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Synthesis of Teleocidins A, B and Their Congeners. Part 3.[1] Synthesis of Dihydroteleocidin B-4 (Dihydroteleocidin B), Teleocidin B-3 and Teleocidin B-4

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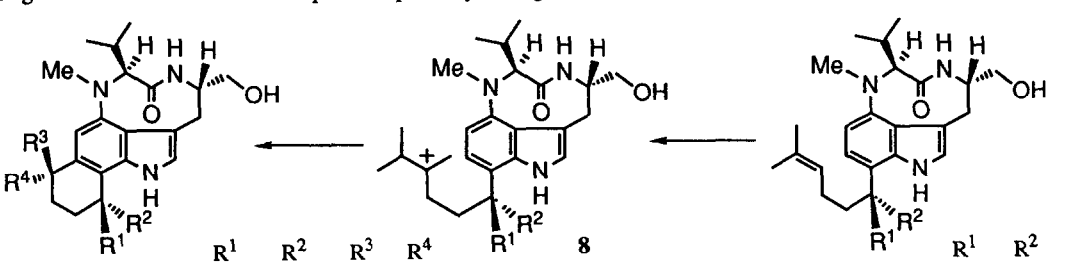
Abstract *— Details of the synthesis method of the tumor promoters teleocidin B-3 (3), teleocidin B-4 (4) and dihydroteleocidin B-4 (9) (=dihydroteleocidin B) from (S)- and (R)-methyl N-methyl-N-[7-(3,6,7-trimethyl-1,6-octadien-3-yl)-4-indolyl]- L-valinates (20b and 20a) are presented*

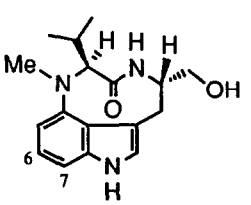
Potent tumor promoters, teleocidins B-1 (**1**), B-2 (**2**), B-3 (**3**) and B-4 (**4**) are isolated from *Streptomyces mediocidicus* together with teleocidins A-1 (**5**) and A-2 (**6**)[2] The teleocidin A family has a linalyl type of monoterpene side chain at the C-7 position of (–)-indolactam V (**7**),[3] whereas the above four teleocidins B have an eleven carbon unit at the 6- and 7-positions of **7**, constituting a six-membered ring and a variety of substituents such as the methyl, isopropyl and vinyl groups with a particular combination of stereochemical arrangement to form B-1 — B-4 In regard to this discrepancy, the extra one carbon atom in question was shown to have originated in L-methionine and a possible pathway through an intermediate **8** was discussed in the biogenesis of



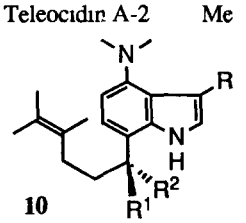
	R^1	R^2	R^3	R^4
1 Teleocidin B-1	vinyl	Me	i-Pr	Me
2 Teleocidin B-2	Me	vinyl	Me	i-Pr
3 Teleocidin B-3	Me	vinyl	i-Pr	Me
4 Teleocidin B-4	vinyl	Me	Me	i-Pr
9 Dihydro-teleocidin B-4	Et	Me	Me	i-Pr

8

	R^1	R^2
5 Teleocidin A-1 =Lyngbyatoxin A	vinyl	Me
6 Teleocidin A-2	Me	vinyl



7 (–)-Indolactam V



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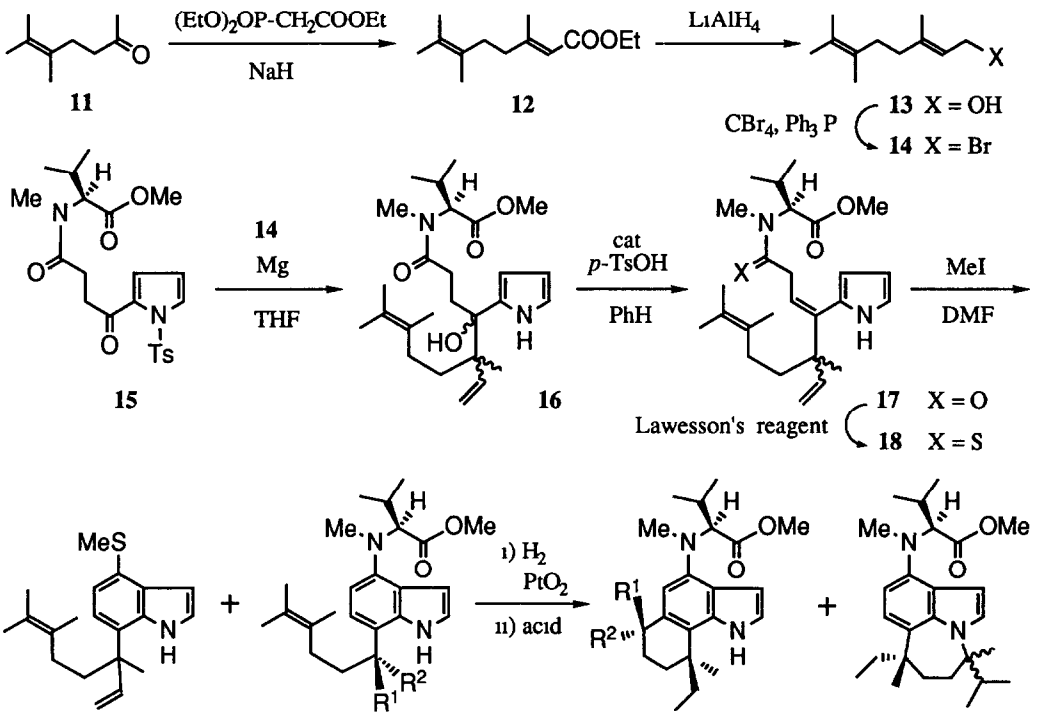
teleocidins B [4] In the synthesis of these alkaloids, we had already made use of the chemical equivalent **10** of the cation **8** and succeeded in the total synthesis of dihydroteleocidin B-4 (**9**), teleocidin B-3 (**3**) and teleocidin B-4 (**4**), as reported in communications [5] Here we describe the details of experiments, whose methodology is closely related to the preceding procedure of the teleocidin A synthesis [1] Total synthesis of racemic **3** and **4** has been reported by Nakatsuka and Goto [6]

Our plan for constructing the fundamental skeleton of the 6,7,8,9-tetrahydrobenz[*g*]indole ring system was to make an acid-catalyzed Friedel-Crafts type of intramolecular cyclization reaction on the compounds having the partial structure **10** So the preparation of indole derivatives **20** was required at first and this task was easily attained as shown in Chart 1, according to the established method described in the two preceding papers [1,9] 3,6,7-Trimethyl-2,6-octadienyl bromide[7] (**14**) was prepared from 5,6-dimethyl-5-hepten-2-one[8] (**11**) in the following three steps in 29% yield i) the Horner-Emmons reaction of **11** with triethyl phosphonoacetate in the presence of sodium hydride, ii) reduction of the diene-ester **12** with lithium aluminum hydride and iii) bromination of the allyl alcohol **13** with carbon tetrabromide and triphenylphosphine Using this bromide **14**, the Grignard reaction was carried out with the L-valine derivative[9] **15** in tetrahydrofuran at -20°C to furnish **16** in 70% yield. This was dehydrated with a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene in 90% yield, and the resulting substance **17** was converted into the corresponding thioamide derivative **18** in 74% yield using the Lawesson's reagent[10] in THF at reflux The indole formation from **18** was performed as before with iodomethane in dimethylformamide at room temperature[9] to give **20a** and **20b** in 38% and 25% yields, respectively, accompanied by the formation of a by-product **19** in 30% yield



19

20a R^1 = vinyl R^2 = Me

20b R^1 = Me R^2 = vinyl

21 R^1 = Et R^2 = Me

22a R^1 = Me R^2 = i-Pr

22b R^1 = i-Pr R^2 = Me

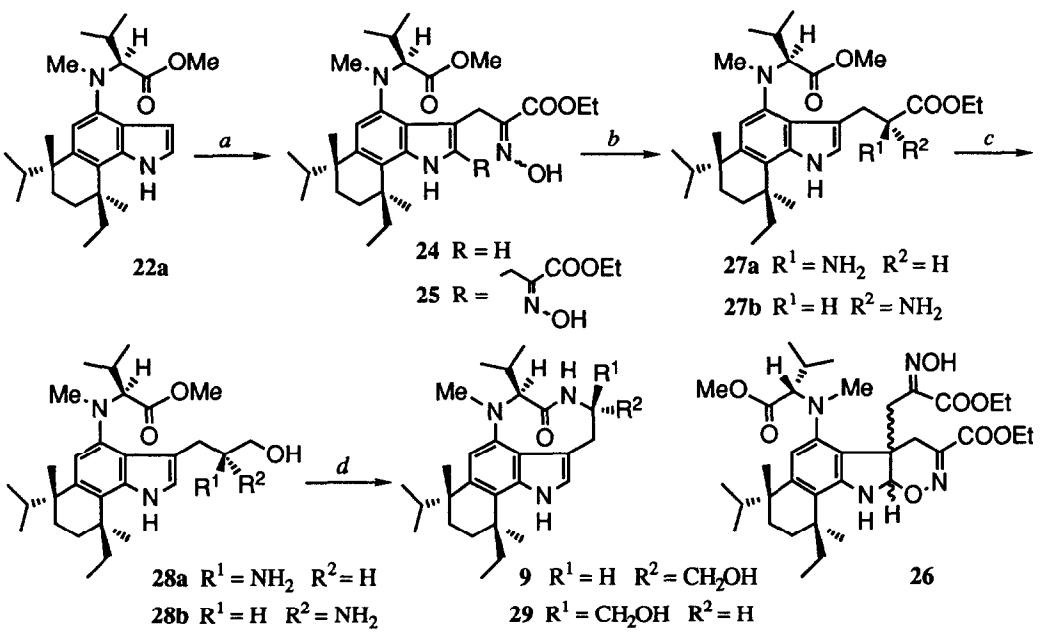
23a, 23b unknown stereochemistry

Chart 1

Table 1 Acid-Catalyzed Intramolecular Cyclization of Methyl *N*-Methyl-*N*-[7-[(*S*)-3,6,7-trimethyl-6-octen-3-yl]-4-indolyl]-L-valinate (**21**)

Acid (mol equiv.)	Solvent	Temperature (°C)	Time (h)	**22a** (%)	**22b** (%)	**23a** (%)	**23b** (%)	Recovery (%)
p-TsOH (1 5)	$CHCl_3$	reflux	15	0	0	0	0	90
$EtAlCl_2$ (12)	CH_2Cl_2	-20 – -10	3		complex mixture			
BF_3OEt_2 (40)	CH_2Cl_2	0 – 20	7	33	19	26	17	0
$SnCl_4$ (50)	CH_2Cl_2	-20 – -10	1 5	36 5	13 5	14	7	0
conc H_2SO_4 (30)	CH_2Cl_2	0	4	40	10	15	8	0

Dihydroteleocidin B-4 (**9**) is a pure crystalline compound obtained accidentally by Takashima and Sakai during their structural investigation of the so-called "teleocidin B,"[11a,11b] which is shown later to be a mixture of four components, teleocidins B-1 (**1**), B-2 (**2**), B-3 (**3**) and B-4 (**4**).[2] Fujiki and co-workers screened this dihydroteleocidin B-4 (**9**) (named "dihydroteleocidin B" at that time[12]) for the first time for tumor promoter activity[13] and started the profound studies concerning the biological activities of this class of indole alkaloids.[3a] To synthesize **9**, the above indole derivative **20a** was reduced catalytically over platinum oxide in methanol. Partial hydrogenation proceeded without trouble and dihydro compound **21** was obtained in 92% yield. The intramolecular cyclization of **21** was then studied using both protonic and the Lewis acids as shown in Table 1. The acids such as *p*-toluenesulfonic acid, trifluoromethanesulfonic acid and dichloroethylaluminium afforded only disappointing results, but boron trifluoride etherate and tin(IV) chloride produced the desired cyclized

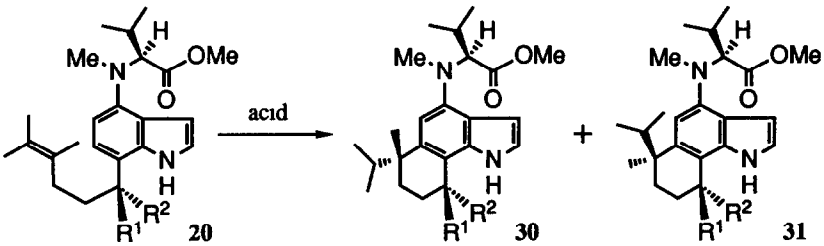


a $BrCH(COOEt)NOH$, Na_2CO_3, CH_2Cl_2 *b* Al-Hg, $THF-H_2O$ *c* $NaBH_4$, LiCl, EtOH-THF

d i) 10% KOH in $MeOH-H_2O$ ii) $Et_3N \cdot HCl$ iii) DPPA, Et_3N, DMF

Chart 2

Table 2 Acid-Catalyzed Intramolecular Cyclization of Methyl (*R*)- and (*S*)-*N*-Methyl-*N*-[7-(3,6,7-trimethyl-1,6-octadien-3-yl)-4-indolyl]-L-valinates (**20a** and **20b**)



20 **30** **31**

a R^1 = vinyl R^2 = Me **b** R^1 = Me R^2 = vinyl

Substrate	Acid (mol equiv)	Solvent	Temperature (°C)	Time	Product (Yield %)
20b	conc H_2SO_4 (63)	CH_2Cl_2	-60	1 h	complex mixture
20b	$SnCl_4$ (35)	CH_2Cl_2	-40	14 min	complex mixture
20a	BF_3OEt_2 (43 5)	CH_2Cl_2	0 → r t	5 5 h	**30a** + **31a** (17) (10 1)
20a	BF_3OEt_2 (40)	$ClCH_2CH_2Cl$	0 → r t	7 5 h	**30a** (20)
20b	BF_3OEt_2 (17)	$ClCH_2CH_2Cl$	0 → r t	7 h	**31b** (14)

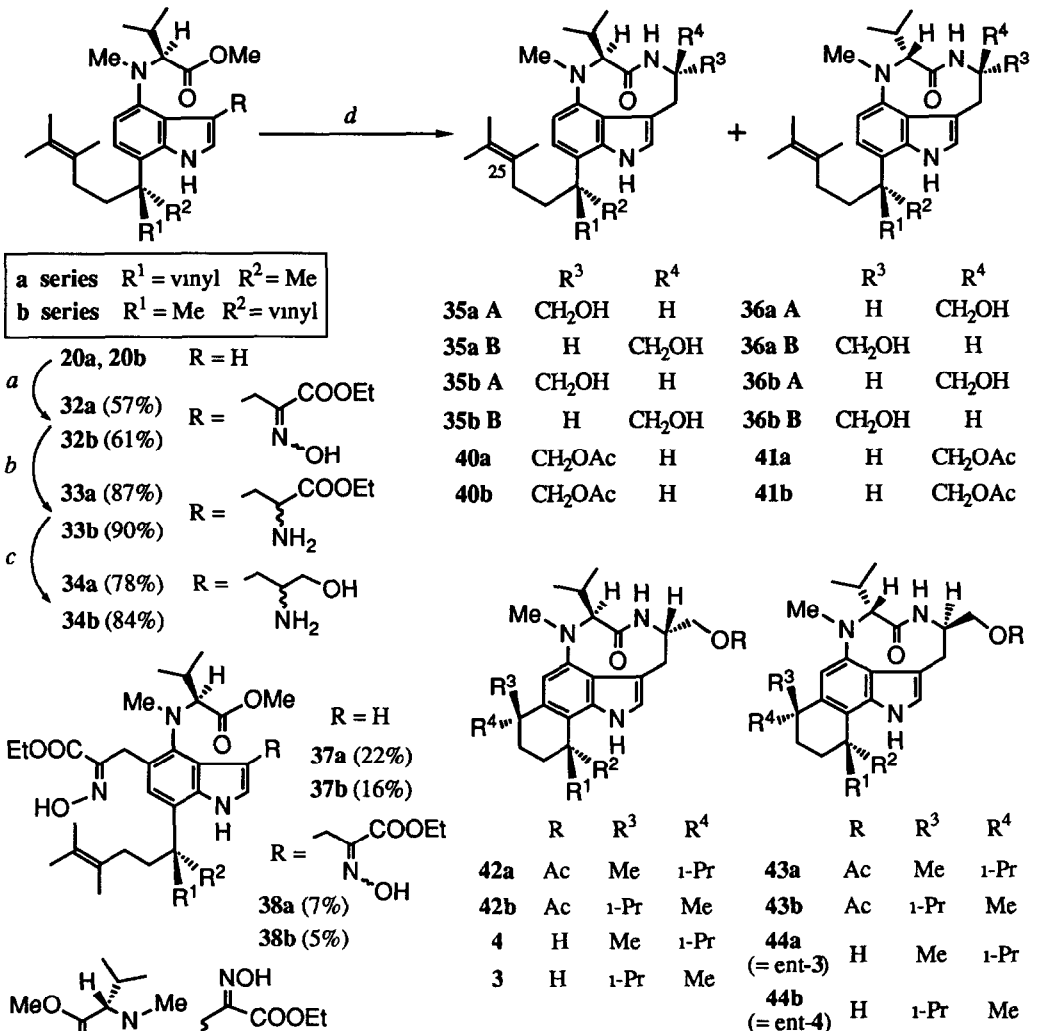
compounds as two diastereoisomers **22a** and **22b**, where the compound **22a** having the bulky alkyl substituents, *i e* , the ethyl and isopropyl groups, at the trans situation was formed in a predominant amount Other tricyclic derivatives **23a** and **23b** were obtained as unwanted by-products The stereochemical arrangement of **22a** and **22b** was uncertain at this stage, and the successful total synthesis of **9** from **22a** revealed this as shown Concentrated sulfuric acid gave the best yield of the required compound **22a** for further synthesis

Treatment of product **22a** with ethyl 3-bromo-2-hydroxyiminopropanoate in the presence of sodium carbonate[14] provided **24**, **25** and **26** in 57%, 2 5% and 9% yields, respectively (Chart 2) The oxime compound **24** was reduced with aluminium-amalgam to give amino-diesters **27a** and **27b** in 40% and 39 5% yields Separation of these two diastereomers at this stage made it easy to purify the final products The amino-diester **27a** was then treated with sodium borohydride in the presence of lithium chloride[15] to give the amino-alcohol **28a**, which was submitted to the next step without further purification, since the chromatography on either silica gel or alumina caused a great loss of the material The last intramolecular amide formation was carried out in the same manner as described in the preceding paper[1] using diphenylphosphoryl azide[16] (DPPA) to afford dihydroteleocidin B-4 (**9**) in 18% yield, calculated from **27a** The synthetic material **9** was identified as authentic dihydroteleocidin B-4 by comparing their mp, MS, IR, ^1H NMR and CD spectra as well as their biological activity In a similar way, the amino-diester **27b** was converted into 9-epidihydroteleocidin B-4 (**29**) via the amino-alcohol **28b** in 13% yield

Contrary to the satisfactory formation of the cyclized compounds **22** having the 6,7,8,9-tetrahydrobenz[*g*]-indole ring system from the dihydro derivative **21**, acid treatment of vinyl compounds **20** gave a rather disappointing result Treatment of **20a** or **20b** with a number of protonic and Lewis acids such as trifluoroacetic acid, trifluoromethanesulfonic acid, tetrafluoroboric acid-diethyl ether complex, concentrated sulfuric acid, boron trichloride, magnesium bromide diethyl etherate, aluminium trichloride, tin(IV) chloride, titanium(IV) chloride, and antimony trichloride gave no definite product, or the recovery of **20** Boron trifluoride etherate was the only reagent which gave a positive result (Table 2), producing the desired compounds **30** and **31** in low yields It is significant that the high selectivity to yield only **30a** or **31b**, bearing the trans relationship between vinyl and isopropyl groups, was done by using 1,2-dichloroethane as a solvent. The rest of the product obtained

in a major amount was an inseparable complex mixture of various type of isomers originating from the acid-catalyzed cyclization reaction of the terpenic side chain So we decided to carry out the six-membered ring cyclization at the final stage of the synthesis by knowing Koshimizu and co-workers' successful conversion of blastmycetin D into olivoretin A [4,17]

25-Methylteleocidins A-1 (**35a A**) and A-2 (**35b A**) were prepared from **20a** and **20b** by way of **32a** and **32b**, **33a** and **33b**, and **34a** and **34b**, according to our established procedure (Chart 3) [1] During introduction of the side chain at the C-3 position of **20a** and **20b**, formation of the by-products **37a** and **37b**, **38a** and **38b**, and



	R³	R⁴		R³	R⁴
35a A	CH_2OH	H	**36a A**	H	CH_2OH
35a B	H	CH_2OH	**36a B**	CH_2OH	H
35b A	CH_2OH	H	**36b A**	H	CH_2OH
35b B	H	CH_2OH	**36b B**	CH_2OH	H
40a	CH_2OAc	H	**41a**	H	CH_2OAc
40b	CH_2OAc	H	**41b**	H	CH_2OAc

	R	R³	R⁴		R	R³	R⁴
42a	Ac	Me	i-Pr	**43a**	Ac	Me	i-Pr
42b	Ac	i-Pr	Me	**43b**	Ac	i-Pr	Me
4	H	Me	i-Pr	**44a** (= ent-3)	H	Me	i-Pr
3	H	i-Pr	Me	**44b** (= ent-4)	H	i-Pr	Me

Chart 3

39a and **39b** was unavoidable as observed in the former cases [1] In view of the poor yield at the cyclization step to dihydroteleocidin B-4 (**9**), diethylphosphoryl cyanide (DEPC)[18] was used for the lactam ring formation to yield **35a A + 36a A** (*ca* 8·1) (33%) and **35a B + 36a B** (28%) from **34a**, and **35b A + 36b A** (*ca* 8 1) (32%) and **35b B + 36b B** (28%) from **34b** The undesired compounds **36a A** and **36b A** were contaminated in 25-methylteleocidins A-1 (**35a A**) and A-2 (**35b A**) due to partial racemization of the L-valine portion during alkaline hydrolysis [1] To protect the hydroxyl group, **35a A + 36a A** and **35b A + 36b A** were acetylated with acetic anhydride in pyridine to get **40a + 41a** and **40b + 41b** in quantitative and 97% yields, and these were subjected to the intramolecular Friedel-Crafts type of cyclization catalyzed with boron trifluoride etherate in 1,2-dichloroethane Compared with the preliminary reaction on **20**, a little improvement of yields was observed here, and the desired compounds **42a + 43a** and **42b + 43b** were obtained in 25% and 24% yields, respectively The acetyl group of **42a + 43a** and **42b + 43b** was removed by alkaline hydrolysis and the resulting mixtures of alcohols were separated by HPLC to afford teleocidin B-4 (**4**) and the enantiomer of teleocidin B-3 (**44a**) in 72% and 7% yields, as well as teleocidin B-3 (**3**) and the enantiomer of teleocidin B-4 (**44b**) in 70 5% and 9% yields The synthetic teleocidins B-3 (**3**) and B-4 (**4**) proved to be identical with the natural specimens by comparing the mp, MS, IR, ^{1}H NMR and CD spectra as well as their biological activities Structural support of **44a** (= ent-**3**) and **44b** (= ent-**4**) was obtained by the antipodal CD curves, together with the identical MS and ^{1}H NMR spectra in comparison with those of **3** and **4**

EXPERIMENTAL

General Procedures — Details were described in the two preceding papers [19]

3,6,7-Trimethyl-2,6-octadienyl Bromide (14) — To a suspension of 50% NaH (5 7 g, 0 12 mol) in dry benzene (60 ml) was added triethyl phosphonoacetate (26 7 g, 0 12 mol) at room temperature to keep the internal temperature below 35°C under Ar atmosphere The mixture was stirred at room temperature for 1 h and then cooled to 0°C 5,6-Dimethyl-5-hepten-2-one (15 0 g, 0 11 mol) in dry benzene (15 ml) was added dropwise and stirring was continued under Ar atmosphere at 0°C — room temperature for 14 h The mixture was poured into NH_4Cl-H_2O, the whole was extracted with Et_2O, and the organic layer was worked up as usual Distillation (95-110°C/4 mmHg) afforded crude **ethyl 3,6,7-trimethyl-2,6-octadienoate (12)** (21 5 g), which contained impurity originating from triethyl phosphonoacetate To a solution of the crude diene-ester **12** (21 5 g) in THF (200 ml) was added portionwise $LiAlH_4$ (3 0 g, 0 08 mol) at 0°C and the mixture was stirred at that temperature for 30 min It was quenched with sat Rochell salt-H_2O, the whole was extracted with Et_2O, and the organic layer was worked up as usual Distillation gave **3,6,7-trimethyl-2,6-octadien-1-ol (13)**, bp 110-116°C/8 mmHg (10 1 g, 56%) as colorless oil IR (film) cm^{-1} 3350, 1667 ^{1}H NMR (90 MHz) δ 4 15 (2H, d, J=7 Hz), 5 42 (1H, t, J=7 Hz) To a cooled solution (0°C) of the above alcohol **13** (15 9 g, 0 095 mol) and Ph_3P (26 0 g, 0 10 mol) in CH_3CN (100 ml) was added portionwise CBr_4 (32 9 g, 0 10 mol), and the solution was stirred at 0°C for 3 h It was extracted with n-hexane and the hexane solution was rinsed several times with a small amount of CH_3CN to remove $CHBr_3$ completely Evaporation of hexane and purification by distillation gave the bromide **14**, bp 86-99°C/4 mmHg (11 1 g, 51%) as colorless oil IR (film) cm^{-1} 1658 ^{1}H NMR (90 MHz) δ 1 66 (9H, s), 1 75 (3H, s), 2 00-2 20 (4H, m), 4 00 (2H, d, J=9 Hz), 5 52 (1H, t, J=9 Hz)

Methyl *N*-[4-Hydroxy-4-(2-pyrrolyl)-5,8,9-trimethyl-5-vinyl-8-decenoyl]-*N*-methyl-L-valinate (16) — In a similar manner as reported previously,[19] L-valine derivative **15** (198 mg, 0 44 mmol) was treated with the above bromide **14** (412 mg, 1 78 mmol) and Mg (85 mg, 3 50 mmol) in THF (8 ml) at 0°C for 3 h to give **16** (118 mg) and *N*-tosylate of **16** (32 mg) The latter was reduced with Mg (29 mg) in MeOH (2 ml) to afford the additional **16** (19 mg), totaling 137 mg (70%) of **16**, colorless syrup MS m/z 428 (M^+–H_2O) IR ($CHCl_3$) cm^{-1} 1735, 1618 ^{1}H NMR (90 MHz) δ 2 80 and 2 83 (3H, s each), 3 62 and 3 66 (3H, s each), 3 80 and 4 90 (1H, d each, J=10 5 Hz), 4 21 (1H, s, OH), 5 04 (1H, d, J=18 Hz), 5 33 (1H, d, J=12 Hz), 6 04 (1H, dd, J=18, 12 Hz), 6 05-6 23 (1H, m), 6 56-6 72 (1H, m), 8 81 (1H, br s)

Methyl *N*-Methyl-*N*-[4-(2-pyrrolyl)-5,8,9-trimethyl-5-vinyl-3,8-decadienoyl]-L-valinate (17) — In a

similar manner as reported previously,[19] the above compound **16** (132 mg, 0 30 mmol) was dehydrated with p-TsOH H_2O (10 mg, 0 05 mmol) in refluxing benzene (5 ml) for 2 min to afford **17** (114 mg, 90%) as colorless syrup HRMS Calcd for $C_{26}H_{40}N_2O_3$ 428 3039 Found. 428.3049. IR ($CHCl_3$) cm^{-1} 1738, 1625. ^1H NMR (90 MHz) δ 0 82, 0.84 and 1 00 (6H, d each, J=7 Hz), 1 21 (3H, s), 1.51 (6H, s), 1 57 (3H, s), 2 87 and 2.91 (3H, s each), 3 04-3 25 (2H, m), 3 70 (3H, s), 3 92 and 4 92 (1H, d each, J=10 5 Hz), 5.67 (1H, t, J=7 5 Hz), 5 95-6 21 (2H, m), 6 57-6 76 (1H, m), 9 50 and 9 54 (1H, br s each)

Methyl *N*-Methyl-*N*-[4-(2-pyrrolyl)-5,8,9-trimethyl-5-vinyl-3,8-decadienthioyl]-L-valinate (18) — In a similar manner as reported previously,[19] the above amide **17** (61 5 mg, 0 14 mmol) was heated with Lawesson's reagent (58 mg, 0 14 mmol) in THF (3 ml) at 85°C for 1 h to afford **18** (47 mg, 74%) as colorless syrup, accompanied by the recovery of **17** (3 mg, 5%) HRMS Calcd for $C_{26}H_{40}N_2O_2S$ 444 2810 Found· 444 2812 IR ($CHCl_3$) cm^{-1} 1738 ^1H NMR (90 MHz) δ 0 73, 0 83, 0 84 and 1 08 (6H, d each, J=7 Hz), 1 53 (6H, s), 1 58 (3H, s), 3 05 and 3 31 (3H, s each), 3 44-3 63 (2H, m), 3 67 and 3 71 (3H, s each), 4 27 and 6 30 (1H, d each, J=10 5 Hz), 5 05 (1H, dd, J=18, 1 Hz), 5 10 (1H, dd, J=11, 1 Hz), 5 70 and 5 73 (1H, t each, J=7 Hz), 5 90-6 21 (2H, m), 6 57-6.75 (1H, m), 8 92 (1H, br s)

Methyl *N*-Methyl-*N*-[7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]-4-indolyl]-L-valinate (20a) and Methyl *N*-Methyl-*N*-[7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]-4-indolyl]-L-valinate (20b) — In a similar manner as reported previously,[19] the thioamide compound **18** (48 mg, 0 11 mmol) was treated with MeI (0 5 ml, 8 03 mmol) in DMF (1 ml) at 19°C for 4 h to yield **20a** (17 mg, 38%) and **20b** (11 mg, 25%) together with **4-(methylthio)-7-(3,6,7-trimethyl-1,6-octadien-3-yl)indole (19)** (10 mg, 30%) **20a** Colorless syrup HRMS Calcd for $C_{26}H_{38}N_2O_2$ 410 2933 Found 410 2936 $[\alpha]_D^{24}$ -140 9° (c 1 248, CH_2Cl_2) IR ($CHCl_3$) cm^{-1} 1728. ^1H NMR (90 MHz) δ 0 93 (3H, d, J=7 Hz), 1 10 (3H, d, J=7 Hz), 1 40 (3H, s), 1 46 (3H, s), 1 56 (6H, s), 2 37 (1H, dqq, J=10 5, 7, 7 Hz), 2 99 (3H, s), 3 57 (3H, s), 4 09 (1H, d, J=10 5 Hz), 5 24 (1H, dd, J=10 5, 1 Hz), 5 26 (1H, dd, J=18, 1 Hz), 6 26 (1H, dd, J=18, 10 5 Hz), 6 60 (1H, d, J=8 Hz), 6 68 (1H, dd, J=3, 2 Hz), 7 00 (1H, d, J=8 Hz), 7 06 (1H, dd, J=3, 3 Hz), 8 62 (1H, br s) **20b** Colorless scales, mp 68-70°C (MeOH-H_2O) Anal Calcd for $C_{26}H_{38}N_2O_2$ C, 76 05, H, 9 32, N, 6 82 Found C, 75 96, H, 9 32, N, 6 80 $[\alpha]_D^{22}$ -180 1° (c 0 784, CH_2Cl_2) IR (KBr) cm^{-1} 1718 ^1H NMR (90 MHz) δ 0 91 (3H, d, J=7 Hz), 1 01 (3H, d, J=7 Hz), 1 38 (3H, s), 1 44 (3H, s), 1 55 (6H, s), 2 37 (1H, dqq, J=10 5, 7, 7 Hz), 3 03 (3H, s), 3 33 (3H, s), 4 10 (1H, d, J=10 5 Hz), 5 24 (1H, dd, J=10 5, 1 Hz), 5 25 (1H, dd, J=18, 1 Hz), 6 24 (1H, dd, J=18, 10 5 Hz), 6 56 (1H, d, J=8 Hz), 6 70 (1H, dd, J=3, 2 Hz), 7 00 (1H, d, J=8 Hz), 7 04 (1H, dd, J=3, 3 Hz), 8 59 (1H, br s) **19** Colorless syrup HRMS Calcd for $C_{20}H_{27}NS$ 313 1864 Found 313 1868 ^1H NMR (90 MHz) δ 1 42 (3H, s) 1 48 (3H, s), 1 57 (6H, s), 2 54 (3H, s), 5 26 (1H, dd, J=10 5, 1 Hz), 5 26 (1H, dd, J=18, 1 Hz), 6 24 (1H, dd, J=18, 10 5 Hz), 6 62 (1H, dd, J=3, 2 Hz), 6 98 (1H, d, J=8 Hz), 7 11 (1H, d, J=8 Hz), 7 13 (1H, dd, J=3, 3 Hz), 8 65 (1H, br s)

Methyl *N*-Methyl-*N*-[7-[(*S*)-3,6,7-trimethyl-6-octen-3-yl]-4-indolyl]-L-valinate (21) — A solution of **20a** (324 mg, 0 79 mmol) in MeOH (25 ml) was stirred in the presence of PtO_2 (45 mg) under an ordinary atmosphere of H_2 at 25°C for 3 h The mixture was filtered on a celite bed, the celite was washed with CH_2Cl_2 and the combined organic layer was evaporated *in vacuo* The residue was purified by PTLC [hexane-EtOAc (20 1)] to give **21** (300 mg, 92%) as colorless syrup HRMS Calcd for $C_{26}H_{40}N_2O_2$ 412 3089 Found 412 3106 IR ($CHCl_3$) cm^{-1} 1725 ^1H NMR (90 MHz) δ 0 66 (3H, t, J=7 Hz), 0 92 (3H, d, J=7 Hz), 1 08 (3H, d, J=7 Hz), 1 30 (3H, s), 1 42 (3H, s), 1 46 (3H, s), 1 54 (3H, s), 2 38 (1H, dqq, J=10 5, 7, 7 Hz), 2 99 (3H, s), 3 56 (3H, s), 4 06 (1H, d, J=10 5 Hz), 6 54 (1H, d, J=8 Hz), 6 69 (1H, dd, J=3, 2 Hz), 6 88 (1H, d, J=8 Hz), 7 07 (1H, dd, J=3, 3 Hz), 8 32 (1H, br s)

Methyl *N*-[(*6R, 9S*)-6,9-Dimethyl-9-ethyl-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indol-4-yl]-*N*-methyl-L-valinate (22a) and Methyl *N*-[(*6S, 9S*)-6,9-Dimethyl-9-ethyl-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indol-4-yl]-*N*-methyl-L-valinate (22b) — To a solution of **21** (24 mg, 0 06 mmol) in CH_2Cl_2 (7 5 ml) was added 95% H_2SO_4 (0 1 ml, 30 equiv) at 0°C and the mixture was stirred at 0°C for 4 h Sat $NaHCO_3$-H_2O was added, the whole was extracted with CH_2Cl_2 and worked up as usual The residue was separated by PTLC [hexane-EtOAc (15 1)] to afford **23a** + **23b** (5 5 mg) and **22a** + **22b** (12 5 mg). The former mixture was further separated by PTLC [hexane-EtOAc (30·1)] to give **Methyl *N*-[(*4ξ, 7S,*)-4,7-Dimethyl-7-ethyl-4-(1-methylethyl)-4,5,6,7-tetrahydro-azepino[*3,2,1-hi*]indol-10-yl]-*N*-methyl-L-valinates (23a)** (3 5

mg, 15%) and **(23b)** (2 mg, 8%) The latter mixture was further separated by PTLC [hexane-DME (49 1)] and purified by recrystallization to furnish **22a** (9 5 mg, 40%) and **22b** (2.5 mg, 10%). **22a** Colorless needles, mp 134-136°C (MeOH-H_2O) Anal. Calcd for $C_{26}H_{40}N_2O_2$ C, 75 68, H, 9 77, N, 6 79. Found C, 75.65, H, 9 60, N, 6 57 HRMS Calcd for $C_{26}H_{40}N_2O_2$ 412.3089 Found 412 3093. $[\alpha]_D^{24}$ -102 0° (c 0 495, CH_2Cl_2). IR (KBr) cm^{-1} 1720 ^1H NMR (90 MHz) δ 0 52 (3H, d, J=7 Hz), 0 54 (3H, t, J=7 Hz), 0 84 (3H, d, J=7 Hz), 0.99 (3H, d, J=7 Hz), 1 11 (3H, d, J=7 Hz), 1 33 (3H, s), 1.40 (3H, s), 2 97 (3H, s), 3 54 (3H, s), 4.01 (1H, d, J=10 5 Hz), 6 57 (1H, s), 6 64 (1H, dd, J=3, 2 Hz), 7.03 (1H, dd, J=3, 3 Hz), 8 28 (1H, br s) **22b**: Colorless prisms, mp 195-196°C (MeOH) Anal Calcd for $C_{26}H_{40}N_2O_2$ C, 75 68, H, 9 77; N, 6 79 Found. C, 75 42; H, 9 59; N, 6 71 HRMS Calcd for $C_{26}H_{40}N_2O_2$ 412 3089 Found· 412 3086 $[\alpha]_D^{24}$ -178 6° (c 0 500, CH_2Cl_2) IR (KBr) cm^{-1} 1735 ^1H NMR (90 MHz) δ. 0 58 (3H, d, J=7 Hz), 0 86 (3H, t, J=7 Hz), 0 95 (6H, d, J=7 Hz), 1 13 (3H, d, J=7 Hz), 1 28 (3H, s), 1 41 (3H, s), 2 94 (3H, s), 3 57 (3H, s), 3 98 (1H, d, J=10.5 Hz), 6 50-6 67 (1H, m), 6.58 (1H, s), 7 05 (1H, dd, J=3, 3 Hz), 8 21 (1H, br s) **23a** Colorless prisms, mp 100-101°C (CH_2Cl_2-MeOH) Anal Calcd for $C_{26}H_{40}N_2O_2$ C, 75 68, H, 9 77, N, 6 79 Found C, 75 75, H, 9 80, N, 6 83 IR (KBr) cm^{-1} 1740, 1730 ^1H NMR (90 MHz) δ 0 28 (3H, d, J=7 Hz), 0 43 (3H, t, J=7 Hz), 0 71 (3H, d, J=7 Hz), 0 83 (3H, d, J=7 Hz), 1 06 (3H, d, J=7 Hz), 1 44 (3H, s), 1 65 (3H, s), 2.97 (3H, s), 3 56 (3H, s), 3 98 (1H, d, J=10 5 Hz), 6.59 (1H, d, J=8 Hz), 6.67 (1H, d, J=3 Hz), 6 85 (1H, d, J=8 Hz), 7 16 (1H, d, J=3 Hz) **23b**· Colorless syrup HRMS Calcd for $C_{26}H_{40}N_2O_2$ 412 3089 Found 412 3078 IR ($CHCl_3$) cm^{-1} 1710 ^1H NMR (90 MHz) δ 0 40 (3H, d, J=7 Hz), 0 81 (3H, d, J=7 Hz), 0 91 (3H, d, J=7 Hz), 0 95 (3H, t, J=7 Hz), 1 10 (3H, d, J=7 Hz), 1 18 (3H, s), 1 61 (3H, s), 3 00 (3H, s), 3 62 (3H, s), 3 82 (1H, d, J=10 5 Hz), 6 64 (1H, d, J=8 Hz), 6 67 (1H, d, J=3 Hz), 6.96 (1H, d, J=8 Hz), 7 11 (1H, d, J=3 Hz)

Ethyl (*6R*, *9S*)-6,9-Dimethyl-9-ethyl-α-(hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indole-3-propanoate (24) — In the same manner as in the preceding paper,[1] **22a** (100 mg, 0 24 mmol) was converted into **24** (75 mg, 57%), **25** (4 mg, 2 5%) and **26** (14 mg, 9%), accompanied by the recovery of **22a** (11 mg, 11%) **24** Colorless syrup MS m/z 541 (M^+) IR ($CHCl_3$) cm^{-1} 1725 ^1H NMR (90 MHz) δ 0 43 (3H, d, J=7 Hz), 0 50 (3H, t, J=7 Hz), 0 91 (3H, d, J=7 Hz), 0 94 (3H, d, J=7 Hz), 1 15 (3H, d, J=7 Hz), 1 20 (3H, t, J=7 Hz), 1 30 (3H, s), 1 37 (3H, s), 2 90 (3H, s), 3 47 (3H, s), 3 62 (1H, d, J=10 Hz), 4 22 (2H, q, J=7 Hz), 4 32 (1H, d, J=15 Hz), 4 54 (1H, d, J=15 Hz), 6 69 (1H, d, J=3 Hz), 6 84 (1H, s), 8 06 (1H, br s), 10 23 (1H, br s, OH) **Diethyl (*6R*, *9S*)-α, α'-Bis(hydroxyimino)-6,9-dimethyl-9-ethyl-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indole-2,3-bispropanoate (25)** Colorless film IR ($CHCl_3$) cm^{-1}. 1732 ^1H NMR (90 MHz) δ 2 88 (3H, s), 3 43 (3H, s), 3 51 (1H, d, J=10 5 Hz), 3 97 (2H, q, J=7 Hz), 4 00 (2H, s), 4 29 (2H, q, J=7 Hz), 4 54 (2H, s), 6 78 (1H, s), 8 93 (1H, br s), 10 08 (2H, br s, OH) **Ethyl (*1S*, *4R*)-1,4-Dimethyl-8-(ethoxycarbonyl)-1-ethyl-1,2,3,4,10a,11-hexahydro-α-(hydroxyimino)-6-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]benz[*g*][*1,2*]oxazino[*6,5-b*]indole-6b(7H)-propanoate (26)** Colorless film MS m/z 670 (M^+) IR ($CHCl_3$) cm^{-1} 1732, 1725 ^1H NMR (90 MHz) δ 2 67 and 2 80 (3H, s each), 3 55 (3H, s), 4 71-4 98 (1H, m, NH), 5 13-5 44 (1H, m), 6 48-6 65 (1H, m), 9 43 (1H, br s, OH)

Ethyl (α*S*, *6R*, *9S*)-α-Amino-6,9-dimethyl-9-ethyl-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]-methylamino]-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indole-3-propanoate (27a) and Ethyl (α*R*, *6R*, *9S*)-α-Amino-6,9-dimethyl-9-ethyl-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indole-3-propanoate (27b) — According to the same procedure as in the preceding paper,[1] **24** (74 mg, 0 14 mmol) was reduced to **27a** (29 mg, 40%) and **27b** (28 5 mg, 39 5%) after separation by PTLC [hexane-EtOAc (1 4)] **27a** Colorless syrup MS m/z 527 (M^+) IR ($CHCl_3$) cm^{-1} 1730 ^1H NMR (90 MHz) δ 0 40 (3H, d, J=7 Hz), 0 50 (3H, t, J=7 Hz), 0 92 (3H, d, J=7 Hz), 0 96 (3H, d, J=7 Hz), 1 13 (3H, d, J=7 Hz), 1 22 (3H, t, J=7 Hz), 1 31 (3H, s), 1 38 (3H, s), 2 83 (3H, s), 3 38 (3H, s), 3 58 (1H, d, J=8 Hz), 4 13 (2H, q, J=7 Hz), 6 77 (1H, s), 6 93 (1H, d, J=2 Hz), 8 20 (1H, br s) **27b** Colorless syrup MS m/z 527 (M^+) IR ($CHCl_3$) cm^{-1} 1730 ^1H NMR (90 MHz) δ. 0 40 (3H, d, J=7 Hz), 0 50 (3H, t, J=7 Hz), 0.94 (6H, d, J=7 Hz), 1 06 (3H, t, J=7 Hz), 1 13 (3H, d, J=7 Hz), 1 30 (3H, s), 1 38 (3H, s), 2 82 (3H, s), 3 37 (3H, s), 3 60 (1H, d, J=8 Hz), 4 04 (2H, q, J=7 Hz), 6 77 (1H, s), 6 92 (1H, d, J=2 Hz), 8 20 (1H, br s)

Dihydroteleocidin B-4 (Dihydroteleocidin B) (9) — The amino-diester **27a** (13 mg, 0 025 mmol) was

reduced to the amino-alcohol **28a** with $NaBH_4$ (19 mg, 0 50 mmol) and LiCl (21 mg, 0 50 mmol) in EtOH-THF (4 3) (2.8 ml) at room temperature In the same manner as in the teleocidin A synthesis,[1] **28a** was converted into dihydroteleocidin B-4 (**9**) (2 mg, 18% form **27a**) as colorless prisms, mp 154-156°C and 232-235°C (decomp) (acetone-H_2O) [lit [11a] mp 154-156°C and 223-224 5°C (decomp), lit [11c] mp 168°C and 233-235°C (decomp)] No mp depression was observed when admixed with the authentic dihydroteleocidin B-4 HRMS Calcd for $C_{28}H_{43}N_3O_2$ 453.3355 Found 453.3358 CD (c 2 23 × 10^{-5}, MeOH, 21°C) $[\theta]_{327}$ 0, $[\theta]_{310}$ +4400, $[\theta]_{297}$ 0, $[\theta]_{262}$ -13000, $[\theta]_{240}$ -12400, $[\theta]_{225}$ -22600, $[\theta]_{215}$ 0 IR (KBr) cm^{-1} 1632 ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ. (major conformer) 0 50 (3H, d, J=7 Hz), 0 60 (3H, t, J=7 Hz), 0 70 (3H, d, J=7 Hz), 0 92 (3H, d, J=7 Hz), 0 99 (3H, d, J=7 Hz), 1 32 (3H, s), 1 39 (3H, s), 2 63 (1H, dqq, J=10 5, 7, 7 Hz), 2 91 (3H, s), 2 94 (1H, dd, J=16, 4 Hz), 3 17 (1H, br d, J=16 Hz), 3 51 (1H, dd, J=11, 9 Hz), 3 74 (1H, dd, J=11, 4 Hz), 4 28-4 37 (1H, m), 4 31 (1H, d, J=10 5 Hz), 6 53 (1H, s), 6.84 (1H, s), 8 14 (1H, br s), (minor conformer) 0 53 (3H, d, J=7 Hz), 0 60 (3H, t, J=7 Hz), 0 94 (3H, d, J=7 Hz), 1.00 (3H, d, J=7 Hz), 1 25 (3H, d, J=7 Hz), 1 35 (3H, s), 1 40 (3H, s), 2 37 (1H, dqq, J=10 5, 7, 7 Hz), 2.69 (1H, d, J=10 5 Hz), 2 73 (3H, s), 2 77 (1H, dd, J=14, 1 Hz), 3 05 (1H, dd, J=14, 5 Hz), 3 44 (1H, dd, J=11, 8 Hz), 3 53 (1H, dd, J=11, 6 Hz), 4 39-4 46 (1H, m), 6 92 (1H, d, J=2 Hz), 7 00 (1H, s), 8 30 (1H, br s)

9-Epidihydroteleocidin B-4 (29) — In the same procedureas above, **29** was obtained in 13% yield from **27b** by way of the amino-alcohol **28b** **29** Colorless prisms, mp 259-261°C (acetone-H_2O) HRMS Calcd for $C_{28}H_{43}N_3O_2$ 453 3355 Found 453 3349 IR (KBr) cm^{-1} 1662 ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ (major conformer) 0 53 (3H, d, J=7 Hz), 0 57 (3H, t, J=7 Hz), 0 76 (3H, d, J=7 Hz), 0 83 (3H, d, J=7 Hz), 1 03 (3H, d, J=7 Hz), 1 26 (3H, s), 1 38 (3H, s), 2 65 (1H, dqq, J=10 5, 7, 7 Hz), 2 89 (1H, br d, J=15 Hz), 3 08 (3H, s), 3 25 (1H, br d, J=15 Hz), 3 88 (1H, d, J=10 5 Hz), (minor conformer) 0 51 (3H, d, J=7 Hz), 0 59 (3H, t, J=7 Hz), 0 95 (3H, d, J=7 Hz), 0.99 (3H, d, J=7 Hz), 1 24 (3H, d, J=7 Hz), 2 34 (1H, dqq, J=10 5, 7, 7 Hz), 2 70 (3H, s), 2 76 (1H, d, J=13 Hz), 2 91 (1H, d, J=10 5 Hz), 3 02 (1H, d, J=13 Hz)

BF_3 OEt_2-Catalyzed Intramolecular Cyclization of 20b — To a solution of **20b** (99 mg, 0 24 mmol) in 1,2-dichloroethane (12 ml) was added BF_3 OEt_2 (0 5 ml, 4 07 mmol) at 0°C, and the mixture was stirred at 0°C for 2 5 h and then at room temperature for 4 5 h Sat $NaHCO_3$-H_2O was added, the whole was extracted with CH_2Cl_2 and worked up as usual to give a residue (103 5 mg) This was separated by PTLC [hexane-EtOAc (34 1)] and purified by recrystallization to afford **methyl *N*-[(*6S*, *9S*)-6,9-dimethyl-9-vinyl-6-(1-methylethyl)-6,7,8,9-tetrahydro-1H-benz[*g*]indol-4-yl]-*N*-methyl-L-valinate (31b)** (14 mg, 14%), mp 135-137°C (MeOH-H_2O), as colorless prisms Anal Calcd for $C_{26}H_{38}N_2O_2$ C, 76 05, H, 9 32, N, 6 82 Found C, 76 12, H, 9 39, N, 6 87 IR (KBr) cm^{-1} 1725 ^1H NMR (400 MHz) δ 0 57 (3H, d, J=7 Hz), 0 97 (3H, d, J=7 Hz), 1 00 (3H, d, J=7 Hz), 1 14 (3H, d, J=7 Hz), 1 32 (3H, s), 1 38-1 52 (2H, m), 1 49 (3H, s), 1 85-1 97 (2H, m), 2 24 (1H, qq, J=7, 7 Hz), 2 37 (1H, dqq, J=11, 7, 7 Hz), 2 94 (3H, s), 3 59 (3H, s), 4 02 (1H, d, J=11 Hz), 5 23 (1H, dd, J=11, 1 Hz), 5 39 (1H, dd, J=18, 1 Hz), 6 18 (1H, dd, J=18, 11 Hz), 6 56 (1H, dd, J=3, 2 Hz), 6 58 (1H, s), 7 01 (1H, dd, J=3, 3 Hz), 8 64 (1H, br s)

Reaction of 20a and 20b with Ethyl 3-Bromo-2-hydroxyiminopropanoate — In the same manner as in the preceding paper,[1] **20a** (97 mg, 0 24 mmol) in CH_2Cl_2 (6 ml) was stirred with ethyl 3-bromo-2-hydroxyiminopropanoate (50 mg, 0 24 mmol) and Na_2CO_3 (50 mg, 0 47 mmol) at 20°C for 16 5 h to afford **32a** (72 5 mg, 57%), **37a** (28 mg, 22%), **38a** (11 mg, 7%) and **39a** (10 5 mg, 7%) Similarly **20b** (103 mg, 0 25 mmol) was converted into **32b** (83 mg, 61%), **37b** (22 mg, 16%), **38b** (8 mg, 5%) and **39b** (8 mg, 5%) **Ethyl α-(Hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-3-propanoate (32a)** Colorless syrup MS m/z 539 (M^+) IR ($CHCl_3$) cm^{-1} 1730 ^1H NMR (90 MHz) δ 0 93 (3H, d, J=7 Hz), 1 13 (3H, d, J=7 Hz), 1 21 (3H, t, J=7 5 Hz), 1 36 (3H, s), 1 45 (3H, s), 1 56 (6H, s), 2 92 (3H, s), 3 53 (3H, s), 3 66 (1H, d, J=9 Hz), 4 20 (2H, q, J=7 5 Hz), 4 35 (1H, d, J=15 Hz), 4 57 (1H, d, J=15 Hz), 5 20 (1H, dd, J=10 5, 1 Hz), 5 22 (1H, dd, J=18, 1 Hz), 6 18 (1H, dd, J=18, 10 5 Hz), 6 69 (1H, d, J=3 Hz), 6 83 (1H, d, J=8 Hz), 6 97 (1H, d, J=8 Hz), 8 40 (1H, br s), 10 26 (1H, br s, OH) **Ethyl α-(Hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-5-propanoate (37a)** Colorless syrup MS m/z 539 (M^+) IR ($CHCl_3$) cm^{-1} 1730, 1725 ^1H NMR (90 MHz) δ 0 92 (3H, d, J=7 Hz), 1 20 (3H, t, J=7 5 Hz), 1 22 (3H, d, J=7 Hz), 1 30 (3H, s), 1 43 (3H, s), 1 54 (6H, s), 3 07 (3H, s), 3 20-3 61 (1H, m), 3 43 (3H, s), 4 15 (2H, q, J=7 5 Hz), 4 41 (1H, d, J=15 Hz), 5 20

(1H, dd, J=10 5, 1.5 Hz), 5.21 (1H, dd, J=18, 1 5 Hz), 6 21 (1H, dd, J=18, 10 5 Hz), 6 44 (1H, dd, J=3, 2 Hz), 6 80 (1H, s), 6.96 (1H, dd, J=3, 3 Hz), 8 47 (1H, br s), 9 75 (1H, br s, OH). **Diethyl α, α'-Bis(hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-3,5-bispropanoate (38a)** Colorless film MS m/z 668 (M^+) IR ($CHCl_3$) cm^{-1} 1725 ^1H NMR (90 MHz) δ. 0 70 (3H, d, J=7 Hz), 0 95 (3H, d, J=7 Hz), 1.25 (6H, t, J=7 5 Hz), 1 26 (6H, s), 1 38 (3H, s), 1 54 (3H, s), 2.97 (3H, s), 3 76 (3H, s), 4 11 (2H, q, J=7 5 Hz), 4 12 (2H, q, J=7 5 Hz), 4.45 (1H, d, J=15 Hz), 4 80 (1H, d, J=15 Hz), 5 17 (1H, d, J=10 5 Hz), 5 20 (1H, d, J=18 Hz), 6 17 (1H, dd, J=18, 10.5 Hz), 6 51-6 71 (1H, m), 6 58 (1H, s), 8 26 (1H, br s), 9 27 (2H, br s, OH) **Ethyl 9,9a-Dihydro-3-(ethoxycarbonyl)-α-(hydroxyimino)-5-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]-1,2-oxazino[*6,5-b*]indole-4a(4H)-propanoate (39a)**. Colorless film MS m/z 668 (M^+) IR ($CHCl_3$) cm^{-1} 1730 ^1H NMR (90 MHz) δ 0.93 (3H, d, J=7 Hz), 2 69 and 2 82 (3H, s each), 3 53 (3H, s), 5 99 (1H, dd, J=18, 10 5 Hz), 6 51 and 6 53 (1H, d each, J=8 Hz), 6 95 (1H, d, J=8 Hz), 9 18 (1H, br s, OH). **Ethyl α-(Hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-3-propanoate (32b)** Colorless syrup MS m/z 539 (M^+) IR ($CHCl_3$) cm^{-1} 1723 ^1H NMR (90 MHz) δ 0 93 (3H, d, J=7 Hz), 1 09 (3H, d, J=7 Hz), 1 19 (3H, t, J=7 5 Hz), 1 37 (3H, s), 1 45 (3H, s), 1 55 (6H, s), 2 89 (3H, s), 3 58 (3H, s), 3 67 (1H, d, J=8 Hz), 4 21 (2H, q, J=7 Hz), 4 36 (1H, d, J=15 Hz), 4 54 (1H, d, J=15 Hz), 5 21 (1H, d, J=10 5 Hz), 5 22 (1H, d, J=17 5 Hz), 6 18 (1H, dd, J=17 5, 10 5 Hz), 6 69 (1H, br d, J=1 5 Hz), 6 85 (1H, d, J=7 5 Hz), 6 98 (1H, d, J=7 5 Hz), 8 40 (1H, br s), 10 20 (1H, br s, OH) **Ethyl α-(Hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-5-propanoate (37b)** Colorless syrup MS m/z 539 (M^+) IR ($CHCl_3$) cm^{-1} 1718 ^1H NMR (90 MHz) δ 0 87 (3H, d, J=7 Hz), 1 20 (3H, d, J=7 Hz), 1 20 (3H, t, J=7 Hz), 1 28 (3H, s), 1 38 (3H, s), 1 44 (3H, s), 1 52 (3H, s), 3 07 (3H, s), 3 23-3 50 (1H, m), 3 37 (3H, s), 4 10 (1H, d, J=15 Hz), 4 19 (2H, q, J=7 Hz), 4 44 (1H, d, J=15 Hz), 5 19 (1H, d, J=10 5 Hz), 5 21 (1H, d, J=17 5 Hz), 6 19 (1H, dd, J=17 5, 10 5 Hz), 6 44 (1H, dd, J=3, 2 Hz), 6 81 (1H, s), 6 98 (1H, dd, J=3, 3 Hz), 8 46 (1H, br s), 9 71 (1H, br s, OH) **Diethyl α, α'-Bis(hydroxyimino)-4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]indole-3,5-bispropanoate (38b)** Colorless film MS m/z 668 (M^+) IR ($CHCl_3$) cm^{-1} 1722 ^1H NMR (90 MHz) δ· 0 73 (3H, d, J=7 Hz), 0 97 (3H, d, J=7 Hz), 1 40 (3H, s), 1 52 (3H, s), 1 54 (3H, s), 2 94 and 3 00 (3H, s each), 3 55 and 3 76 (3H, s each), 5 18 (1H, d, J=10 5 Hz), 5 20 (1H, d, J=18 Hz), 6 16 (1H, dd, J=18, 10 5 Hz), 6 57 and 6 70 (1H, s each), 6 62 (1H, d, J=3 Hz), 8 26 (1H, br s), 9 26 (2H, br s, OH) **Ethyl 9,9a-Dihydro-3-(ethoxycarbonyl)-α-(hydroxyimino)-5-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]-methylamino]-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]-1,2-oxazino[*6,5-b*]indole-4a(4H)-propanoate (39b)** Colorless film MS m/z 668 (M^+) IR ($CHCl_3$) cm^{-1} 1720 ^1H NMR (90 MHz) δ 0 94 and 0 96 (3H, d each, J=7 Hz), 2 68 and 2 76 (3H, s each), 3 59 and 3 64 (3H, s each), 5 91 and 5 95 (1H, dd each, J=18, 10 5 Hz), 6 48 and 6 52 (1H, d each, J=7 5 Hz), 6 96 (1H, d, J=7 5 Hz), 9 33 (1H, br s, OH)

Reduction of 32a and 32b with Al-Hg — According to the procedure reported in the preceding paper,[1] the oxime derivative **32a** (55 mg, 0 10 mmol) was reduced with Al-Hg [prepared from Al (83 mg, 3 07 mmol)] in THF-H_2O (9 1) (6 ml) under Ar atmosphere at 40°C for 1 h to afford **33a** (46 5 mg, 87%) A similar treatment of **32b** (65 mg, 0 12 mmol) gave **33b** (57 mg, 90%) **Ethyl 4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]tryptophanate (33a)** Colorless syrup MS m/z 525 (M^+) IR ($CHCl_3$) cm^{-1} 1728 ^1H NMR (90 MHz) of two diastereoisomers (*ca* 1 1) δ 0 94 (3H, d, J=7 Hz), 1 14 (3H, t, J=7 5 Hz), 1 16 and 1 20 (3H, d each, J=7 Hz), 1 36 (3H, s), 1 47 (3H, s), 2 87 (3H, s), 2 98 (1H, dd, J=14, 9 Hz), 3 43 (3H, s), 4 08 and 4 15 (2H, q each, J=7 5 Hz), 5 22 (1H, d, J=10 5 Hz), 5 22 (1H, d, J=18 Hz), 6 22 (1H, dd, J=18, 10 5 Hz), 6 80 (1H, d, J=8 Hz), 6 95 (1H, d, J=8 Hz), 8 50 (1H, br s) **Ethyl 4-[[(*S*)-1-(methoxycarbonyl)-2-methylpropyl]methylamino]-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]tryptophanate (33b)** Colorless syrup MS m/z 525 (M^+) IR ($CHCl_3$) cm^{-1} 1725 ^1H NMR (90 MHz) of two diastereoisomers (*ca* 1 1) δ 0 95 (3H, d, J=7 Hz), 1 08 and 1 10 (3H, d each, J=7 Hz), 1 15 and 1 17 (3H, t each, J=7 Hz), 1 31 (3H, s), 1 35 (3H, s), 1 44 (3H, s), 1 54 (3H, s), 1 70 (2H, s, NH_2), 2 11- 2 54 (1H, m), 2 83 (3H, s), 2 97 (1H, dd, J=15, 9 Hz), 3 45 (3H, s), 3 64 (1H, d, J=7 Hz), 4 09 and 4 15 (2H, q each, J=7 Hz), 5 22 (1H, dd, J=10 5, 1 5 Hz), 5 22 (1H, dd, J=18, 1 5 Hz), 6 18 (1H, dd, J=18, 10 5 Hz), 6 81 (1H, d, J=7 5 Hz), 6 90-

6 98 (1H, br s), 6 96 (1H, d, J=7 5 Hz), 8 50 (1H, br s)

Methyl *N*-[3-(2-Amino-3-hydroxypropyl)-7-[(*R*)-3,6,7-trimethyl-1,6-octadien-3-yl]-4-indolyl]-*N*-methyl-L-valinate (34a) and Methyl *N*-[3-(2-Amino-3-hydroxypropyl)-7-[(*S*)-3,6,7-trimethyl-1,6-octadien-3-yl]-4-indolyl]-*N*-methyl-L-valinate (34b) — In a similar manner as in the preceding paper,[1] reduction of **33a** (46 mg, 0.088 mmol) with $NaBH_4$ (66 mg, 1.75 mmol) was carried out in the presence of LiCl (74 mg, 1 75 mmol) in EtOH-THF (4:3) (6.3 ml) under Ar atmosphere at 20°C for 12 h to give **34a** (33 mg, 78%) Similarly **34b** (27 mg, 84%) was prepared from **33b** (35 mg, 0 067 mmol) **34a**: Colorless syrup MS m/z 483 (M^+) IR ($CHCl_3$) cm^{-1} 1725 ^1H NMR (90 MHz) of two diastereoisomers (*ca* 1 1) δ 0 88 (3H, d, J=7 Hz), 1 10 and 1 13 (3H, d each, J=7 Hz), 1 32 (3H, s), 1 44 (3H, s), 2 71 (3H, s, NH_2 and OH), 2 80 and 2 82 (3H, s each), 3 39 and 3 43 (3H, s each), 5 23 (1H, d, J=10 5 Hz), 5 24 (1H, d, J=18 Hz), 6 20 (1H, dd, J=18, 10 5 Hz), 6 77 (1H, d, J=8 Hz), 6 80-6 97 (1H, m), 6 95 (1H, d, J=8 Hz), 8 50 (1H, br s). **34b** Colorless syrup MS m/z 483 (M^+) IR ($CHCl_3$) cm^{-1} 1727 ^1H NMR (90 MHz) of two diastereoisomers (*ca* 1 1) δ 0 93 (3H, d, J=7 Hz), 1 09 and 1 12 (3H, d each, J=7 Hz), 1 26 (3H, s), 1 33 (3H, s), 1 46 (3H, s), 1 55 (3H, s), 2 36-2 59 (3H, m, NH_2 and OH), 2 81 and 2 83 (3H, s each), 3 44 and 3 46 (3H, s each), 3 68 (1H, d, J=7 Hz), 5 23 (1H, dd, J=18, 1 5 Hz), 5 24 (1H, dd, J=10, 1 5 Hz), 6 19 (1H, dd, J=18, 10 Hz), 6 78 (1H, d, J=8 Hz), 6 88-6 97 (1H, m), 6 95 (1H, d, J=8 Hz), 8 50 (1H, br s)

(*R*)-7-(3,6,7-Trimethyl-1,6-octadien-3-yl)-(–)-indolactam V (25-Methylteleocidin A-1) (35a A) and (*R*)-7-(3,6,7-Trimethyl-1,6-octadien-3-yl)-9-epi-(–)-indolactam V (35a B) — The same procedure using DEPC (diethylphosphoryl cyanide) as in the preceding paper[1] was applied to the amino-alcohol **34a** (45 5 mg, 0 094 mmol) to give **35a A** containing **36a A** (**35a A** **36a A**=*ca* 8 1) (14 mg, 33%) and **35a B** containing **36a B** (10 5 mg, 28%) **35a A** with a contaminant **36a A** Colorless syrup MS m/z 451 (M^+) IR ($CHCl_3$) cm^{-1} 1658 ^1H NMR (400 MHz, $CDCl_3$-D_2O) of **35a A** δ (major conformer) 0 65 (3H, d, J=7 Hz), 0 92 (3H, d, J=7 Hz), 1 47 (3H, s), 1 48 (3H, s), 1 59 (3H, s), 1 60 (3H, s), 2 59 (1H, dqq, J=10 5, 7, 7 Hz), 2 91 (3H, s), 3 02 (1H, dd, J=17 5, 3 Hz), 3 15 (1H, d, J=17 5 Hz), 3 55 (1H, dd, J=11, 8 Hz), 3 73 (1H, dd, J=11, 3 Hz), 4 27-4 38 (1H, m), 4 34 (1H, d, J=10 5 Hz), 5 30 (1H, d, J=11 Hz), 5 31 (1H, d, J=18 Hz), 6 17 (1H, dd, J=18, 11 Hz), 6 48 (1H, d, J=8 Hz), 6 82 (1H, s), 7 00 (1H, d, J=8 Hz), 8 52 (1H, br s), (minor conformer) 0 94 (3H, d, J=7 Hz), 1 25 (3H, d, J=7 Hz), 1 50 (3H, s), 1 58 (3H, s), 2 39 (1H, dqq, J=10 5, 7, 7 Hz), 2 73 (3H, s), 2 81 (1H, dd, J=15, 1 Hz), 3 07 (1H, dd, J=15, 4 Hz), 3 39 (1H, dd, J=11, 7 Hz), 3 46 (1H, dd, J=11, 7 Hz), 4 38-4 47 (1H, m), 5 34 (1H, d, J=11 Hz), 5 35 (1H, d, J=18 Hz), 6 23 (1H, dd, J=18, 11 Hz), 6 95 (1H, s), 7 01 (1H, d, J=8 Hz), 7 11 (1H, d, J=8 Hz), 8 76 (1H, br s) ^1H NMR (400 MHz, $CDCl_3$-D_2O) of **36a A** δ (major conformer) 0 58 (3H, d, J=7 Hz), 2 91 (3H, s), 8 55 (1H, br s), (minor conformer) 2 74 (3H, s) The ratio between **35a A** and **36a A** was estimated from the integrated values of the signals at 0 65 (d) and 0 58 (d) of each major conformer **35a B** with a contaminant **36a B** Colorless syrup MS m/z 451 (M^+) IR ($CHCl_3$) cm^{-1} 1658 ^1H NMR (400 MHz, $CDCl_3$-D_2O) of **35a B** δ (major conformer) 0 71 (3H, d, J=7 Hz), 0 75 (3H, d, J=7 Hz), 1 47 (3H, s), 1 48 (3H, s), 1 57 (3H, s), 1 60 (3H, s), 2 61 (1H, dqq, J=10 5, 7, 7 Hz), 2 91 (1H, d, J=16 Hz), 3 09 (3H, s), 3 25 (1H, d, J=16 Hz), 3 91 (1H, d, J=10 5 Hz), 5 28 (1H, d, J=10 5 Hz), 5 30 (1H, d, J=18 Hz), 6 16 (1H, dd, J=18, 10 5 Hz), 6 73 (1H, d, J=8 Hz), 6 81 (1H, s), 6 97 (1H, d, J=8 Hz), 8 44 (1H, br s), (minor conformer) 0 65 (3H, d, J=7 Hz), 0 95 (3H, d, J=7 Hz), 2 37 (1H, dqq, J=10 5, 7, 7 Hz), 2 71 (3H, s), 2 78 (1H, d, J=14 Hz), 6 22 (1H, dd, J=18, 10 5 Hz), 7 00 (1H, s), 7 01 (1H, d, J=8 Hz), 7 12 (1H, d, J=8 Hz) ^1H NMR (400 MHz, $CDCl_3$-D_2O) of **36a B** δ (major conformer) 0 65 (3H, d, J=7 Hz), 6 96 (1H, d, J=8 Hz)

(*S*)-7-(3,6,7-Trimethyl-1,6-octadien-3-yl)-(–)-indolactam V (25-Methylteleocidin A-2) (35b A) and (*S*)-7-(3,6,7-Trimethyl-1,6-octadien-3-yl)-9-epi-(–)-indolactam V (35b B) — The same procedure using DEPC (diethylphosphoryl cyanide) as in the preceding paper[1] was applied to the amino-alcohol **34b** (46 5 mg, 0 096 mmol) to give **35b A** containing **36b A** (**35b A** **36b A**=*ca* 8 1) (14 mg, 32%) and **35b B** containing **36b B** (12 mg, 28%) **35b A** with a contaminant **36b A** Colorless syrup MS m/z 451 (M^+) IR ($CHCl_3$) cm^{-1} 1657 ^1H NMR (400 MHz, $CDCl_3$-D_2O) of **35b A** δ (major conformer) 0 58 (3H, d, J=7 Hz), 0 90 (3H, d, J=7 Hz), 1 32 (3H, s), 1 45 (3H, s), 1 52 (3H, s), 1 56 (3H, s), 2 56 (1H, dqq, J=10 5, 7, 7 Hz), 2 89 (3H, s), 3 06 (1H, dd, J=15, 3 Hz), 3 14 (1H, d, J=15 Hz), 3 57 (1H, dd, J=11 5, 8 Hz), 3 72 (1H, dd, J=11 5, 3 Hz), 4 28-4 40 (1H, m), 4 35 (1H, d, J=10 5 Hz), 5 26 (1H, d, J=11 Hz), 5 30 (1H, d, J=18 Hz), 6 22 (1H, dd, J=18, 11 Hz), 6 47 (1H, d, J=8

Hz), 6 82 (1H, s), 6 97 (1H, d, J=8 Hz), 8 54 (1H, br s), (minor conformer) 0.93 (3H, d, J=7 Hz), 1 25 (3H, d, J=7 Hz), 2 37 (1H, dqq, J=10.5, 7, 7 Hz), 2.74 (3H, s), 2 82 (1H, dd, J=15, 1 Hz), 2 99 (1H, d, J=10 5 Hz), 3.33 (1H, dd, J=11, 7 5 Hz), 3 41 (1H, dd, J=11, 7 Hz), 4 40-4.47 (1H, m), 5 32 (1H, d, J=11 Hz), 5 33 (1H, d, J=18 Hz), 6 17 (1H, dd, J=18, 11 Hz), 7 01 (1H, d, J=8 Hz), 7 11 (1H, d, J=8 Hz), 8 77 (1H, br s) ^{1}H NMR (400 MHz, $CDCl_3$-D_2O) of **36b A** δ· (major conformer) 0.65 (3H, d, J=7 Hz), 2 91 (3H, s), 7 00 (1H, d, J=8 Hz), (minor conformer) 2.72 (3H, s) The ratio between **35b A** and **36b A** was estimated from the integrated values of the signals at 0 58 (d) and 0 65 (d) of each major conformer **35b B** with a contaminant **36b B**· Colorless syrup MS m/z 451 (M^+) IR ($CHCl_3$) cm^{-1} 1655 ^{1}H NMR (400 MHz, $CDCl_3$-D_2O) of **35b B** δ (major conformer) 0 66 (3H, d, J=7 Hz), 0 73 (3H, d, J=7 Hz), 1 33 (3H, s), 1 44 (3H, s), 1 53 (3H, s), 1 57 (3H, s), 2.59 (1H, dqq, J=10 5, 7, 7 Hz), 2 89 (1H, dd, J=16, 2 Hz), 3 09 (3H, s), 3 26 (1H, dd, J=16, 2 Hz), 3 91 (1H, d, J=10.5 Hz), 5 27 (1H, dd, J=11, 1 Hz), 5.29 (1H, dd, J=18, 1 Hz), 6 23 (1H, dd, J=18, 11 Hz), 6.73 (1H, d, J=8 Hz), 6.81 (1H, d, J=2 Hz), 6 96 (1H, d, J=8 Hz), 8 45 (1H, br s), (minor conformer) 0 95 (3H, d, J=7 Hz), 2.35 (1H, dqq, J=10.5, 7, 7 Hz), 2 73 (3H, s), 2.78 (1H, d, J=14 Hz), 3 02 (1H, d, J=10 5 Hz), 6 16 (1H, dd, J=18, 11 Hz), 7.01 (1H, d, J=8 Hz), 7 12 (1H, d, J=8 Hz), 8 72 (1H, br s) ^{1}H NMR (400 MHz, $CDCl_3$-D_2O) of **36b B** δ (major conformer) 0 77 (3H, d, J=7 Hz), 6.73 (1H, d, J=8 Hz), 6 97 (1H, d, J=8 Hz), 8 44 (1H, br s)

(*R*)-14*O*-Acetyl-7-(3,6,7-trimethyl-1,6-octadien-3-yl)-(−)-indolactam V (40a) and (*S*)-14*O*-Acetyl-7-(3,6,7-trimethyl-1,6-octadien-3-yl)-(−)-indolactam V (40b) — To a solution of **35a A** + **36a A** (114 5 mg, 0 254 mmol) in pyridine (1 5 ml) and CH_2Cl_2 (1 ml) was added Ac_2O (0.75 ml, 7 96 mmol) at 0°C, and the mixture was stirred at 0°C for 1 h The solvent was evaporated, sat $NaHCO_3$-H_2O was added and the whole was extracted with CH_2Cl_2 Usual work-up and PTLC [hexane-EtOAc (2 1)] afforded **40a** with a contaminant **41a** (125 mg, 100%) Similarly **35b A** + **36b A** (128 mg) gave **40b** with a contaminant **41b** (135 5 mg, 97%) **40a** with **41a** Colorless syrup MS m/z 493 (M^+) IR ($CHCl_3$) cm^{-1} 1740, 1658 ^{1}H NMR (90 MHz) δ 0 94 (3H, d, J=7 Hz), 2 02 and 2 10 (3H, s each), 2 74 and 2 98 (3H, s each), 6 16 and 6 23 (1H, dd, J=18, 10 5 Hz), 6 47 (1H, d, J=8 Hz), 6 80 and 6 87 (1H, d each, J=2 Hz), 8 51 and 8 72 (1H, br s each) **40b** with **41b** Colorless syrup MS m/z 493 (M^+) IR ($CHCl_3$) cm^{-1} 1737, 1652 ^{1}H NMR (90 MHz) δ 0 92 and 0 93 (3H, d each, J=7 Hz), 2 03 and 2 09 (3H, s each), 2 74 and 2 92 (3H, s each), 6 22 (1H, dd, J=18, 10 5 Hz), 6 47 (1H, d, J=8 Hz), 8 53 and 8 72 (1H, br s each).

14*O*-Acetylteleocidin B-4 (42a) and 14*O*-Acetylteleocidin B-3 (42b) — To a solution of **40a** + **41a** (125 mg, 0 254 mmol) in 1,2-dichloroethane (37 5 ml) was added BF_3 OEt_2 (1 25 ml, 10 2 mmol) at 0°C and the mixture was stirred at 0°C for 1 h Sat $NaHCO_3$-H_2O was added, the whole was extracted with CH_2Cl_2 and worked up as usual PTLC [hexane-$CHCl_3$-i-PrOH (86 10 4)] of the residue afforded the crude products (33 5 mg), which was purified by PTLC [hexane-EtOAc (2 1)] to give **42a** containing a contaminant **43a** (31 5 mg, 25%) Similarly **42b** with a contaminant **43b** (31 mg, 24%) was obtained from **40b** + **41b** (130 mg) **42a** with **43a** Colorless syrup MS m/z 493 (M^+) IR ($CHCl_3$) cm^{-1} 1735, 1653 ^{1}H NMR (90 MHz) (two conformers) δ 0 55, 0 62, 0 70, 0 94 and 1 01 (Me protons of the two i-Pr groups, d each, J=7 Hz), 1 35 (3H, s), 1 51 (3H, s), 1 91 and 2 08 (3H, s each), 2 73 and 2 92 (3H, s each), 5 22 (1H, d, J=10 5 Hz), 5 35 (1H, d, J=18 Hz), 6.14 and 6 17 (1H, dd each, J=18, 10 5 Hz), 6 50 and 6 99 (1H, s each), 6 74 and 6 79 (1H, d each, J=3 Hz), 8 68 and 8 73 (1H, br s each) **42b** with **43b** Colorless syrup MS m/z 493 (M^+) IR ($CHCl_3$) cm^{-1} 1740, 1655, 1652 ^{1}H NMR (90 MHz) (two conformers) δ 0 58, 0 66, 0 92 and 1 03 (Me protons of the two i-Pr groups, d each, J=7 Hz), 1 31 1 33 (3H, s each), 1 46 and 1 51 (3H, s each), 2 04 and 2 08 (3H, s each), 2 74 and 2 91 (3H, s each), 6 20 (1H, dd, J=18, 10 5 Hz), 6 47 and 7 00 (1H, s each), 8 64 and 8 77 (1H, br s each)

Teleocidin B-4 (4) — A solution of **42a** + **43a** (34 mg, 0 069 mmol) in MeOH (5 ml) was stirred with K_2CO_3 (48 mg, 0 35 mmol) at 0°C for 40 min Sat NH_4Cl-H_2O was added, the whole was extracted with CH_2Cl_2 and worked up as usual to give a residue (36 5 mg), which was separated by HPLC [column YMC A-324, ODS, S-5, 10 × 300 mm, mobile phase MeOH-H_2O-$CHCl_3$ (78 20 2), flow rate 2 ml/min] to afford **4** (25 5 mg, retention time 130 8 min) and **44a** (3 5 mg, retention time 120 4 min) The former compound was further purified by PTLC [hexane-EtOAc (1 1)] and recrystallization from CH_2Cl_2-i-Pr_2O to give **teleocidin B-4 (4)** (22 5 mg, 72%), colorless prisms, mp 233-235°C (lit [3b] mp 230-232 5°C) No depression of mp was observed on admixture with the authentic sample of **4** Similarly ent-teleocidin B-3 (**44a**) (2 5 mg, 8%) was obtained **The**

synthetic 4 HRMS Calcd for $C_{28}H_{41}N_3O_2$: 451.3198. Found. 451.3212. CD (c 2.26×10^{-5}, MeOH, 21°C): $[\theta]_{327}$ 0, $[\theta]_{311}$ +4000, $[\theta]_{302}$ 0, $[\theta]_{260}$ -24500, $[\theta]_{255}$ -23300, $[\theta]_{252}$ -24000, $[\theta]_{249}$ -23500, $[\theta]_{240}$ -37000, $[\theta]_{235}$ -30500, $[\theta]_{225}$ -50500, $[\theta]_{210}$ 0. IR (KBr) cm^{-1}: 1640. ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ: (major conformer) 0.53 (3H, d, J=7 Hz), 0 69 (3H, d, J=7 Hz), 0.91 (3H, d, J=7 Hz), 1.01 (3H, d, J=7 Hz), 1.35 (3H, s), 1.51 (3H, s), 2 25 (1H, qq, J=7, 7 Hz), 2.61 (1H, dqq, J=10.5, 7, 7 Hz), 2.91 (3H, s), 2.97 (1H, dd, J=17 5, 4 Hz), 3.12 (1H, d, J=17 5 Hz), 3 51 (1H, dd, J=11, 9 Hz), 3.71 (1H, dd, J=11, 4 Hz), 4.27-4.36 (1H, m), 4 31 (1H, d, J=10.5 Hz), 5 25 (1H, dd, J=10.5, 1 Hz), 5 41 (1H, dd, J=18, 1 Hz), 6.16 (1H, dd, J=18, 10.5 Hz), 6 51 (1H, s), 6.76-6.80 (1H, m), 8.68 (1H, br s), (minor conformer) 0.61 (3H, d, J=7 Hz), 0.93 (3H, d, J=7 Hz), 1.03 (3H, d, J=7 Hz), 1.24 (3H, d, J=7 Hz), 1 50 (3H, s), 2 37 (1H, dqq, J=10 5, 7, 7 Hz), 2 73 (3H, s), 2.74 (1H, dd, J=15, 1 Hz), 2 85 (1H, d, J=10.5 Hz), 3 03 (1H, dd, J=15, 5 Hz), 3.42 (1H, dd, J=11, 7 Hz), 4.38-4.46 (1H, m), 5.28 (1H, d, J=10.5 Hz), 5.42 (1H, d, J=18 Hz), 6 21 (1H, dd, J=18, 10.5 Hz), 6.87 (1H, d, J=2 Hz), 7.02 (1H, s), 8.77 (1H, br s). Ent-teleocidin B-3 (**44a**). Colorless prisms, mp 155-158°C (CH_2Cl_2-i-Pr_2O). HRMS Calcd for $C_{28}H_{41}N_3O_2$: 451 3198. Found· 451 3192 CD (c $2\ 33 \times 10^{-5}$, MeOH, 21°C) $[\theta]_{322}$ 0, $[\theta]_{302}$ -6500, $[\theta]_{294}$ 0, $[\theta]_{262}$ +18000, $[\theta]_{258}$ +16000, $[\theta]_{253}$ +19500, $[\theta]_{247}$ +17500, $[\theta]_{240}$ +24000, $[\theta]_{236}$ +18000, $[\theta]_{223}$ +27500, $[\theta]_{214}$ 0 ^1H NMR spectrum (400 MHz) was identical with that of teleocidin B-3 (**3**) described below

Teleocidin B-3 (3) — The same treatment as above yielded teleocidin B-3 (**3**) (20 mg, 70 5%) and ent-teleocidin B-4 (**44b**) (2 5 mg, 9%) from **42b** + **43b** (31 mg) **The synthetic 3**· Colorless prisms, mp 155-158°C (CH_2Cl_2-i-Pr_2O) (lit [3b] mp 160-162°C) No depression of mp was observed on admixture with the authentic sample of **3**. HRMS Calcd for $C_{28}H_{41}N_3O_2$· 451.3198 Found. 451 3210. CD (c $2\ 26 \times 10^{-5}$, MeOH, 21°C) $[\theta]_{323}$ 0, $[\theta]_{307}$ +7500, $[\theta]_{294}$ 0, $[\theta]_{258}$ -20000, $[\theta]_{247}$ -19000, $[\theta]_{240}$ -27000, $[\theta]_{235}$ -19000, $[\theta]_{225}$ -30000, $[\theta]_{212}$ 0. IR (KBr) cm^{-1}· 1638 ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ (major conformer) 0.62 (3H, d, J=7 Hz), 0.64 (3H, d, J=7 Hz), 0 91 (3H, d, J=7 Hz), 1.01 (3H, d, J=7 Hz), 1.30 (3H, s), 1 46 (3H, s), 2.27 (1H, qq, J=7, 7 Hz), 2 60 (1H, dqq, J=10.5, 7, 7 Hz), 2 89 (3H, s), 2.93 (1H, dd, J=18.5, 4 Hz), 3 13 (1H, d, J=18 5 Hz), 3.51 (1H, dd, J=11, 9 Hz), 3 75 (1H, dd, J=11, 4 Hz), 4.28 (1H, d, J=10 5 Hz), 4 28-4 36 (1H, m), 5 24 (1H, dd, J=10 5, 1 Hz), 5 37 (1H, dd, J=18, 1 Hz), 6 22 (1H, dd, J=18, 10.5 Hz), 6.47 (1H, s), 6 76 (1H, s), 8 46 (1H, br s); (minor conformer) 0 58 (3H, d, J=7 Hz), 0 93 (3H, d, J=7 Hz), 1.02 (3H, d, J=7 Hz), 1 24 (3H, d, J=7 Hz), 1 33 (3H, s), 1 50 (3H, s), 2 24 (1H, qq, J=7, 7 Hz), 2 38 (1H, dqq, J=11 5, 7, 7 Hz), 2 73 (3H, s), 2 78 (1H, dd, J=15, 1 Hz), 2.91 (1H, d, J=11.5 Hz), 3 05 (1H, dd, J=15, 5 Hz), 3 45 (1H, dd, J=11 5, 7 5 Hz), 3.50 (1H, dd, J=11.5, 6 Hz), 4.36-4 46 (1H, m), 5 30 (1H, d, J=10.5 Hz), 5 44 (1H, d, J=18 Hz), 6.19 (1H, dd, J=18, 10 5 Hz), 6 89 (1H, d, J=3 Hz), 7.03 (1H, s), 8 79 (1H, br s) Ent-teleocidin B-4 (**44b**): Colorless prisms, mp 231-234°C (CH_2Cl_2-i-Pr_2O) HRMS Calcd for $C_{28}H_{41}N_3O_2$ 451 3198 Found 451 3187 CD (c $2\ 00 \times 10^{-5}$, MeOH, 21°C) $[\theta]_{322}$ 0, $[\theta]_{314}$ -2500, $[\theta]_{302}$ 0, $[\theta]_{255}$ +19000, $[\theta]_{248}$ +17500, $[\theta]_{240}$ +28000, $[\theta]_{235}$ +23000, $[\theta]_{224}$ +37000, $[\theta]_{210}$ 0 ^1H NMR spectrum (400 MHz) was identical with that of teleocidin B-4 (**4**) described above

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REFERENCES AND NOTES

1 Part 2· Muratake, H , Okabe, K ; Natsume, M *Tetrahedron* preceding paper

2 (a) Sakai, S ; Aimi, N , Yamaguchi, K.; Hitotsuyanagi, Y., Watanabe, C.; Yokose, K.; Koyama, Y., Shudo, K, Itai, A. *Chem Pharm Bull* **1984**, *32*, 354-357. (b) Hitotsuyanagi, Y.; Fujiki, H.; Suganuma, M ; Aimi, N ; Sakai, S ; Endo, Y.; Shudo, K , Sugimura, T. *Chem. Pharm Bull* **1984**, *32*, 4233-4236

3 (a) Fujiki, H , Sugimura, T. *Cancer Surveys* **1983**, 2, 539-556. (b) Sakai, S.; Hitotsuyanagi, Y ; Aimi, N , Fujiki, H , Suganuma, M ; Sugimura, T , Endo, Y , Shudo, K *Tetrahedron Lett* **1986**, *27*, 5219-5220.

4 Irie, K.; Kajiyama, S.; Funaki, A.; Koshimizu, K , Hayashi, H.; Arai, M. *Tetrahedron* **1990**, *46*, 2773-2788.

5. (a) Muratake, H.; Okabe, K.; Natsume, M. *Tetrahedron Lett.* **1988**, *29*, 6267-6270. (b) Okabe, K., Muratake, H.; Natsume, M. *Chem. Pharm. Bull.* **1989**, *37*, 563-564.

6 Nakatsuka, S., Masuda, T.; Goto, T *Terahedron Lett.* **1987**, *28*, 3671-3674.

7 This bromide was already reported. Muntyan, G. E , Vaskan, R. N. *Izv Akad Nauk Mold SSR, Ser Biol Khim. Nauk* **1978**, 65-70 [*Chem. Abstr.* **1978**, *89*, 75405g] Actually the product was an inseparable *ca.* 1.1 mixture of **14** and 3,6,7-trimethyl-1,6-octadien-3-yl bromide. Using this mixture, the Grignard reaction product **16** was obtained only in a poor yield.

8 Saucy, G., Marbet, R. *Helv Chim Acta* **1967**, *50*, 2091-2095

9 Part 1: Muratake, H ; Natsume, M. *Tetrahedron* preceding paper.

10 Scheibye, S.; Pedersen, B. S ; Lawesson, S. O. *Bull Soc Chim. Belg.* **1978**, *87*, 229-238.

11 (a) Takashima, M., Sakai, H., Arima, K. *Agric Biol Chem* **1962**, *26*, 660-668. (b) Takashima, M., Sakai, H., Mori, R.; Arima, K. *Agric Biol Chem.* **1962**, *26*, 669-678 (c) Harada, H.; Nakata, H ; Hirata, Y *Nippon Kagaku Zasshi* **1966**, *87*, 86-92

12 See the description in Part 1 [9]

13 Fujiki, H.; Mori, M., Nakayasu, M., Terada, M , Sugimura, T. *Biochem Biophys Res Commun.* **1979**, *90*, 976-983

14 Gilchrist, T. L ; Lingham, D A.; Roberts, T G *J Chem Soc , Chem Commun.* **1979**, 1089-1090

15 Hamada, Y.; Shioiri, T. *Chem Pharm Bull.* **1982**, *30*, 1921-1924.

16. Shioiri, T.; Ninomiya, K., Yamada, S -i. *J Am Chem Soc.* **1972**, *94*, 6203-6205

17 Irie, K ; Hagiwara, N ; Funaki, A., Hayashi, H , Arai, M., Koshimizu, K. *Agric Biol Chem.* **1987**, *51*, 1733-1735

18 Yamada, S -i.; Kasai, Y.; Shioiri, T. *Tetrahedron Lett* **1973**, 1595-1598

19 Okabe, K.; Muratake, H., Natsume, M. *Tetrahedron* **1990**, *46*, 5113-5120