Hz), 5.45 (m, 1H), 6.62 (br d, 1H, J=7.6 Hz), 6.89 (br s, 1H), 6.98 (br s, 1H), 7.30—7.36 (m, 10H), 7.52 and 7.55 (br d, 1H, J=7.7 Hz), 7.65 (br s, 1H), 7.76 (br s, 1H), 8.31 and 8.32 (br d, 1H, J=6.8 Hz), 9.10 and 9.11 (br s, 1H). Found: C, 54.77; H, 6.71; N, 10.95%. Calcd for $C_{51}H_{79}N_9O_{17}\cdot 2H_2O$: C, 55.06 H, 7.02; N, 11.11%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Abu–ΔIle–Ser–OBzl (21f). Yield 70%. $[\alpha]_D^{25}$ −25.6° (c 0.522, MeOH). IR (KBr) 3328, 2974, 2938, 1656, 1533 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.88 (t, 3H, J=7.3 Hz), 0.93 and 0.94 (t, 3H, J=7.6 Hz), 1.20 (d, 3H, J=7.3 Hz), 1.35 (s, 9H), 1.50—1.85 (m, 2H), 1.64 and 1.94 (s, 3H), 2.05—2.16 (m, 2H), 2.03 and 2.32 (q, 6H, J=7.6 Hz), 3.19 and 3.21 (s, 6H), 3.60—3.88 (m, 6H), 4.18—4.42 (m, 4H), 4.48—4.57 (m, 6H), 4.86—4.89 (m, 1H), 4.96—5.04 (m, 3H), 5.13 (ABq, 2H, J=13.4 Hz), 5.47 (m, 1H), 6.61 (br d, 1H, J=8.6 Hz), 6.10 (br s, 1H), 6.98 (br s, 1H), 7.36—7.30 (m, 10H), 7.58 and 7.62 (br d, 1H, J=7.3 Hz), 7.80 (br s, 1H), 8.21 and 8.22 (br d, 1H, J=6.7 Hz), 9.13 and 9.15 (br s, 1H). Found: C, 56.37; H, 6.86; N, 11.16%. Calcd for $C_{53}H_{77}N_9O_{17}\cdot H_2O$: C, 56.32; H, 7.05; N, 11.15%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Nva–ΔIle–Ser–OBzl (21g). Yield 73%. $[\alpha]_D^{25}$ −21.5° (c 0.536, MeOH). IR (KBr) 3334, 2962, 2938, 1719, 1659, 1530 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.86 (t, 3H, J=7.4 Hz), 0.92—0.96 (m, 3H), 1.20 (d, 3H, J=6.7 Hz), 1.30—1.70 (s, 13H), 1.70—1.86 (m, 2H), 1.64 and 1.92 (s, 3H), 2.00—2.10 (m, 2H), 2.03 and 2.32 (q, 6H, J=7.5 Hz), 3.19 and 3.21 (s, 6H), 3.60—3.85 (m, 6H), 4.08—4.30 (m, 8H), 4.86—4.89 (m, 1H), 4.95—5.05 (m, 3H), 5.13 (ABq, 2H, J=12.8 Hz), 5.23 (m, 1H), 6.60 (br d, 1H, J=8.6 Hz), 6.89 (br s, 1H), 6.97 (br s, 1H), 7.30—7.36 (m, 10H), 7.55 and 7.59 (br d, 1H, J=7.3 Hz), 7.64 (br d, 1H), 7.80 (br s, 1H), 8.21 and 8.22 (br d, 1H, J=7.1 Hz), 9.17 and 9.18 (br s, 1H). Found: C, 57.39; H, 6.98; N, 10.96%. Calcd for $C_{54}H_{79}N_9O_{17}$: C, 57.59; H, 7.07; N, 11.19%.

Boc–HMSer(MOM)$_2$–Ala–Dab(Cbz)–Pya–Leu–ΔIle–Ser–OBzl (21h). Yield 62%. $[\alpha]_D^{25}$ −17.9° (c 0.514, MeOH). IR (KBr) 3334, 2962, 2938, 1719, 1656, 1530 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.83 and 0.89 (d, 6H, J=6.7 Hz), 0.92—0.96 (m, 3H), 1.20 (d, 3H, J=7.9 Hz), 1.30—1.50 (m, 12H), 1.70—1.90 (m, 2H), 1.64 and 1.92 (s, 3H), 2.05—2.20 (m, 2H), 3.19 and 3.21 (s, 6H), 3.60—3.85 (m, 6H), 4.05—4.58 (m, 8H), 4.80—5.03 (m, 4H), 5.13 (s, 2H), 5.50 (m, 1H), 6.59 (br d, 1H, J=8.6 Hz), 6.89 (br s, 1H), 6.97 (br s, 1H), 7.54 and 7.58 (br d, 1H, J=7.3 Hz), 7.31—7.36 (m, 10H), 7.64 (br d, 1H), 7.80 (br s, 1H), 8.25 and 8.27 (br d, 1H, J=7.3 Hz), 9.15 and 9.17 (br s, 1H). Found: C, 57.24; H, 7.13; N, 10.64%. Calcd for $C_{55}H_{81}N_9O_{17}\cdot H_2O$: C, 57.08; H, 7.14; N, 10.64%.

Hydrogenolytic Deprotection of 3. Typical Procedure: A suspension of **3** (0.1 mmol) in MeOH (0.1 ml) was hydrogenolyzed catalytically with 5% Pd/C (10 mg) at room temperature for 20 min. After removal of Pd/C, the filtrate was concentrated in vacuo to give crude crystals, which were recrystallized from hexane–EtOAc to give colorless prisms or solid.

Boc–Ala–ΔVal–Ser–OH from 3a. Yield 89%, mp 171—173 °C. $[\alpha]_D^{25}$ −14.8° (c 0.520, MeOH). IR (KBr) 3340, 3286, 1749, 1659, 1524 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=1.21 (d, 3H, J=7.3 Hz), 1.37 (s, 9H), 1.68 and 1.98 (s, 6H), 3.33 (br s, 1H, OH), 3.68 (m, 2H), 4.00 (dq, 1H, J=7.3 and 7.7 Hz), 4.27 (dt, 1H, J=3.3 and 6.6 Hz), 7.00 (br d, 1H, NH, J=6.6 Hz), 7.38 (br d, 1H, NH, J=7.7 Hz), 9.02 (br s, 1H, NH), 12.00 (br s, 1H, COOH). Found: C, 51.25; H, 7.10; N, 11.08%. Calcd for $C_{16}H_{27}N_3O_7$: C, 51.47; H, 7.29; N, 11.25%.

Boc–Ala–ΔIle–Ser–OH from 3e. Colorless solid, yield 92%. $[\alpha]_D^{25}$ −15.9° (c 0.887, MeOH). IR (KBr) 3340, 1662, 1524 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=0.94 and 1.00 (t, 3H, J=7.7 Hz), 1.22 (d, 3H, J=7.0 Hz), 1.45 (s, 9H), 1.67—2.52 (m, 5H), 3.58 and 3.73 (m, 2H), 4.00 (dq, 1H, J=7.0 Hz), 4.27 (dt, 1H, J=3.2 Hz), 7.00 (d, 1H, NH, J=6.4 Hz), 7.30 (d, 1H, NH, J=7.0 Hz), 7.30 (br s, 1H, NH). Found: C, 50.11; H, 7.46; N, 10.11%. Calcd for $C_{17}H_{29}N_3O_7\cdot H_2O$: C, 50.36; H, 7.71; N, 10.36%.

H–Ala–ΔVal–Ser–OMe from 3i. Yield 89%, mp 136—138 °C. $[\alpha]_D^{25}$ +25.0° (c 0.404, MeOH). IR (KBr) 3328, 1755, 1653, 1632, 1506 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=1.36 (d, 3H, J=7.0 Hz), 1.85 and 2.02 (s, 6H), 2.68 (br s, 1H, NH), 3.60 (q, 1H, J=7.0 Hz), 3.78 (s, 3H), 4.63 (dt, 1H, J=3.5 and 11.9 Hz), 6.96 (br d, 1H, NH, J=7.0 Hz), 7.33 (br s, 1H, NH). Found: C, 49.19; H, 7.15; N, 14.60%. Calcd for $C_{12}H_{21}N_3O_5\cdot 1/4H_2O$: C, 49.39; H, 7.43; N, 14.40%.

H–Ala–ΔVal–Ser–OH from 3j. Yield 87%, mp 205—207 °C (decomp). $[\alpha]_D^{25}$ +62.7° (*c* 0.623, MeOH). IR (KBr) 3388, 3220, 1758, 1686, 1659, 1587, 1512 cm^{-1}. ^1H NMR (CD_3OD) δ=1.57 (d, 3H, *J*=7.5 Hz), 1.79 and 2.07 (s, 6H), 3.86 (d, 2H, *J*=4.2 Hz), 4.05 (q, 1H, *J*=7.5 Hz), 4.30 (t, 1H, *J*=4.2 Hz). Found: C, 46.84; H, 6.83; N, 15.16%. Calcd for $C_{11}H_{19}N_3O_3 \cdot 1/2H_2O$: C, 46.80; H, 7.14; N, 14.89%.

H–Ala–ΔIle–Ser–OH from 3k. Colorless solid, yield 92%. $[\alpha]_D^{25}$ +67.2° (*c* 0.568, MeOH). IR (KBr) 3394, 1758, 1623, 1536 cm^{-1}. ^1H NMR (CD_3OD) δ=1.04 and 1.10 (t, 3H, *J*=7.3 Hz), 1.57 (d, 3H, *J*=7.0 Hz), 1.79 and 2.03 (s, 3H), 2.18 and 2.45 (q, 2H, *J*=7.3 Hz), 3.85 (d, 2H, *J*=4.2 Hz), 4.12 (q, 1H, *J*=7.0 Hz), 4.27 (t, 1H, *J*=4.2 Hz). Found: C, 47.17; H, 7.28; N, 13.45%. Calcd for $C_{13}H_{21}N_3O_5 \cdot H_2O$: C, 47.21; H, 7.59; N, 13.76%.

Antrimycins Av (la) and Dv (1d). A solution of an appropriate protected antrimycin **21** (0.10 g, 0.10 mmol) in MeOH (1 ml) and acetic acid (0.3 ml) was hydrogenolyzed catalytically with 10% Pd/C at room temperature for 2 h under vigorous stirring. Pd/C was filtered off and the filtrate was concentrated in vacuo. The obtained residue was dissolved in 70% TFA (2.6 ml) and the resulting solution was stirred at room temperature for 12 h. After concentration in vacuo, the crude peptide obtained was purified by HPLC using Tosoh TSK gel ODS-120T (21.5 mm i.d.×30 cm) column with 15% CH_3CN–H_2O 0.05% TFA by the flow rate 6.0 ml min^{-1} to give **1** as a colorless amorphous solid.

Antrimycin Av (la). Yield 73%. IR (KBr) 3400, 1674, 1530 cm^{-1}. ^1H NMR (D_2O) δ=1.15 (d, 3H, *J*=7.0 Hz, Dab –CH_3), 1.31 (d, 3H, *J*=7.3 Hz, Ala –CH_3), 1.34 (d, 3H, *J*=7.0 Hz, Ala –CH_3), 1.79 and 1.92 (s, 6H, ΔVal –CH_3), 2.15—2.23 (m, 2H, Pya ring-H), 3.75 and 3.85 (dABq, 2H, *J*=4.6 and 12.0 Hz, Ser –CH_2–), 3.88 (dq, 1H, *J*=7.0 and 4.6 Hz, Dab β-H), 3.80 and 3.92 (ABq, 2H, *J*=12.5 Hz, HMSer –CH_2O–), 3.81 and 3.93 (ABq, 2H, *J*=12.5 Hz, HMSer –CH_2O–), 4.23 (q, 1H, *J*=7.3 Hz, Ala α-H), 4.37 (q, 1H, *J*=7.0 Hz, Ala α-H), 4.44 (dd, 1H, *J*=4.6 Hz, Ser α-H), 4.96 (t, 1H, Pya α-H), 5.58 (d, 1H, *J*=4.6 Hz, Dab α-H), 7.07 (d, 1H, *J*=3.9 Hz, Pya H-6). ^{13}C NMR (D_2O) δ=13.92, 17.01, 17.24, 20.04, 20.61, 20.71, 21.27, 21.27, 48.84, 50.69, 51.69, 52.99, 53.70, 55.69, 61.49, 62.04, 66.99, 122.45, 144.51, 149.18, 168.36, 169.53, 170.02, 172.54, 174.09, 175.16, 176.04. TLC (*Rf*): 0.12 (BuOH : AcOH : H_2O=4 : 1 : 2). Ninhydrin: positive.

Found: C, 38.88; H, 5.26; N, 12.88%. Calcd for $C_{27}H_{45}N_9O_{11} \cdot 3CF_3COOH$: C, 39.10; H, 4.77; N, 12.44%.

Antrimycin Dv (1d). Yield 68%. IR (KBr) 3436, 1680, 1530 cm^{-1}. ^1H NMR (D_2O) δ=0.93 and 0.98 (d, 6H, *J*=6.4 Hz, Leu –CH_3), 1.28 (d, 3H, *J*=7.0 Hz, Dab –CH_3), 1.44 (d, 3H, *J*=7.3 Hz, Ala –CH_3), 1.64—1.75 (m, 3H, Leu β-H, γ-H), 1.79 and 2.05 (s, 6H, ΔVal –CH_3), 2.01—2.08 (m, 2H, Pya ring-H), 2.25—2.37 (m, 2H, Pya ring-H), 3.88 and 3.99 (dABq, 2H, *J*=4.0 and 11.6 Hz, Ser –CH_2O–), 3.94 and 4.05 (ABq, 2H, *J*=12.5 Hz, HMSer –CH_2O–), 3.95 and 4.07 (ABq, 2H, *J*=12.2 Hz, HMSer –CH_2O–), 4.09 (dq, 1H, *J*=7.0 and 4.6 Hz, Dab β-H), 4.41 (dd, 1H, *J*=4.9 and 9.2 Hz, Leu α-H), 4.51 (q, 1H, *J*=7.3 Hz, Ala α-H), 4.56 (dd, 1H, *J*=4.3 Hz, Ser α-H), 5.10 (t, 1H, Pya α-H), 5.72 (d, 1H, *J*=4.6 Hz, Dab α-H), 7.21 (d, 1H, *J*=3.7 Hz, Pya H-6). ^{13}C NMR (D_2O) δ=14.30, 17.67, 20.35, 20.99, 21.16, 21.69, 21.99, 23.27, 25.63, 40.89, 49.22, 51.57, 53.41, 53.84, 54.10, 56.17, 61.91, 61.94, 62.42, 67.40, 122.91, 144.92, 149.48, 168.83, 169.95, 170.41, 173.20, 174.57, 175.30, 176.47. TLC-(*Rf*): 0.28 (BuOH : AcOH : H_2O=4 : 1 : 2). Ninhydrin: positive.

Found: C, 40.63; H, 5.28; N, 11.70%. Calcd for $C_{30}H_{51}N_9O_{11} \cdot 3CF_3COOH$: C, 40.95; H, 5.16; N, 11.94%.

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