Available online at www.sciencedirect.com
SCIENCE DIRECT®
Bioorganic & Medicinal Chemistry 12 (2004) 337–361
Bioorganic & Medicinal Chemistry

Structure–activity relationships of globomycin analogues as antibiotics

Toshihiro Kiho,[a] Mizuka Nakayama,[a] Kayo Yasuda,[b] Shunichi Miyakoshi,[b] Masatoshi Inukai[b] and Hiroshi Kogen[a,*]

[a]*Exploratory Chemistry Research Laboratories, Sankyo Co., Ltd., 2-58, Hiromachi 1-chome, Sinagawa-ku, Tokyo 140-8710, Japan*
[b]*Lead Discovery Research Laboratories, Sankyo Co., Ltd., 2-58, Hiromachi 1-chome, Sinagawa-ku, Tokyo 140-8710, Japan*

Received 6 September 2003; revised 30 October 2003; accepted 31 October 2003

Abstract—Globomycin (**1a**), a signal peptidase II inhibitor, and its derivatives show potent antibacterial activity against Gram-negative bacteria. The synthesis and antimicrobial activity of novel globomycin analogues are reported. The hydroxyl group in the L-Ser residue was essential for the antimicrobial activity and the length of the alkyl side chain greatly influenced the activity. In addition, derivatives that had a modified cyclic core exhibited weak activity. One of the analogues showed a wider antimicrobial spectrum, effective against not only Gram-negative but also Gram-positive bacteria.

1. Introduction

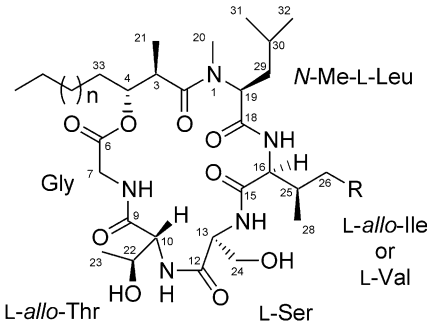
Globomycin (**1a**)[1] and its congeners, SF-1902 A_2–A_5,[2] isolated by different researchers as antibiotics against only Gram-negative bacteria, are 19-membered cyclic depsipeptides.[1,2] The major component, **1a**, has only been proven to be a specific inhibitor of signal peptidase II, a prolipoprotein-processing enzyme,[3] that processes the acylated precursor form of lipoprotein into apolipoprotein and a signal peptide in *Escherichia coli*.[4] Inhibition of signal peptidase II leads to the accumulation of the lipoprotein precursor in the cytoplasmic membrane and consequently to the death of the cell.[5] Signal peptidase II represents an attractive target because the mechanism is different from currently available drugs. Previously, we reported the absolute structure of **1a** obtained by X-ray analysis and the first asymmetric total synthesis of globomycin (**1a**) and SF-1902A_5 (**1b**).[1d,e] In a recent communication, we also reported on new synthetic globomycin analogues that have more potent inhibitory activity.[1f] Structurally, these congeners were constructed from four natural amino acids, one *N*-methyl amino acid and a β-hydroxy-α-methyl carboxylic acid. Naturally occurring globomycin congeners have the structure shown in Figure 1. The minor congeners, SF-1902 A_3 and A_{4b}, have an L-Val in the place of L-*allo*-Ile, and the other congeners, SF-1902 A_2, A_{4a} and A_{4b}, have a shorter or longer alkyl side chain in the fatty acid unit than that of **1a**. It was reported that the antibacterial activity is quite sensitive to the length of the alkyl side chain, either in the fatty acid or amino acid.[2] The congeners which have a longer side chain, **1b**, SF-1902 A_{4a} and A_{4b}, are more potent than **1a** (MIC: **1a**, 6.25 μg/mL; **1b**, 1.56 μg/mL against *E. coli* NIHJ JC-2). However, SF-1902 A_2 with the shortest side chain showed the weakest activity.[2b] Furthermore, the congeners containing an L-Val, SF-1902 A_3 and A_{4b}, are less active compared with **1a** and **1b**, respectively. In addition, based on ^{1}H NMR analysis, **1a** exists as a mixture of rotational isomers derived from the acyl *N*-methyl amide group. The major isomer was ascribed to be in the *trans* form while the minor isomer was considered to adopt a *cis* form.[1d,e] The *cis*/*trans* ratio may affect the antibacterial activity. Now, we wish to report the full structure–activity relationships (SARs) of newly synthesized globomycin analogues.

2. Chemistry

Three fragments (*Fragments A*, *B* and *C*) were synthesized and assembled to construct various globomycin

* Corresponding author. Tel.: +81-3-3492-3131; fax: +81-3-5436-8561; e-mail: hkogen@shina.sankyo.co.jp

0968-0896/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bmc.2003.10.055



	R	n
Globomycin (**1a**)	CH_3	3
SF-1902 A_5 (**1b**)	CH_3	5
SF-1902 A_{4a}	CH_3	4
SF-1902 A_2	CH_3	1
SF-1902 A_3	H	3
SF-1902 A_{4b}	H	5

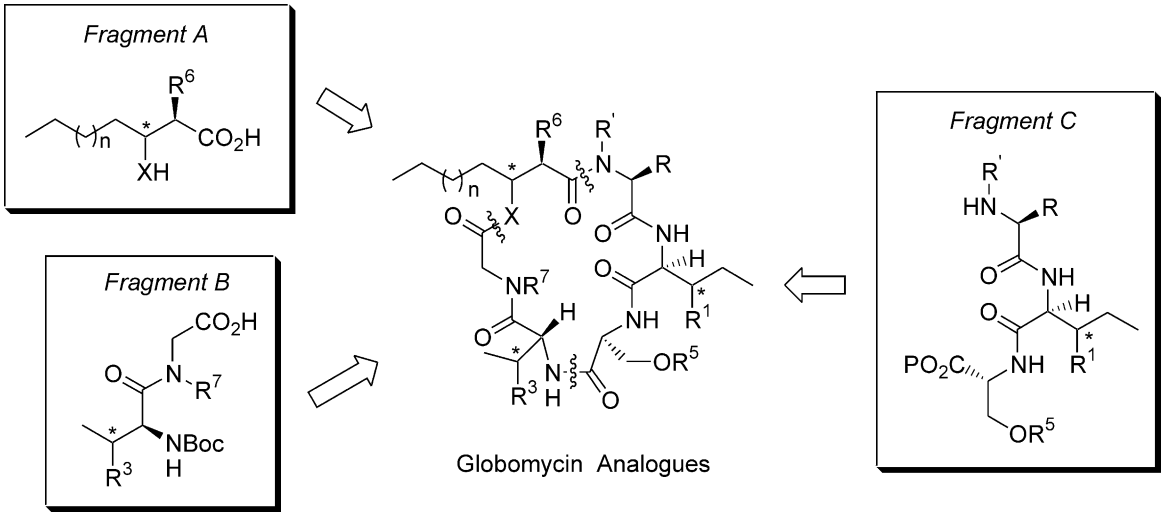
Figure 1. Structure of naturally occurring globomycin (**1a**) and its congeners.

analogues as shown in Scheme 1. Each fragment was prepared with the corresponding method used in the total synthesis of globomycin (**1a**).[1d] *Fragment A* is an optically active β-hydroxy or β-amino carboxylic acid. *Fragments B* and *C* are dipeptidyl and tripeptidyl compounds, respectively. *Fragment A*, the only non-amino acid containing part, was prepared as shown in Scheme 2. Compound **3**[1d,e] was prepared by an *anti*-selective boron-mediated asymmetric aldol reaction developed by Abiko and Masamune.[6] The *anti*-aldol product **3c** was obtained in good yield and with high diastereoselectivity ($n=7$: 76%, 89% *de*). The hydroxyl ester **3c** was hydrolyzed with aqueous LiOH in THF to give **4c** without epimerization in good yield (86%). On the other hand, the *syn* isomer **7** was prepared by a *syn*-selective Evans aldol method[7] with a chiral oxazolidinone **5**. The aldol product **6** (93%) was hydrolyzed to give an acid **7**[7c] in the usual manner (100%). The hydroxyl group in **6** was converted to an azide group by Mistunobu inversion to afford **8** (81%). Removal of the chiral auxiliary followed by the reduction in the presence of Boc_2O gave (2*R*,3*S*)-3-Boc-amino-2-methylnonanoic acid **9** (46%, two steps). Finally, (3*R*)-hydroxynonanoic acid **11**[8] was produced by asymmetric hydrogenation of β-ketoester **10** with a BINAP ruthenium catalyst[9] followed by hydrolysis (96%, two steps). The optical purity was confirmed by ^1H NMR analysis after the conversion to (*R*)- and (*S*)-MTPA ester.

The dipeptide unit, *Fragment B* (**15a–15e**), was prepared from commercially available L-*allo*-threonine (L-*allo*-Thr-OH), Boc-L-threonine [Boc-L-Thr-OH (**12a**)] or Boc-L-α-aminobutyric acid (Boc-L-Abu-OH). Scheme 3 shows the preparation of compound **15b** as an example and a representative structure of *Fragment B*. The protection of **12** with TBSOTf (88%) followed by condensation with glycine benzyl ester (**13**) afforded fully protected dipeptide **14b** (87%). Compound **14b** was hydrogenated to give the dipeptide *Fragment B* **15b** (98%). In the case of **15c**, *N*-Me-Gly-OBn was used in place of **13**. Dipeptide **15e** was also synthesized with Boc-L-*allo*-Thr(Me)-OH (**12b**) prepared from L-*allo*-Thr-OH.

The tripeptide **19a–19f**, *Fragment C*, was synthesized from Boc-protected L-Serine derivatives **16** as shown in Scheme 4. An allyl or benzyl group was selected to protect the carboxylic acid in **16** ($P^1=Me$, $P^2=Bn$ or $P^1=Bn$, $P^2=$allyl). The esterification of **16** followed by the deprotection of the Boc group with 4 N HCl in EtOAc gave the ester **17** as an HCl salt. Coupling of this salt with Boc-L-*allo*-isoleucine (Boc-L-*allo*-Ile-OH) mediated by (benzotriazolyloxy) tris(pyrrolydino)phosphonium hexafluorophosphate (PyBOP)[10] was conducted to give dipeptide **18** (100%). After the removal of the Boc group in **18**, the coupling with a variety of Boc-protected amino acid followed by the treatment with 4 N HCl in EtOAc gave tripeptides **19a–19e**. Tripeptide **19g** was also prepared in the same manner but by using Boc-L-Ile-OH in palce of Boc-L-*allo*-Ile-OH.

The novel synthetic analogues **1c–1q** were prepared by the convergent macrolactamization method using the

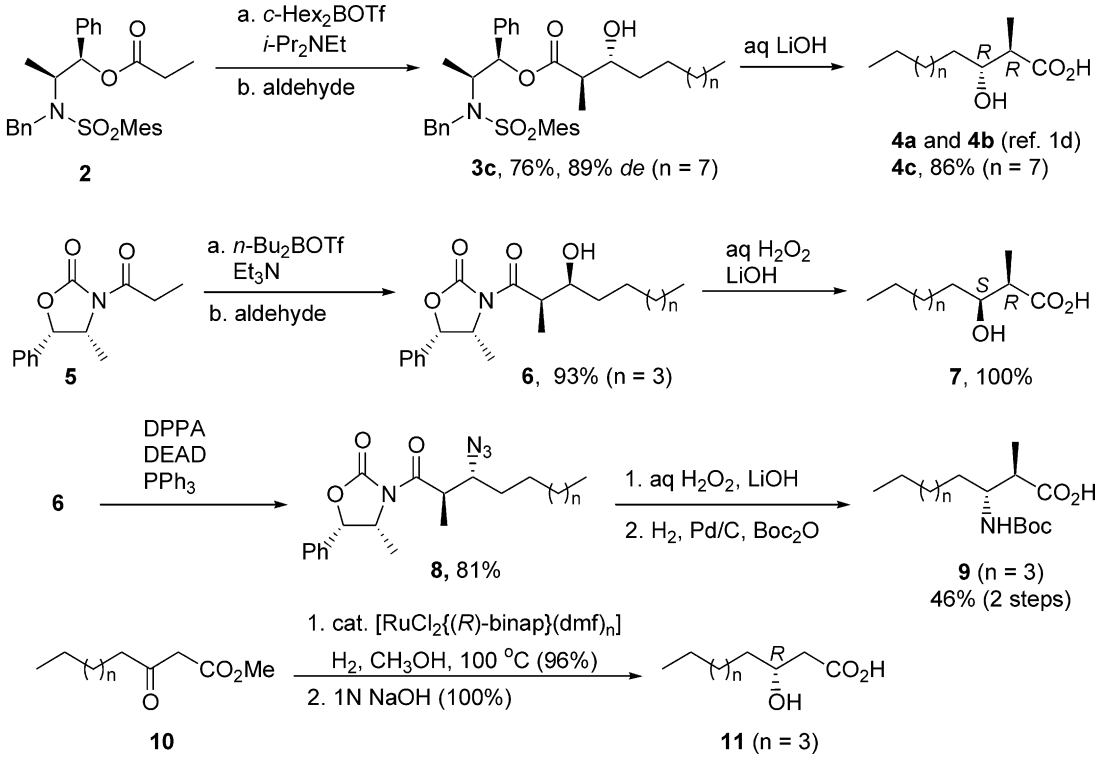


Scheme 1. Synthetic strategy for globomycin analogues.

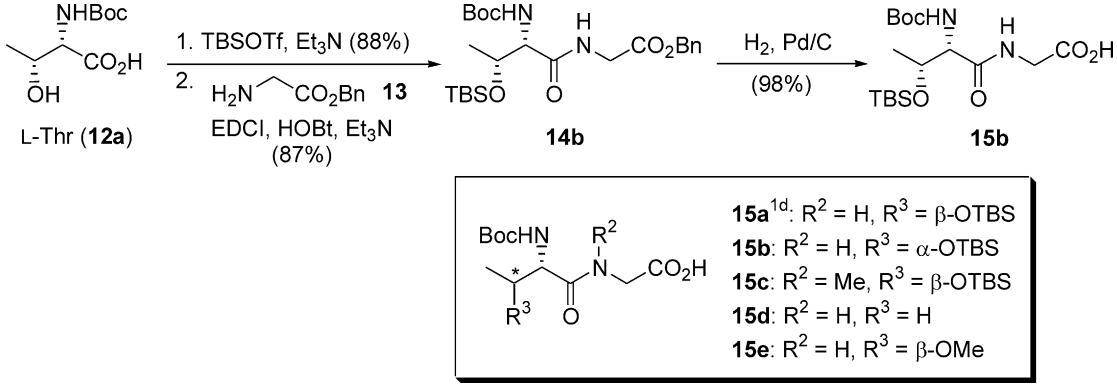
three fragments (*Fragments A*, *B* and *C*). As an example, synthesis of the most potent analogue **1c** is shown in Scheme 5. Condensation of *Fragment C* (**19b**) with *Fragment A* (**4c**) mediated by diethylcyanophosphate (DEPC)[11] was carried out to give the acylated tripeptide **20c** (99%). Esterification of **20** was performed with diisopropylcarbodiimide (DIPC) and *Fragment B* (**15a**) under Keck's condition[12] to afford depsipeptide **21c** (97%). After the treatment of **21c** with TBAF in the presence of AcOH (91%), the removal of the allyl (91%) and Boc group with a Pd catalyst and TFA respectively, provided the macrocyclization precursors. The macrolactamization was performed with *O*-(7-azabenzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU)[13] to give *O*-Bn cyclic derivatives under highly diluted conditions (33%, two steps). Finally, the removal of the benzyl group by hydrogenolysis yielded **1c** (90%). The other analogues **1d–1q** were also synthesized by the same route.[14] The reagent, 2-(1*H*-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU),[13] was also used for macrocyclization. The newly obtained globomycin analogues are shown in Figure 2. The ^{1}H NMR analysis indicated these analogues were present as a mixture of rotamers, but the *N*-demethyl derivative **1j** was found to be single isomer.[15]

3. Antibacterial activity

The antibacterial activities of the synthetic globomycin analogues **1a–1q** against Gram-negative bacteria are summarized in Table 1. As a result, **1c**[1f] possessing the longest alkyl side chain showed the most potent activity among the analogues (MIC: **1a**, 12.5 μg/mL; **1b**, 3.13 μg/mL; **1c**, 1.56 μg/mL against *E. coli* SANK 70569).

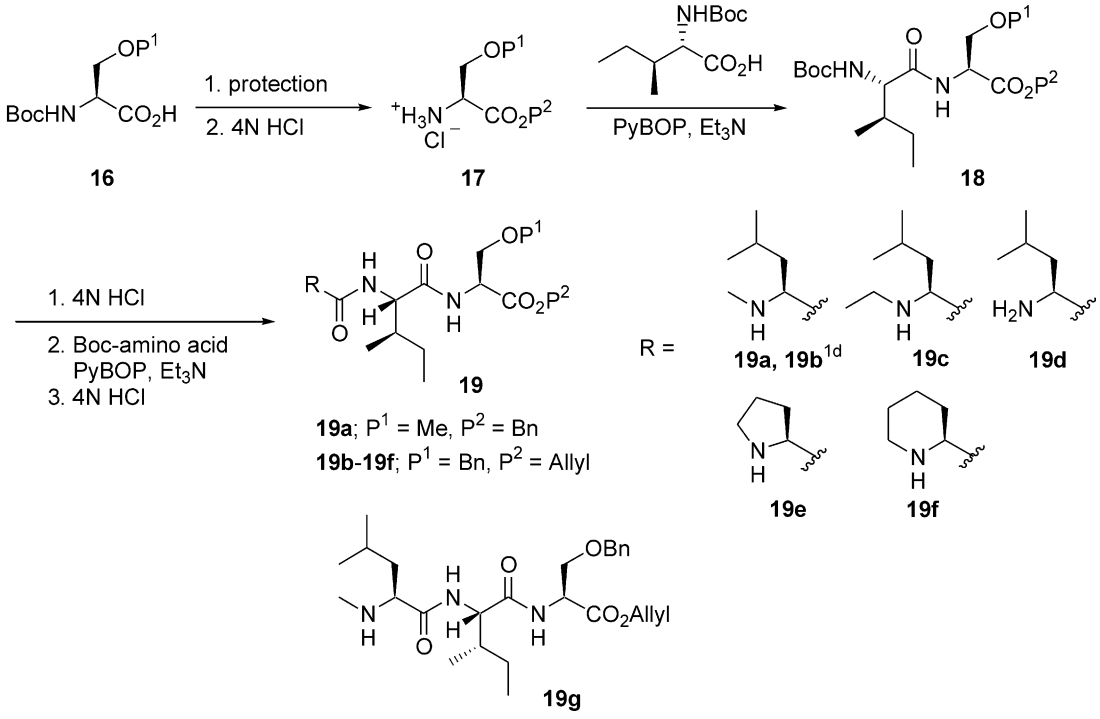


Scheme 2. Synthesis of *Fragment A*.

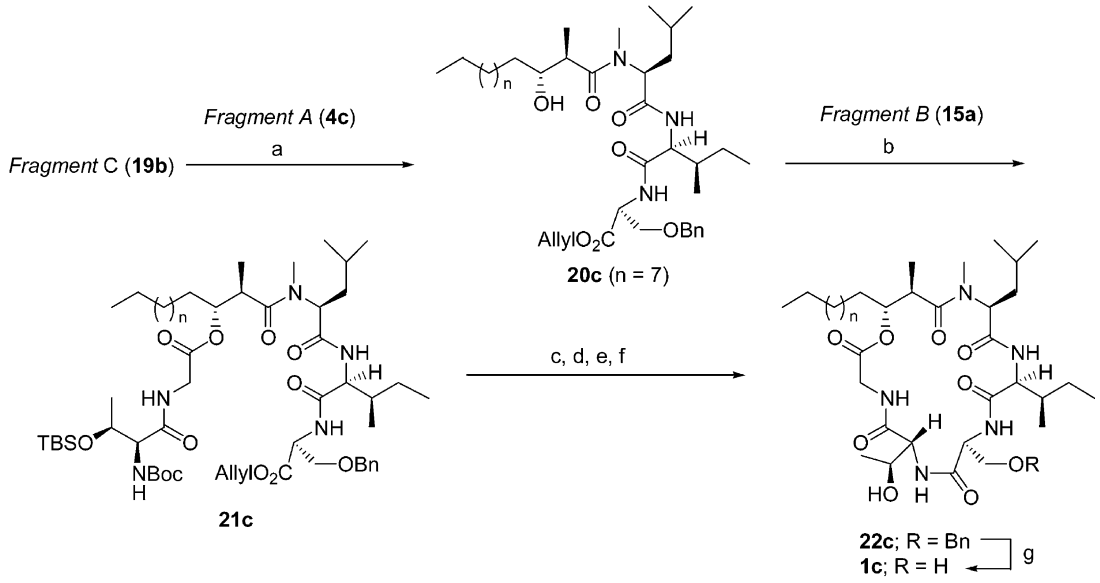


Scheme 3. Synthesis of the dipeptide *Fragment B*.

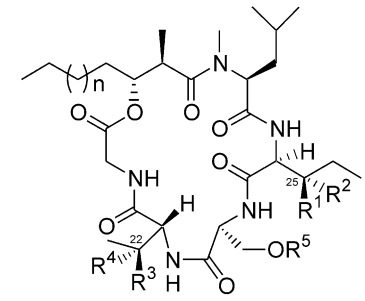
The length of the alkyl side chain greatly affected the antibacterial activity. A four-carbon increase in the fatty acid side chain enhanced the activity by 4- to 8-fold compared with **1a** while the *cis*/*trans* geometric ratio was almost constant among these three compounds. The hydrophobicity seemed to be important for the antibacterial activity, therefore, it may be possible to produce other more potent inhibitors. With regard to stereochemistry, the activity of **1d**, C(25)-epimer, was diminished and the activities of **1e**, C(22)-epimer, and **1f**, stereoisomer at C(22) and C(25) positions, were completely lost. In particular, the stereochemistry of the hydroxyl group in L-Thr was quite important for the activity. Compound **1e** was inactive although the deoxy derivative **1g** and methyl ether derivative **1h** retained their activity. Therefore, the hydroxyl group in L-*allo*-Thr is



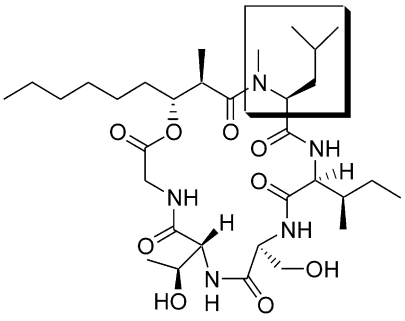
Scheme 4. Synthesis of the tripeptide *Fragment C*.

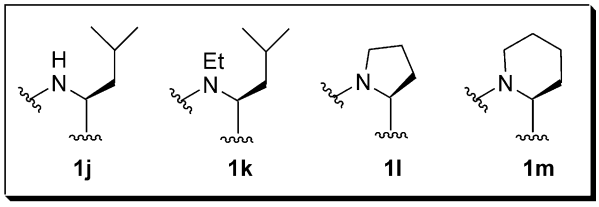


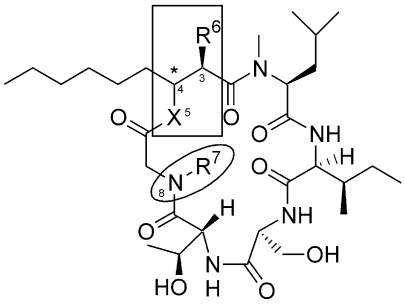
Scheme 5. Synthesis of the globomycin derivative **1c**. Reagents and conditions: (a) DEPC, Et_3N,THF, 0°C to rt, 99%; (b) DIPC, CSA, DMAP, CH_2Cl_2, 0°C to rt, 97%; (c) TBAF, AcOH, 91%; (d) cat $Pd(PPh_3)_4$, morpholine, 94%; (e) TFA, CH_2Cl_2; (f) HATU or TBTU, *i*-Pr_2NEt, 33% (two steps); (g) H_2, $Pd(OH)_2$, 90%.



Compounds		n	R^1	R^2	R^3	R^4	R^5
globomycin	**1a**	3	Me	H	OH	H	H
SF-1902 A_5	**1b**	5	Me	H	OH	H	H
	1c	7	Me	H	OH	H	H
	1d	3	H	Me	OH	H	H
	1e	3	Me	H	H	OH	H
	1f	3	H	Me	H	OH	H
	1g	3	Me	H	H	H	H
	1h	3	Me	H	OMe	H	H
	1i	3	Me	H	OH	H	Me



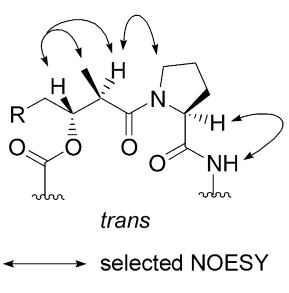




	R^6	R^7	X
1n	H	H	α-O
1o	Me	H	α-NH
1p	Me	H	β-O
1q	Me	Me	α-O

Figure 2. Structures of globomycin (**1a**) and the synthetic analogues (**1b–1q**).

not essential for the activity. On the other hand, the hydroxyl group in L-Ser is essential because generating a methyl ether derivative, such as **1i**, lost the activity.[16] Among derivatives with a modified *N*-alkyl moiety, **1i–1m**, only *N*-ethyl derivative **1k** showed weak activity. However the other derivatives, **1j**, **1l** and **1m** did not



ratio of rotamers	
1a	5.9/1
1j*	single isomer
1k	>20/1
1l	5.2/1

* in CD_3OD

Figure 3. Selected NOESY Structure of **1l** and the ratio of rotamers in $CDCl_3$.

(MIC: **1k**, 25 μg/mL against *E. coli* SANK 70569). ^1H NMR analysis of these compounds suggested that the conformation of **1k** was similar to that of globomycin (**1a**)[17] but the conformations of **1j**, **1l** and **1m** were quite different. Furthermore, the NOESY experiments of these compounds indicated that conformation of the major isomer at the acyl *N*-H or *N*-alkyl amide moiety was trans form which is the same as **1a**, as shown in Figure 3. These results suggested that modifications at the *N*-Me position caused a conformational change at another site in the molecule. Taking this into account, lactam **1o**, *syn* **1p** and *N*-Me-Gly derivative **1q** were inactive because of a conformational change ascribed to a modification of the cyclic core.

Surprisingly, **1c** showed moderate activity against all Gram-positive bacteria tested such as *Staphylococcus aureus* (MRSA) (MIC = 12.5 μg/mL) even though **1a** and **1b** were almost inactive as shown in Table 2. This is the first globomycin analogue that has a wide anti-

Table 1. Antibacterial spectra of globomycin (**1a**), SF-1902 A_5 (**1b**) and the synthetic analogues (**1c–1i**)

Compd	MIC (μg/mL)							
	Organism							
	Escherichia coli SANK 70569 (NIHJ JC-2)	*Escherichia coli* SANK 72290	*Salmonella enteritidis* SANK 72390	*Klebsiella pneumoniae* SANK 72490	*Enterobacter cloacae* 846	*Enterobacter cloacae* SANK 72690	*Serratia marcescens* SANK 72790	*Pseudomonas aeruginosa* SANK 73190
Ampicillin	50	>100	12.5	>100	100	>100	50	>100
Streptomycin, sulfate	12.5	>100	3.13	6.25	6.25	3.13	3.13	50
1a	12.5	12.5	25	25	6.25	50	100	>100
1b	3.13	3.13	6.25	3.13	1.56	12.5	12.5	>100
1c	1.56	1.56	3.13	1.56	1.56	3.13	3.13	>100
1d	12.5	12.5	50	25	6.25	50	>100	>100
1e	>100	>100	>100	>100	100	>100	>100	>100
1f	>100	>100	>100	>100	>100	>100	>100	>100
1g	25	25	100	50	12.5	>100	>100	>100
1h	25	25	50	50	12.5	100	>100	>100
1i	>100	>100	>100	>100	>100	>100	>100	>100
1j	>100	>100	>100	>100	100	>100	>100	>100
1k	25	25	50	50	12.5	100	>100	>100
1l	>100	>100	>100	>100	>100	>100	>100	>100
1m	>100	>100	>100	>100	>100	>100	>100	>100
1n	>100	>100	>100	>100	>100	>100	>100	>100
1o	>100	>100	>100	>100	>100	>100	>100	>100
1p	>100	>100	>100	>100	>100	>100	>100	>100
1q	>100	>100	>100	>100	>100	>100	>100	>100

bacterial spectrum which also includes Gram-positive bacteria. These results suggest that lipoproteins are essential for not only Gram-negative bacteria but also Gram-positive bacteria and that signal peptidase II inhibitors would probably be effective against all bacteria. Finding such an inhibitor would lead to the development of a new class of antibiotics. Finally, the antifungal activity of these analogues was tested. However, no activity was observed against *Candida albicans*, *Candida glabrata* and *Aspergillus clavatus* (>50 μg/mL).

In summary, new globomycin analogues were synthesized and their antibacterial activities against Gram-negative bacteria were evaluated. SAR studies were conducted based on the NMR spectroscopic analysis of the analogues. Compound **1c** possessing the longest alkyl side chain showed the most potent activity among the synthesized analogues and the antibacterial spectrum was expanded to also includes Gram-positive bacteria. These results were promising in the search to find a more potent and effective antibiotic.

3.1. Measurement of antibacterial activity

Bacteria were inoculated on Nutrient Agar (Eiken Chemical Co., Ltd.) and the MICs of the synthesized analogues were determined by the agar dilution method.[18]

4. Experimental

4.1. General procedure

All moisture-sensitive reactions were carried out under a N_2 atmosphere. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Other anhydrous solvents were purchased from Aldrich or Kanto Kagaku. All reagents were commercially available and used as obtained unless otherwise stated. Preparative flash column chromatography was performed using Merck Silica gel 60 (230–400 mesh). NMR spectra were obtained on a JEOL ECP-500, JNM-GSX-400, Varian Inova-500, Mercury-400. All ^{1}H NMR spectra are reported in ppm downfield from tetramethylsilane as an internal standard. All ^{13}C NMR spectra are reported in ppm relative to the central line for $CDCl_3$ (δ 77.0) or CD_3OD (δ 49.0). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, m = multiplet, br = broadened. In the NMR spectral lists, chemical shifts which are assigned to the minor conformer are marked with an asterisk.

4.1.1. *Fragment A*: (2*R*,3*R*)-3-hydroxy-2-methyltridecanoic acid (1*R*,2*S*)-2-[benzyl-(2,4,6-trimethyl-benzenesulfonyl)amino]-1-phenylpropyl ester (3c). To a stirred solution of (1*R*,2*S*)-**2** (701 mg, 1.46 mmol) in CH_2Cl_2 (15 mL) was added Et_3N (0.52 mL, 3.73 mmol). The solution was cooled to −78 °C and to this was transferred via cannula a solution of *c*-Hex_2BOTf (1.0 M in hexane, 3.05 mL, 3.05 mmol), which was precooled to −78 °C. The resulting solution was stirred at −78 °C for 2 h to complete enolization. A solution of undecylic aldehyde (615 mg, 3.61 mmol) in CH_2Cl_2 (5 mL) was added dropwise to the enolate solution and the reaction mixture was stirred at −78 °C for 4 h and at 0 °C for 2 h. The reaction was quenched by the addition of pH 7 buffer solution (6 mL) followed by CH_3OH (15 mL) and 30% H_2O_2 (1.5 mL). The mixture was stirred overnight vigorously at room temperature. The resulting solution was extracted with ether. The organic extracts were

Table 2. Antibacterial spectra of globomycin (**1a**–**1c**) against Gram-positive bacteria

Compd	MIC (μg/mL)			
	Organism			
	Staphylococcus aureus SANK 70668	*Staphylococcus aureus* SANK 71790	*Staphylococcus aureus* SANK 71890[a]	*Enterococcus faecalis*[a] SANK 71990
Ampicillin	0.78	1.56	>100	12.5
Streptomycin, sulfate	1.56	3.13	>100	100
1a	>100	>100	>100	>100
1b	50	50	50	100
1c	6.25	6.25	12.5	12.5

[a] MRSA.

combined, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was partially purified by silica gel flash column chromatography with a 10:1 mixture of hexane and EtOAc as an eluent to afford a mixture of aldol products (825 mg, 1.27 mmol, 87%, 89% *de*). The ratio of the diastereomers (94.67:5.06:0.25) was determined by HPLC analysis (Daicel Chiralcel AD 0.46 cm×25 cm, *n*-hexane/*i*-PrOH = 92:8, 1.0 mL/min, 40 °C). Purification of the diastereomers by silica gel flash column chromatography with a 10:1 mixture of hexane and EtOAc as an eluent to give compound **3c** as a colorless oil (705 mg, 1.08 mmol, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 0.88 (t, 3H, J = 6.6 Hz), 1.13 (d, 3H, J = 7.3 Hz), 1.18 (d, 3H, J = 7.3 Hz), 1.20–1.47 (m, 19H), 2.28 (s, 3H), 2.43–2.51 (m, 1H); 2.48 (s, 6H), 3.60–3.64 (m, 1H), 4.12 (dq, 1H, J = 7.3 Hz), 4.54 and 4.76 (AB type d's, each 1H, J = 16.9 Hz) 5.83 (d, 1H, J = 4.4 Hz) 6.86-6.88 (m, 4H), 7.16–7.30 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 13.5, 14.1, 20.9, 22.66, 22.69, 25.4, 29.3, 29.6, 29.6, 31.6, 31.9, 34.5, 45.5, 48.3, 56.7, 73.2, 78.2, 126.0, 127.2, 127.7, 128.0, 128.3, 128.4, 132.1, 133.4, 138.2, 138.4, 140.3, 142.6, 174.6; IR ($CHCl_3$) cm^{-1}: 2982, 2928, 2856, 1729, 1605, 1456, 1382, 1322, 1153, 855; HRMS calcd for $C_{39}H_{55}NO_5SNa$ $(M+Na)^+$ calcd 672.3698, found 672.3716; $[\alpha]_D^{25}$ +19.7 (*c* 1.16, $CHCl_3$).

4.1.2. (2*R*,3*R*)-3-hydroxy-2-methyltridecanoic acid (4c). A solution of **3c** (204 mg, 0.313 mmol) and $LiOH{\cdot}H_2O$ (65.9 mg, 1.57 mmol) in THF–CH_3OH–H_2O (2:3:2, 7.0 mL) was stirred at room temperature overnight. The mixture was poured into water (5 mL) and extracted with CH_2Cl_2. The aqueous layer was acidified with 10% aqueous $KHSO_4$ solution and extracted with CH_2Cl_2. The extracts were washed with brine, dried with $MgSO_4$, filtered and evaporated. The residue was purified by silica gel flash column chromatography with a gradient elution system, a 3:1–1:0 mixture of hexane and EtOAc as eluents to give **4c** (65.8 mg, 0.269 mmol, 86%) as a colorless solid (mp 44–45 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.88 (t, 3H, J = 6.9 Hz), 1.25 (d, 3H, J = 7.0 Hz), 1.26–1.50 (m, 16H), 1.50–1.60 (m, 2H), 2.56 (qu, 1H, J = 7.0 Hz), 3.68–3.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 14.1, 14.2, 22.7, 25.4, 29.3, 29.5, 29.6, 31.9, 34.6, 45.2, 73.3, 180.9; IR (KBr) cm^{-1}: 3252, 2916, 2849, 2617, 1710, 1689, 1465, 1283, 1265, 1091; HRMS calcd for $C_{14}H_{29}O_3$ $(M+H)^+$ calcd 245.2117, found 245.2121. Anal. calcd for $C_{14}H_{28}O_3{\cdot}1/6H_2O$: C, 67.97; H, 11.54; Found: C, 68.11; H, 11.79; $[\alpha]_D^{24}$ +2.7 (*c* 1.03, $CHCl_3$).

4.1.3. (4*R*,5*S*)-3-[(2*R*,3*S*)-(3-Hydroxy-2-methylnonanoyl)]-4-methyl-5-phenyloxazolidin-2-one (6). A chiral oxazolidione **5** (2.90 g, 12.4 mmol) was dissolved in CH_2Cl_2 (25 mL) and cooled at 0 °C. To this solution were added *n*-Bu_2BOTf (1.0 M solution in CH_2Cl_2, 13.7 mL, 13.7 mmol) and Et_3N (2.10 mL, 15.1 mmol) at 0 °C. The The resulting solution was stirred at 0 °C for 15 min and at-15 °C for 15 min. After the mixture was cooled to −78 °C, heptanal (1.56 g, 13.7 mmol) was added dropwise to the enolate solution. The reaction mixture was stirred at −78 °C for 2 h, at −10 °C for 20 min and then at 0 °C for 2 h. The reaction was quenched by the addition of aqueous phospahte buffer solution (14 mL) followed by CH_3OH (40 mL) and 30% H_2O_2 (15 mL). The mixture was stirred at 0 °C for 1 h and then evaporated. The resulting solution was extracted with ether. The organic extracts were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by silica gel flash column chromatography with a gradient elution system, a 6:1–5:1 mixture of hexane and EtOAc as eluents to give **6** (4.01 g, 11.5 mmol, 93%) as a colorless crystal (mp 108–109 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89 (t, 3H, J = 7.0 Hz), 0.90 (d, 3H, J = 6.8 Hz), 1.24 (d, 3H, J = 7.0 Hz), 1.29–1.59 (m, 10H), 2.88 (d, 1H, J = 3.0 Hz) 3.78 (dq, 1H, J = 2.7, 7.0 Hz), 3.94–3.99 (m, 1H), 4.80 (qu, 1H, J = 6.8 Hz), 5.69 (d, 1H, J = 7.3 Hz), 7.30–7.32 (m, 2H), 7.36–7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 10.2, 14.1, 14.4, 22.6, 26.0, 29.2, 31.8, 33.9, 42.2, 54.8, 71.6, 78.9, 125.6, 128.8, 128.9, 133.2, 152.6, 177.5; IR (KBr) cm^{-1}: 3462, 2949, 2922, 1787, 1690, 1370, 1346, 1242, 1195, 1154; HRMS calcd for $C_{20}H_{30}NO_4$ $(M+H)^+$ calcd 348.2175, found 348.2177. Anal. calcd for $C_{20}H_{29}NO_4$: C, 69.14; H, 8.41, N, 4.03; Found: C, 69.43; H, 8.38, N, 4.06; $[\alpha]_D^{25}$ +18.0 (*c* 1.14, $CHCl_3$).

4.1.4. (4*R*,5*S*)-3-{(2*R*,3*R*)-(3-Azide-2-methylnonanoyl)}-4-methyl-5-phenyloxazolidin-2-one (8). To a solution of **6** (198 mg, 0.569 mmol) in THF (3.0 mL) were DEAD (99 μL, 0.626 mmol) Ph_3P (164 mg, 0.626 mmol) at room temperature. After being stirred for 5 min, DPPA (35 μL, 0.626 mmol) was added. This reaction mixture was stirred over night and evaporated. The residue was purified by silica gel flash column chromatography with

a 10:1 mixture of hexane and EtOAc as an eluent to give **8** (171 mg, 0.458 mmol, 81%) as a colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.87–0.94 (m, 6H), 1.20 (d, 3H, J = 6.9 Hz), 1.24–1.55 (m, 9H), 1.66–1.74 (m, 1H), 3.70 (dt, 1H, J = 2.8, 9.1 Hz), 3.80–3.88 (m, 1H), 4.83 (qu, 1H, J = 6.9 Hz), 5.72 (d, 1H, J = 7.2 Hz), 7.31–7.33 (m, 2H), 7.36–7.45 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 14.1, 14.3, 14.6, 22.6, 25.6, 29.1, 31.3, 31.7, 42.3, 55.1, 64.9, 79.0, 125.6, 128.76, 128.81, 133.2, 152.6, 174.7; IR ($CHCl_3$) cm^{-1}: 2930, 2859, 2104, 1781, 1698, 1456, 1386, 1345, 1254, 1121; HRMS calcd for $C_{20}H_{29}N_4O_3$ $(M+H)^+$ 373.2240, found 373.2249; $[\alpha]_D^{26}$ −5.12 (*c* 1.35, $CHCl_3$).

4.1.5. (2*R*,3*R*)-3-Boc-amino-2-methylnonanoic acid (9). Compound **8** (193 mg, 0.518 mmol) was dissolved in THF–H_2O (4:1.3, 4.3 mL). To this solution were added $LiOH{\cdot}H_2O$ (44.0 mg, 1.04 mmol) and 30% aqueous H_2O_2 (0.1 mL) at °C. After being stirred at the same temperature for 2 h, 10% $Na_2S_2O_3$ aqueous solution was added. The reaction mixture was acidified with 10% aqueous $KHSO_4$ solution and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and evaporated to give (2*R*,3*R*)-3-azide-2-methyltnonanoic acid (83.5 mg, 0.391 mmol, 76%) as a colorless oil.

This azide (280 mg, 1.31 mmol) and Boc_2O (343 mg, 1.57 mmol) were dissolved in EtOAc (3.0 mL). To this solution, 10% Pd/C (cat) was added and the resulting mixture was stirred at room temperature for 10 h under H_2 atmosphere. Pd/C was removed by filtration and the filtrate was evaporated. The residue was purified by column chromatography with a gradient elution system, a 1:0-20:1 mixture of CH_2Cl_2 and CH_3OH as eluents to give **9** (231 mg, 3.95 mmol, 61%) as a colorless solid (mp, 84 °C). ^{1}H NMR (400 MHz, $CDCl_3$, two conformers (major/minor = 3.0/1)) δ ppm: 0.86–0.89 (m, 3H), 1.17–1.31 (m, 13H), 1.44 (s, 27/4H), 1.46 (s, 9/4H), 2.63-2.74 (m, 1H), 3.65-3.78 (m, 1H), 5.06 (br d, 3/4H, J = 10.0 Hz), 5.56 (br d, 1/4H, J = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 14.1, 14.6, 16.8, 22.56, 22.64, 26.3, 27.2, 28.2, 28.4, 29.06, 29.14, 29.5, 31.7, 31.8, 33.5, 34.0, 39.3, 42.9, 52.5, 79.2, 80.3, 156.1, 180.6; IR (KBr) cm^{-1}: 3211, 2979, 2926, 1726, 1687, 1519, 1461, 1388, 1249, 1178; HRMS calcd for $C_{15}H_{29}NO_4Na$ $(M+Na)^+$ 310.1994, found 310.2008. Anal. calcd for $C_{15}H_{29}NO_4$: C, 62.69; H, 10.17; N, 4.87; Found: C 62.98; H, 10.51; N, 4.76; $[\alpha]_D^{25}$ +11.7 (*c* 1.64, $CHCl_3$).

4.1.6. (*R*)-3-Hydroxynonanoic acid (11). Methyl 3-oxononanoate (**10**) (1.38 g, 7.41 mmol) was placed in a dry Schlenk and dissolved in CH_3OH (15 mL). To this solution was added the in situ prepared (*R*)-BINAP-Ru complex (24.5 mg) under N_2 atmosphere. The resulting solution was transferred by cannula to autoclave with N_2 gas. Hydrogen was introduced into the reaction vessel until the pressure gauge indicated 6 atm. This mixture was vigorously stirred at 100 °C for 4 h. After the reaction mixture was cooled, hydrogen was carefully released. The mixture was evaporated and the oil residue was purified by silica gel flash column chromatography with a gradient elution system, a 10:1–8:1 mixture of hexane and EtOAc as eluents to give methyl (*R*)-3-hydroxynonanoate (1.34 g, 7.12 mmol, 96%) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.88 (t, 3H, J = 7.0 Hz), 1.25–1.38 (m, 7H), 1.38–1.56 (m, 3H), 2.41 (dd, 1H, J = 8.9, 16.3 Hz) 2.52 (dd, 1H, J = 3.3, 16.3 Hz), 2.87 (br s, 1H), 3.72 (s, 3H), 3.97–4.04 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 14.0, 22.6, 25.4, 29.2, 31.7, 36.5, 41.1, 51.7, 68.0, 173.5; IR ($CHCl_3$) cm^{-1}: 3596, 2956, 2931, 2859, 1724, 1439, 1404, 1335, 1267, 1174; HRMS calcd for $C_{10}H_{21}O_3$ $(M+H)^+$ calcd 189.1491, found 189.1481; $[\alpha]_D^{24}$−20.0 (*c* 1.33, $CHCl_3$).

To the solution of this ester (557 mg, 2.96 mmol) in CH_3OH (20.0 mL) was added 1 N NaOH aqueous solution (6.0 mL, 6.0 mmol) at 0 °C. The mixture was stirred at the same temperature for 30 min and at room temperature for an additional 3 h. The solution was acidified with 5% aqueous HCl solution and extracted with EtOAc. The organic extracts were washed with brine, dried with $MgSO_4$, filtered and evaporated to give **11** (514 mg, 2.95 mmol, 100%) as a colorless solid (mp 49–50 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89 (t, 3H, J = 7.1 Hz), 1.25–1.40 (m, 7H), 1.40–1.50 (m, 2H), 1.52–1.60 (m, 1H), 2.48 (dd, 1H, J = 8.9, 16.3 Hz) 2.58 (dd, 1H, J = 3.4, 16.3 Hz), 4.01–4.07 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 14.0, 22.6, 25.4, 29.1, 31.7, 36.5, 41.0, 68.0, 177.8; IR (KBr) cm^{-1}: 3481, 3121, 2956, 2927, 2857, 1740, 1717, 1683, 1414, 1176; HRMS calcd for $C_9H_{19}O_3$ $(M+H)^+$ calcd 175.1334, found 175.1322. Anal. calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41; Found: C, 61.75; H, 10.20; $[\alpha]_D^{24} = -20.5$ (*c* 1.14, $CHCl_3$).

4.1.7. *Fragment B*: Boc-L-Thr(Me)-OH (12b). Boc-L-*allo*-Thr-OBn (2.19 g, 7.08 mmol) was dissolved in CH_2Cl_2 (40 mL) and cooled at 0 °C. To this solution were added Me_3OBF_4 (1.57 g,10.6 mmol) and then Proton-Sponge (2.28 g, 10.6 mmol). After being stirred at 0 °C for 2 h and at room temperature for an additional 10 h, the reaction mixture was filtered and the filtrate was washed with 10% $KHSO_4$, saturated $NaHCO_3$ aqueous solution and brine. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The oil residue was purified by column chromatography with a 6:1 mixture of hexane and EtOAc as an eluent to give benzyl ester of **12b** (1.23 g, 3.80 mmol, 54%) as a colorless oil.

This ester (1.06 g, 3.28 mmol) was dissolved in CH_3OH (15 mL). To this solution, 10% Pd/C (100 mg) was added and the resulting mixture was stirred at room temperature for 4 h under H_2 atmosphere. Pd/C was removed by filtration and the filtrate was evaporated to give **12b** (0.76 g, 3.26 mmol, 99%) as a colorless oil. ^{1}H NMR (400 MHz, CD_3OD) δ ppm: 1.16 (d, 3H, J = 6.3 Hz), 1.45 (s, 9H), 3.35 (s, 3H), 3.63–3.72 (m, 1H), 4.34 (d, 1H, J = 4.7 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: 15.8, 28.7, 57.0, 57.9, 78.2, 80.7, 97.3, 158.0, 174.0; IR ($CHCl_3$) cm^{-1}: 3442, 2982, 2934, 1759, 1713, 1501, 1393, 1369, 1252, 1163; HRMS calcd for $C_{10}H_{20}NO_5$ $(M+H)^+$ 234.1341, found 234.1333; $[\alpha]_D^{24}$−3.9 (*c* 1.11, CH_3OH).

4.1.8. Boc-L-Thr(TBS)-Gly-OBn (14b). To the solution of Boc-L-Threonine (**12a**) (2.00 g, 9.13 mmol) in CH_2Cl_2 (18 mL) were added Et_3N (3.8 mL, 27.2 mmol) and TBSOTf (5.2 mL, 22.6 mmol) at 0 °C. The mixture was stirred at the same temperature for 2 h. After being stirred at room temperature for an additional 2 h, aqueous K_2CO_3 solution was added. The resulting mixture was vigorously stirred over night. The solution was acidified with 10% aqueous $KHSO_4$ solution and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude oil was purified by column chromatography with a 4:1 mixture of hexane and EtOAc as an eluent to give Boc-L-*allo*-Thr(TBS)-OH (2.69 g, 8.05 mmol, 88%) as a colorless solid (mp 129–130 °C).

This product (2.46 g, 7.37 mmol) and glycine benzyl ester *p*-toluenesulfonate (**13**) (2.50 g, 7.41 mmol) were dissolved in CH_2Cl_2 (30 mL) and then Et_3N (2.55 mL, 18.2 mmol) and 1-hydroxybenzotriazole (1.23 g, 9.10 mmol) were added. To the solution was added EDCI·HCl (1.55 g, 8.09 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for an additional 13 h. After a saturated $NaHCO_3$ aqueous solution was added, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography with a gradient elution system, a 5:1–4:1 mixture of hexane and EtOAc as eluents to give **14b** (3.08 g, 6.41 mmol, 87%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.08 (s, 3H), 0.10 (s, 3H), 0.87 (s, 9H), 1.13 (d, 3H, J = 6.2 Hz), 1.46 (s, 9H), 4.03 (dd, 1H, J = 4.5, 18.5 Hz), 4.12–4.18 (m, 2H), 4.40 (dq, 1H, J = 2.8, 6.3 Hz), 5.19 (s, 2H), 5.31 (d, 1H, J = 6.3 Hz), 7.16 (br s, 1H), 7.31–7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.1, −4.7, 17.9, 18.9, 25.7, 28.3, 41.4, 59.4, 67.2, 68.3, 80.1, 128.4, 128.5, 128.6, 135.2, 155.8, 169.3, 170.4; IR ($CHCl_3$) cm^{-1}: 3423, 2980, 2956, 2931, 2858, 1747, 1713, 1678, 1485, 1167; HRMS calcd for $C_{24}H_{41}N_2O_6Si$ $(M+H)^+$ calcd 481.2734, found 481.2735; $[\alpha]_D^{25}$ +3.5 (*c* 1.07, $CHCl_3$).

4.1.9. Boc-L-*allo*-Thr(TBS)-*N*-Me-Gly-OBn (14c). 85%, a slightly yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, two rotamers (major/minor = 2.7/1)) δ ppm: −0.04* (s, 3/4H), −0.03 (s, 9/4H), 0.03* (s, 3/4H), 0.04 (s, 9/4H), 0.83* (s, 9/4H), 0.84 (s, 27/4H), 1.21 (d, 3H, J = 6.1 Hz), 1.40* (s, 9/4H), 1.42 (s, 27/4H), 2.98* (s, 3/4H), 3.19 (s, 9/4H), 3.75 (d, 3/4H, J = 17.3 Hz), 3.81–3.90 (m, 5/4H), 4.39* (t, 1/4H, J = 9.2 Hz), 4.58 (d, 3/4H, J = 17.3 Hz), 6.25 (t, 3/4H, J = 8.6 Hz), 4.73* (d, 1/4H, J = 18.5 Hz), 5.15 and 5.16 (AB type d's, each 1H, J = 12.3 Hz), 5.25 (d, 1H, J = 9.8 Hz), 7.30–7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamer) δ ppm: −5.2, −5.0, −4.81, −4.77, 14.1, 17.81, 17.84, 20.5, 20.7, 25.63, 25.67, 28.27, 28.31, 31.6, 35.2, 36.9, 49.6, 51.9, 55.4, 55.6, 66.9, 67.3, 70.8, 71.4, 77.5, 79.5, 79.6, 128.3, 128.4, 128.6, 135.2, 135.3, 155.0, 155.2, 168.61, 168.64, 172.5, 172.8; IR ($CHCl_3$) cm^{-1}: 3434, 2957, 2931, 2858, 1749, 1710, 1650, 1499, 1258, 1170; HRMS calcd for $C_{25}H_{43}N_2O_6Si$ $(M+H)^+$ calcd 495.2891, found 495.2874; $[\alpha]_D^{25}$ +13.1 (*c* 1.12, $CHCl_3$).

4.1.10. Boc-L-Abu-Gly-OBn (14d). 97%, a colorless crystal (mp, 80–81 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.95 (t, 3H, J = 7.5 Hz), 1.44 (s, 9H), 1.59–1.71 (m, 1H), 1.83–1.94 (m, 1H), 4.03–4.15 (m, 1H), 4.09 (d, 2H, J = 5.5 Hz), 5.02 (br d, 1H, J = 4.6 Hz), 5.18 (s, 2H), 6.64 (br s, 1H), 7.34–7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 9.9, 25.7, 28.3, 41.3, 55.7, 67.2, 80.1, 128.4, 128.55, 128.64, 135.1, 155.7, 169.5, 172.3; IR (KBr) cm^{-1}: 3321, 2970, 1739, 1684, 1658, 1555, 1529, 1278, 1254, 1172. Anal. calcd for $C_{18}H_{26}N_2O_5$: C, 61.70; H, 7.48; N, 7.99; Found: C, 61.73; H, 7.57; N, 7.87; HRMS calcd for $C_{18}H_{27}N_2O_5$ $(M+H)^+$ 351.1920, found 351.1912; $[\alpha]_D^{24}$ −20.2 (*c* 1.39, $CHCl_3$).

4.1.11. Boc-L-*allo*-Thr(Me)-Gly-OBn (14e). 98%, a colorless solid (mp 74–76 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 1.20 (d, 3H, J = 6.3 Hz), 1.45 (s, 9H), 3.34 (s, 3H), 3.60–3.66 (m, 1H), 4.10 (d, 2H, J = 5.2 Hz), 4.25 (br t, 1H, J = 6.6 Hz), 5.15 (br s, 1H), 5.18 (s, 2H), 6.85 (br s, 1H), 7.30–7.41 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 15.2, 28.2, 41.2, 41.3, 56.6, 67.2, 80.3, 128.4, 128.5, 128.6, 135.1, 155.8, 169.4, 170.6; IR (KBr) cm^{-1}: 3329, 2982, 2934, 1740, 1681, 1657, 1534, 1369, 1307, 1175; HRMS calcd for $C_{19}H_{29}N_2O_6$ $(M+H)^+$ 381.2026, found 381.2027. Anal. calcd for $C_{19}H_{28}N_2O_6$: C, 59.99; H, 7.42; N, 7.36; Found: C 59.89; H, 7.42; N, 7.34; $[\alpha]_D^{24}$−7.4 (*c*1.27, $CHCl_3$).

4.1.12. Boc-L-Thr(TBS)-Gly-OH (15b). Compound **14b** (1.93 g, 4.02 mmol) was dissolved in C_2H_5OH (15 mL). To this solution, 10% Pd/C (210 mg) was added and the resulting mixture was stirred at room temperature for 2.5 h under H_2 atmosphere. Pd/C was removed by filtration and the filtrate was evaporated to give **15b** (1.54 g, 3.95 mmol, 98%) as a colorless amorphous foam. ^{1}H NMR (400 MHz, CD_3OD) δ ppm: 0.04 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.18 (d, 3H, J = 6.3 Hz), 1.47 (s, 9H), 3.84 (d, 1H, J = 17.9 Hz), 4.01 (d, 1H, J = 17.9 Hz), 4.07 (d, 1H, J = 3.0 Hz), 4.34 (dq, 1H, J = 3.0, 6.3 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: −4.9, −4.5, 18.8, 20.9, 26.3, 28.7, 41.9, 61.5, 70.2, 81.1, 157.8, 172.4, 173.2; IR (KBr) cm^{-1}: 3332, 2955, 2931, 2858, 1722, 1668, 1505, 1255, 1170, 837; HRMS calcd for $C_{17}H_{35}N_2O_6Si$ $(M+H)^+$ calcd 391.2264, found 391.2266. Anal. calcd for $C_{17}H_{34}N_2O_6Si{\cdot}1/5H_2O$: C, 51.80; H, 8.80; N, 7.11; Found: C, 51.82; H, 8.52; N, 7.33; $[\alpha]_D^{24}$ = −0.7 (*c* 1.09, CH_3OH).

4.1.13. Boc-L-*allo*-Thr(TBS)-*N*-Me-Gly-OH (15c). 99%, a colorless amorphous foam, ^{1}H NMR (400 MHz, CD_3OD, two rotamers (major/minor = 2.0/1)) δ ppm: 0.004 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.17–1.20 (m, 3H), 1.41* (s, 3H), 1.43 (s, 6H), 2.96* (s, 1H), 3.23 (s, 2H), 3.80 (d, 2/3H, J = 17.2 Hz), 3.92–4.05 (m, 4/3H), 4.36 (d, 1H, J = 17.2 Hz), 4.53–4.61 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD, both rotamer) δ ppm: −4.8, −4.5, −4.4, −3.6, 14.4, 18.7, 20.9, 23.7, 26.2, 26.3, 28.0, 28.7, 32.7, 35.6, 37.5, 50.7, 52.5, 57.1, 70.9, 71.5, 80.6, 80.7, 97.3, 157.5, 172.0, 172.1, 174.3, 174.4; IR ($CHCl_3$) cm^{-1}: 3432, 2981, 2957, 2931, 2859, 1711, 1651, 1500, 1257, 1164; HRMS calcd for $C_{18}H_{37}N_2O_6Si$ $(M+H)^+$ calcd 405.2421, found 405.2447. Anal. calcd for $C_{18}H_{36}N_2O_6Si{\cdot}1/5H_2O$: C, 52.97; H, 8.99; N, 6.86;

Found: C, 52.82; H, 9.07; N, 6.65; $[\alpha]_D^{25}$ −2.1 (*c* 1.11, CH_3OH).

4.1.14. Boc-L-Abu-Gly-OH (15d). 100%, a colorless amorphous foam, ^1H NMR (400 MHz, CD_3OD) δ ppm: 0.97 (t, 3H, *J* = 7.4 Hz), 1.44 (s, 9H), 1.56–1.68 (m, 1H), 1.77–1.87 (m, 1H), 3.86 and 3.96 (AB type d's, each 1H, *J* = 17.8 Hz), 3.97–4.00 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: 10.6, 26.7, 28.7, 41.8, 57.4, 80.6, 157.9, 172.7, 175.5; IR ($CHCl_3$) cm^{-1}: 3433, 3368, 2980, 2936, 1730, 1672, 1502, 1370, 1251, 1162; HRMS calcd for $C_{11}H_{21}N_2O_5$ $(M+H)^+$ 261.1450, found 261.1463; $[\alpha]_D^{24}$ −26.4 (*c* 1.18, CH_3OH).

4.1.15. Boc-L-*allo*-Thr(Me)-Gly-OH (15e). 100%, a colorless solid, (mp 50 °C), ^1H NMR (400 MHz, CD_3OD) δ ppm: 1.15 (d, 3H, *J* = 6.3 Hz), 1.45 (s, 9H), 3.35 (s, 3H), 3.65–3.68 (m, 1H), 3.92 and 3.94 (AB type d's, each 1H, *J* = 17.8 Hz), 4.33 (br d, 1H, *J* = 4.8 Hz), ^{13}C NMR (125 MHz, CD_3OD) δ pm: 15.5, 28.7, 41.8, 57.0, 58.5, 78.1, 80.8, 97.3, 157.9, 172.6, 173.3; IR (KBr) cm^{-1}: 3322, 3091, 2980, 2935, 1719, 1663, 1528, 1368, 1248, 1168; HRMS calcd for $C_{12}H_{23}N_2O_6$ $(M+H)^+$ 291.1556, found 291.1565. Anal. calcd for $C_{12}H_{22}N_2O_6$: C, 49.65; H, 7.64; N, 9.65; Found: C 49.36; H, 7.85; N, 9.43; $[\alpha]_D^{25}$ −13.0 (*c* 1.03, CH_3OH).

4.1.16. *Fragment C*: L-Ser(Me)-OBn·HCl (17a). The benzyl ester (2.87 g, 9.28 mmol) prepared from Boc-L-Ser(Me)-OH (**16a**) was treated with 4 N HCl in EtOAc (40 mL) and the mixture was stirred at room temperature for 2 h. The solvents were removed in vacuo and dissolved in EtOAc. The mixture was evaporated and dissolved in EtOAc again. This procedure was repeated tree times and the resulting crude product was dried under reduced pressure to give a hydrochloride salt (2.28 g, 9.28 mmol, 100%) as a colorless solid (mp 101–102 °C). ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 3.34 (s, 3H), 3.92 (dd, 1H, *J* = 3.6, 10.4 Hz), 4.03 (dd, 1H, *J* = 2.7, 10.4 Hz), 4.45 (br s, 1H), 5.16 and 5.29 (AB type d's, each 1H, *J* = 12.2 Hz), 7.28–7.37 (m, 5H), 8.77 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 53.6, 59.3, 68.2, 69.2, 128.3, 128.58, 128.60, 134.7, 167.5; IR (KBr) cm^{-1}: 2941, 2883, 1963, 1753, 1576, 1487, 1225, 1107, 968; HRMS calcd for $C_{11}H_{16}NO_3$ $(M+H)^+$ 210.1130, found 210.1119. Anal. calcd for $C_{11}H_{16}ClNO_3$: C, 53.77; H, 6.56; N, 5.74; Cl, 14.43; Found: C, 53.44; H, 6.59; N, 5.74; Cl, 14.72; $[\alpha]_D^{25}$ −23.1 (*c* 1.15, $CHCl_3$).

4.1.17. Boc-L-*allo*-Ile-L-Ser(Me)-OBn (18a). Compound **17** (2.22 g, 9.04 mmol) and Boc-L-Ile-OH (1.99 g, 8.60 mmol) were dissolved in CH_2Cl_2 (30 mL). To this solution were added Et_3N (3.02 mL, 21.7 mmol) and PyBOP (4.70 g, 9.04 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for an additional 10 h. After saturated $NaHCO_3$ aqueous solution was added, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and evaporated. The oil residue was purified by column chromatography with a gradient elution system, a 3:1–1:1 mixture of hexane and EtOAc as eluents to give **18a** (3.63 g, 8.61 mmol, 95%) as a colorless solid (mp 56–57 °C). ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.84 (d, 3H, *J* = 7.1 Hz), 0.92 (t, 3H, *J* = 7.4 Hz), 1.44 (s, 9H), 1.92 (br s, 1H), 3.29 (s, 3H), 3.60 (dd, 1H, *J* = 3.1, 9.4 Hz), 3.84 (dd, 1H, *J* = 3.0, 9.4 Hz), 4.18 (brd, 1H, *J* = 3.8 Hz), 4.76–4.80 (m, 1H), 5.05 (br d, 1H, *J* = 8.1 Hz), 5.14 and 5.26 (AB type d's, each 1H, *J* = 12.3 Hz), 6.64 (br d, 1H, *J* = 6.9 Hz), 7.39–7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.1, 26.3, 38.3, 37.8, 52.7, 57.9, 59.2, 67.3, 72.1, 79.9, 128.2, 128.4, 128.6, 135.3, 155.8, 169.9, 171.6; IR (KBr) cm^{-1}: 3321, 2967, 2932, 1746, 1658, 1522, 1366, 1243, 1168; HRMS calcd for $C_{22}H_{35}N_2O_6$ $(M+H)^+$ 423.2495, found 423.2495. Anal. calcd for $C_{22}H_{34}O_6N_2$: C, 62.54; H, 8.11; N, 6.03; Found: C, 62.43; H, 7.89; N, 6.71; $[\alpha]_D^{24}$ +3.5 (*c* 1.44, $CHCl_3$).

4.1.18. Boc-L-Ile-L-Ser(Bn)-OAllyl (18g). 99%, a colorless solid, (mp 59–60 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.91 (t, 3H, *J* = 7.4 Hz), 0.95 (d, 3H, *J* = 6.7 Hz), 1.10–1.21 (m, 1H), 1.40–1.52 (m, 1H), 1.45 (s, 9H), 1.85–1.92 (m, 1H), 3.68 (dd, 1H, *J* = 3.3, 9.5 Hz), 3.93 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.04 (br t, 1H, *J* = 6.5 Hz), 4.48 and 4.55 (AB type d's, each 1H, *J* = 12.2 Hz), 4.60–4.69 (m, 2H), 4.77 (dt, 1H, *J* = 3.0, 8.0 Hz), 5.08 (br d, 1H, *J* = 7.9 Hz), 5.23 (dt, 1H, *J* = 1.2, 10.3 Hz), 5.31 (dt, 1H, *J* = 1.3, 17.5 Hz), 5.82–9.92 (m, 1H), 6.63 (br d, 1H, *J* = 7.5 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.5, 15.4, 24.6, 28.3, 37.7, 52.6, 59.1, 66.2, 69.6, 73.3, 79.8, 118.8, 127.7, 127.9, 128.4, 131.5, 137.4, 155.6, 169.6, 171.2; IR (KBr) cm^{-1}: 3334, 2966, 2934, 1747, 1687, 1652, 1548, 1524, 1245, 1173; HRMS calcd for $C_{24}H_{37}N_2O_6$ $(M+H)^+$ calcd 449.2652, found 449.2651. Anal. calcd for $C_{24}H_{36}N_2O_6$: C, 64.26; H, 8.09; N, 6.25; Found: C, 64.48; H, 8.15; N, 6.25; $[\alpha]_D^{27}$ +8.6 (*c* 1.01, $CHCl_3$).

4.1.19. Boc-19a. Deprotection procedure of Boc group in **18a** was almost the same in the synthesis of **17a** to give a hydrochloride salt (3.00 g) as a colorless solid (mp 169 °C).

This salt (1.53 g, 4.28 mmol) and Boc-*N*-Me-L-leucine (1.10 g, 4.49 mmol) were dissolved in CH_2Cl_2 (15 mL). To this solution were added Et_3N (1.43 mL, 10.3 mmol) and PyBOP (2.34 g, 4.49 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for an additional 10 h. After a saturated $NaHCO_3$ aqueous solution was added, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and evaporated. The oil residue was purified by column chromatography with a 2:1 mixture of hexane and EtOAc as an eluent to give Boc-**19a** (2.26 g, 41.1 mmol, 96%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.83 (d, 3H, *J* = 6.8 Hz), 0.89 (t, 3H, *J* = 6.9 Hz), 0.91 (d, 3H, *J* = 6.5 Hz), 0.95 (d, 3H, *J* = 6.6 Hz), 1.06–1.17 (m, 1H), 1.33–1.46 (m, 2H), 1.48 (s, 9H), 1.65–1.71 (m, 2H), 1.83–1.97 (m, 1H), 2.75 (s, 3H), 3.29 (s, 3H), 3.58 (dd, 1H, *J* = 3.2, 9.0 Hz), 3.84 (br d, 1H, *J* = 8.3 Hz), 4.49 (dd, 1H, *J* = 4.4, 9.0 Hz), 4.63–4.68 (m, 1H), 4.75–4.77 (m, 1H), 5.13 and 5.25 (AB type d's, each 1H, *J* = 12.2 Hz), 6.47 (br s, 1H), 6.66–6.74 (m, 1H), 7.31–7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$)

δ ppm: 11.7, 14.2, 22.1, 23.1, 23.2, 24.5, 24.8, 26.3, 28.4, 29.6, 29.9, 36.2, 36.3, 37.3, 52.6, 56.1, 59.2, 67.3, 72.0, 80.5, 128.2, 128.4, 128.6, 135.3, 156.8, 169.8, 171.0, 170.1, 171.5; IR ($CHCl_3$) cm^{-1}: 3432, 296ss4, 2934, 1746, 1676, 1501, 1390, 1323, 1152, 1118; HRMS calcd for $C_{29}H_{48}N_3O_3$ $(M+H)^+$ 550.3492, foundd 550.3462; $[\alpha]_D^{26}$ −61.3 (*c* 1.27, $CHCl_3$).

4.1.20. *N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Me)-OBn (19a). Compound **Boc-19a** (2.19 g, 3.98 mmol) was treated with 4N HCl in EtOAc (20 mL) and the mixture was stirred at room temperature for 1.3 h. The reaction mixture was concentrated under reduced pressure, diluted with EtOAc and washed with saturated $NaHCO_3$ aqueous solution. The organic layer was dried over Na_2SO_4, filtered and evaporated to give **19a** (1.66 mg, 3.69 mmol, 93%) as a colorless solid (mp, 110–111 °C). This free amine was directly used in the following reaction without further purification. ^1H NMR (400 MHz, CD_3OD) δ ppm: 0.86–0.91 (m, 12H), 0.94 (d, 1H, $J=6.6$ Hz), 1.10–1.21 (m, 1H), 1.35–1.52 (m, 3H), 1.60–1.70 (m, 1H), 1.84–1.94 (m, 1H), 2.31 (s, 3H), 3.13 (t, 1H, $J=7.2$ Hz), 3.32 (s, 3H), 3.62 (dd, 1H, $J=3.7$, 9.6 Hz), 3.80 (dd, 1H, $J=5.0$, 9.6 Hz), 4.51 (d, 1H, $J=6.0$ Hz), 4.67 (t, 1H, $J=4.3$ Hz), 4.13 and 5.21 (AB type d's, each 1H, d, $J=12.2$ Hz), 7.29–7.40 (m, 5H); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: 11.9, 14.8, 22.9, 23.1, 25.7, 27.4, 33.7, 38.6, 42.8, 54.2, 57.9, 59.3, 63.0, 68.1, 72.7, 129.28, 129.33, 129.5, 137.1, 171.1, 173.3; IR (KBr) cm^{-1}: 3287, 2960, 2930, 1742, 1634, 1547, 1456, 1390, 1208, 1118; HRMS calcd for $C_{24}H_{40}N_3O_5$ $(M+H)^+$ 450.5916, found 450.2954. Anal. calcd for $C_{24}H_{39}N_3O_5$: C, 64.12; H, 8.74; N, 9.35; Found: C, 64.44; H, 8.72; N, 9.36; $[\alpha]_D^{25}$ −23.0 (*c* 1.07, $CHCl_3$).

4.1.21. Boc-19c. 94%, a colorless oil, ^1H NMR (400 MHz, CD_3OD) δ ppm: 0.88–0.95 (m, 12H), 1.11 (t, 3H, $J=7.0$ Hz), 1.24–1.34 (m, 2H), 1.45–1.55 (m, 2H), 1.49 (s, 9H), 1.64–1.67 (m, 1H), 1.88–1.98 (m, 1H), 3.15–3.30 (m, 2H), 3.74 (dd, 1H, $J=3.7$, 9.6 Hz), 3.89 (dd, 1H, $J=5.1$, 9.6 Hz), 4.47 (d, 1H, $J=5.1$ Hz), 4.48 and 4.57 (AB type d's, each 1H, $J=11.8$ Hz), 4.62–4.64 (m, 3H), 4.69 (dd, 1H, $J=3.8$, 4.8 Hz), 5.20 (dd, 1H, $J=1.4$, 11.6 Hz), 5.32 (dd, 1H, $J=1.4$, 17.6 Hz), 5.85–5.95 (m, 1H), 7.27–7.33 (m, 5H); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: 12.0, 14.4, 14.8, 23.3, 23.7, 26.0, 27.4 28.7, 32.7, 38.7, 54.3, 57.6, 67.0, 70.4, 74.2, 97.3, 118.7, 128.8, 128.9, 129.4, 133.2, 139.1, 170.9, 173.6; IR ($CHCl_3$) cm^{-1}: 3432, 2964, 2874, 1746, 1676, 1502, 1368, 1287, 1156, 1115; HRMS calcd for $C_{32}H_{51}N_3O_7Na$ $(M+Na)^+$ 612.3625, found 612.3635; $[\alpha]_D^{24}$ −49.4 (*c* 1.38, $CHCl_3$).

4.1.22. *N*-Et-L-Leu-L-*allo*-Ile-L-Ser(Me)-OBn (19c). 97%, a colorless solid (mp 112–113 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.90 (d, 3H, $J=6.7$ Hz), 0.92–1.01 (m, 9H), 1.08 (t, 3H, $J=7.0$ Hz), 1.11–1.26 (m, 1H), 1.35–1.49 (m, 2H), 1.56–1.77 (m, 3H), 1.94–2.06 (m, 1H), 2.55–2.68 (m, 2H), 3.14 (dd, 1H, $J=4.5$, 9.2 Hz), 3.67 (dd, 1H, $J=3.2$, 9.3 Hz), 3.93 (dd, 1H, $J=3.2$, 9.3 Hz), 4.46–4.49 (m, 1H), 4.47 and 4.56 (AB type d's, each 1H, $J=12.2$ Hz), 4.59–4.73 (m, 2H), 4.75–4.79 (m, 1H), 5.23 (dd, 1H, $J=1.3$, 8.5 Hz), 5.30 (dd, 1H, $J=1.3$, 17.5 Hz), 5.81–5.91 (m, 1H), 6.62 (d, 1H, $J=8.2$ Hz), 7.25–7.36 (m, 5H), 7.88 (d, 1H, $J=9.1$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.3, 15.4, 21.8, 23.2, 25.2, 26.4, 37.6, 43.1, 43.2, 52.6, 55.8, 61.6, 66.2, 69.6, 73.3, 118.7, 127.6, 127.8, 128.4, 131.5, 137.4, 169.6, 171.2; IR (KBr) cm^{-1}: 3282, 3070, 2959, 2872, 1740, 1633, 1551, 1393, 1215, 1102; HRMS calcd for $C_{27}H_{44}N_3O_5$ $(M+H)^+$ 490.3281, found 490.3291. Anal. calcd for $C_{27}H_{43}N_3O_5$: C, 66.23; H, 8.85; N, 8.58; Found: C 66.03; H, 8.64; N, 8.68; $[\alpha]_D^{25}$ −11.7 (*c* 1.04, $CHCl_3$).

4.1.23. Boc-19d. 95%, a colorless solid (mp, 108–109 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.90–0.94 (m, 12H), 1.12–1.23 (m, 1H), 1.38–1.53 (m, 2H), 1.44 (s, 9H), 1.63–1.68 (m, 2H), 1.96 (br, 1H), 3.65 (dd, 1H, $J=3.2$, 9.5 Hz), 3.93 (dd, 1H, $J=3.1$, 9.5 Hz), 4.11 (br, 1H), 4.49 (dd, 1H, $J=4.8$, 8.9 Hz), 4.47 and 4.56 (AB type d's, each 1H, $J=12.1$ Hz), 4.59–4.68 (m, 2H), 4.75 (dt, 1H, $J=3.4$, 8.4 Hz), 4.88 (br d, 1H, $J=7.3$ Hz), 5.23 (dd, 1H, $J=1.3$, 10.6 Hz), 5.30 (dt, 1H, $J=1.3$, 16.9 Hz), 5.81–5.91 (m, 1H), 6.63 (br d, 1H, $J=7.6$ Hz), 6.68 (br d, 1H, $J=8.2$ Hz), 7.26–7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.2, 22.0, 22.9, 24.7, 26.1, 28.3, 37.8, 40.6, 52.6, 53.2, 56.4, 66.2, 69.5, 73.3, 80.1, 118.8, 127.7, 127.9, 128.4, 131.5, 137.3, 155.7, 169.5, 171.8, 172.5; IR (KBr) cm^{-1}: 3283, 2961, 2932, 2874, 1745, 1695, 1644, 1543, 1523, 1173; HRMS calcd for $C_{30}H_{48}N_3O_7$ $(M+H)^+$ calcd 562.3492, found 562.3492. Anal. calcd for $C_{30}H_{47}N_3O_7$: C, 64.15; H, 8.43; N, 7.48; Found: C, 64.11; H, 8.65; N, 7.53; $[\alpha]_D^{28}=-23.5$ (*c* 1.18, $CHCl_3$).

4.1.24. L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (19d). 98%, a colorless solid (mp, 90–91 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89–0.99 (m, 12H), 1.13–1.24 (m, 1H), 1.31–1.39 (m, 1H), 1.41–1.51 (m, 1H), 1.57–1.80 (m, 4H), 1.93–2.02 (m, 1H), 3.43 (dd, 1H, $J=3.1$, 9.5 Hz), 3.68 (dd, 1H, $J=3.1$, 9.5 Hz), 3.93 (dd, 1H, $J=3.1$, 9.5 Hz), 4.46 (dd, 1H, $J=5.1$, 9.1 Hz), 4.48 and 4.55 (AB type d's, each 1H, $J=12.2$ Hz), 4.59–4.69 (m, 2H), 4.75 (dt, 1H, $J=3.1$, 8.0 Hz), 5.24 (dd, 1H, $J=1.2$, 10.3 Hz), 5.29–5.34 (m, 1H), 5.82–5.92 (m, 1H), 6.69 (d, 1H, $J=8.1$ Hz), 7.26–7.36 (m, 5H), 7.86 (d, 1H, $J=9.1$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.4, 21.3, 23.4, 24.9, 26.3, 37.6, 44.1, 52.6, 53.7, 56.1, 66.2, 69.5, 73.3, 118.8, 127.7, 127.9, 128.4, 131.4, 137.3, 169.7, 171.3, 175.7; IR (KBr) cm^{-1}: 3299, 2959, 2932, 2873, 1743, 1636, 1546, 1237, 1210, 1106; HRMS calcd for $C_{25}H_{40}N_3O_5$ $(M+H)^+$ calcd 462.2968, found 462.2975. Anal. calcd for $C_{25}H_{39}N_3O_5$: C, 65.05; H, 8.52; N, 9.10; Found: C, 64.84; H, 8.65; N, 8.90; $[\alpha]_D^{23}$ –13.3 (*c* 1.08, $CHCl_3$).

4.1.25. Boc-19e. 97%, a colorless solid, (mp 56–58 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.87–0.91 (m, 6H), 1.11–1.22 (m, 1H), 1.47 (s, 9H), 1.76 (br s, 1H), 1.84–2.20 (br m, 4H), 2.37 (br s, 1H), 3.31–3.55 (br m, 2H), 3.69 (br d, 1H, $J=6.8$ Hz), 3.91 (br d, 1H, $J=7.2$ Hz), 4.25 (br s, 1/2H), 4.35 (br s, 1/2H), 4.44–4.52 (m, 2H), 4.56 (d, 1H, $J=12.2$ Hz), 4.59–4.68 (m, 2H), 4.76 (dt, 1H, $J=3.2$, 8.1 Hz), 5.23 (d, 1H, $J=10.2$ Hz), 5.28–5.33 (m, 1H), 5.82–5.91 (m, 1H), 6.50 (br s, 1/4H), 6.64 (br s, 1/4H), 6.84 (br s, 1/2H), 7.26–7.36 (m, 11/2H), 7.47 (br

s, 1/2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.1, 24.7, 26.3, 27.8, 28.4, 37.0, 47.0, 47.1, 52.6, 56.7, 59.9, 66.1, 69.6, 73.3, 80.5, 118.7, 127.7, 127.8, 128.4, 131.5, 137.5, 169.6, 171.1, 172.1; IR ($CHCl_3$) cm^{-1}: 2979, 2936, 1744, 1679, 1514, 1503, 1460, 1394, 1271, 1168; HRMS calcd for $C_{29}H_{44}N_3O_7$ $(M+H)^+$ calcd 546.3179, found 546.3181; $[\alpha]_D^{24}$ −51.3 (*c* 1.06, $CHCl_3$).

4.1.26. L-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (19e). 95%, a colorless solid, (mp, 93–95 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89 (d, 3H, *J* = 6.8 Hz), 0.93 (t, 3H, *J* = 7.4 Hz), 1.11–1.22 (m, 1H), 1.39–1.49 (m, 1H), 1.71 (qu, 2H, *J* = 6.8 Hz), 1.88–2.19 (m, 4H), 2.92 (dt, 1H, *J* = 6.2, 10.2 Hz), 3.03 (dt, 1H, *J* = 6.9, 10.2 Hz), 3.68 (dd, 1H, *J* = 3.4, 9.5 Hz), 3.76 (dd, 1H, *J* = 5.0, 9.2 Hz), 3.93 (dd, 1H, *J* = 3.4, 9.5 Hz), 4.40 (dd, 1H, *J* = 5.1, 9.1 Hz), 4.47 and 4.55 (AB type d's, each 1H, *J* = 12.2 Hz), 4.59–4.69 (m, 2H), 4.75 (dt, 1H, *J* = 3.4, 8.0 Hz), 5.27 (dd, 1H, *J* = 1.4, 8.5 Hz), 5.29–5.34 (m, 1H), 5.82–5.92 (m, 1H), 6.71 (d, 1H, *J* = 8.1 Hz), 7.26–7.37 (m, 5H), 8.19 (d, 1H, *J* = 9.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.4, 26.2, 26.4, 31.0, 37.5, 47.3, 52.7, 56.1, 60.6, 66.2, 69.6, 73.3, 118.8, 127.7, 127.9, 128.4, 131.5, 137.4, 169.7, 171.3, 175.3; IR ($CHCl_3$) cm^{-1}: 3433, 3326, 2968, 2936, 2876, 1746, 1665, 1511, 1502, 1105; HRMS calcd for $C_{24}H_{36}N_3O_5$ $(M+H)^+$ calcd 446.2655, found 446.2653. Anal. calcd for $C_{24}H_{35}N_3O_5$: C, 64.70; H, 7.92; N, 9.43; Found: C, 64.39; H, 7.75; N, 9.32; $[\alpha]_D^{27}$ −24.3 (*c* 1.01, $CHCl_3$).

4.1.27. Boc-19f. 97%, a colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.88 (d, 3H, *J* = 6.8 Hz), 0.94 (t, 3H, *J* = 7.3 Hz), 1.14–1.21 (m, 1H), 1.42–1.56 (m, 4H), 1.48 (s, 9H), 1.60–1.72 (br, 2H), 1.95 (br, 1H), 2.27 (br, 1H), 2.80 (br, 1H), 3.65 (dd, 1H, *J* = 3.0, 9.5 Hz), 3.93 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.02 (br s, 1/2H), 4.14 (br s, 1/2H), 4.49 (br s, 1H), 4.47 and 4.56 (AB type d's, each 1H, *J* = 12.2 Hz), 4.58–4.68 (m, 2H), 4.76 (dt, 2H, *J* = 3.0, 8.2 Hz), 5.23 (dt, 1H, *J* = 1.3, 10.3 Hz), 5.31 (dq, 1H, *J* = 1.4, 16.9 Hz), 5.81–5.91 (m, 1H), 6.60 (br s, 3/2H), 6.79 (br s, 1/2H), 7.26–7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.8, 14.1, 14.5, 20.5, 22.7, 25.0, 26.4, 28.4, 31.6, 52.5, 52.6, 56.4, 66.2, 69.5, 73.4, 77.5, 80.8, 118.8, 127.7, 127.9, 128.5, 131.5, 137.3, 169.6, 170.8; IR ($CHCl_3$) cm^{-1}: 3432, 2968, 2939, 2876, 1746, 1676, 1501, 1411, 1367, 1161; HRMS calcd for $C_{30}H_{46}N_3O_7$ $(M+H)^+$ calcd 560.3335; Found 560.3340; $[\alpha]_D^{24}$ −48.6 (*c* 1.13, $CHCl_3$).

4.1.28. L-homo-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (19f). 97%, a colorless solid, (mp 111–112 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.92 (d, 3H, *J* = 6.8 Hz), 0.94 (t, 3H, *J* = 7.4 Hz), 1.16–1.26 (m, 1H), 1.37-1.59 (m, 5H), 1.75–1.81 (m, 1H), 1.91–2.05 (m, 3H), 2.67 (dt, 1H, *J* = 3.1, 11.7 Hz), 3.02 (dt, 1H, *J* = 2.9, 11.7 Hz), 3.25 (dd, 1H, *J* = 3.1, 9.6 Hz), 3.67 (dd, 1H, *J* = 3.3, 9.5 Hz), 3.93 (dd, 1H, *J* = 3.4, 9.5 Hz), 4.48 (dd, 1H, *J* = 5.3, 9.0 Hz), 4.47 and 4.55 (AB type d's, each 1H, *J* = 12.0 Hz), 4.59–4.69 (m, 2H), 4.74 (dt, 1H, *J* = 3.1, 8.1 Hz), 5.24 (dt, 1H, *J* = 1.3, 11.5 Hz), 5.29–5.34 (m, 1H), 5.82–5.92 (m, 1H), 6.65 (d, 1H, *J* = 8.1 Hz), 7.23–7.37 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.5, 23.9, 25.8, 26.3, 30.1, 37.7, 45.6, 52.6, 56.0, 60.2, 66.2, 69.5, 73.3, 118.8, 127.7, 127.9, 128.5, 131.5, 137.4, 169.7, 171.2, 174.2; IR (KBr) cm^{-1}: 3278, 2959, 2922, 2875, 2853, 1738, 1636, 1544, 1452, 1220; HRMS calcd for $C_{25}H_{38}N_3O_5$ $(M+H)^+$ calcd 460.2812, found 460.2783. Anal. calcd for $C_{25}H_{37}N_3O_5$: C, 65.34; H, 8.12; N, 9.14; Found: C, 65.62; H, 8.02; N, 9.10; $[\alpha]_D^{26}$ −13.4 (*c* 1.05, $CHCl_3$).

4.1.29. Boc-19g. 100%, a colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89–0.93 (m, 12H), 1.12–1.20 (m, 1H), 1.43–1.55 (m, 2H), 1.49 (s, 9H), 1.60–1.75 (m, 2H), 1.82–1.94 (m, 1H), 2.76 (s, 3H), 3.66 (dd, 1H, *J* = 3.4, 9.5 Hz), 3.93 (br d, 1H, *J* = 8.2 Hz), 4.35 (t, 1H, *J* = 6.5 Hz), 4.47 and 4.56 (AB type d's, each 1H, *J* = 12.2 Hz), 4.59–4.72 (m, 3H), 4.74–4.77 (m, 1H), 5.23 (d, 1H, *J* = 10.1 Hz), 5.30 (dt, 1H, *J* = 1.3, 15.6 Hz), 5.81–5.91 (m, 1H), 6.49 (br s, 1H), 6.62–6.73 (br m, 1H), 7.26–7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.3, 15.4, 21.9, 23.1, 24.5, 24.8, 28.3, 29.9, 36.1, 37.1, 52.6, 57.4, 66.2, 69.5, 73.3, 80.4, 118.8, 127.7, 127.9, 128.4, 131.5, 137.3, 169.5, 170.6, 171.3, 171.5; IR ($CHCl_3$) cm^{-1}: 3432, 2964, 2934, 2874, 1746, 1676, 1501, 1391, 1368, 1153; HRMS calcd for $C_{31}H_{50}N_3O_7$ $(M+H)^+$ calcd 576.3649, found 576.3638; $[\alpha]_D^{24}$ −56.7 (*c* 1.08, $CHCl_3$).

4.1.30. *N*-Me-L-Leu-L-Ile-L-Ser(Bn)-OAllyl (19g). 94%, a colorless solid, (mp 91–92 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89–0.97 (m, 12H), 1.11–1.22 (m, 1H), 1.35–1.43 (m, 1H), 1.46–1.61 (m, 3H), 1.64–1.74 (m, 1H), 1.89–1.99 (m, 1H), 2.36 (s, 3H), 3.00 (dd, 1H, *J* = 4.9, 9.2 Hz), 3.66 (dd, 1H, *J* = 3.1, 9.5 Hz), 3.93 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.35 (dd, 1H, *J* = 6.4, 9.2 Hz), 4.47 and 4.55 (AB type d's, each 1H, *J* = 12.2 Hz), 4.59–4.68 (m, 2H), 4.76 (dt, 1H, *J* = 3.3, 8.2 Hz), 5.23 (dt, 1H, *J* = 1.3, 9.9 Hz), 5.30 (dt, 1H, *J* = 1.3, 17.5 Hz), 5.81–5.91 (m, 1H), 6.64 (d, 1H, *J* = 8.2 Hz), 7.26–7.36 (m, 5H), 7.70 (d, 1H, *J* = 9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 11.3, 15.6, 21.9, 23.2, 24.7, 25.2, 35.5, 37.3, 43.0, 52.6, 57.0, 63.7, 66.2, 69.6, 73.4, 118.8, 127.7, 127.9, 128.5, 131.5, 137.4, 169.6, 171.1, 174.9; IR ($CHCl_3$) cm^{-1}: 3290, 2961, 2933, 2874, 1744, 1651, 1633, 1547, 1211, 1114; HRMS calcd for $C_{26}H_{42}N_3O_5$ $(M+H)^+$ calcd 476.3125, found 476.3130. Anal. calcd for $C_{26}H_{41}N_3O_5 \cdot 1/5H_2O$: C, 65.16; H, 8.71; N, 8.77; Found: C, 65.23; H, 8.51; N, 8.90; $[\alpha]_D^{24}$ −21.3 (*c* 1.06, $CHCl_3$).

4.1.31. (2*R*,3*R*)-3-Hydroxy-2-methyltridecanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20c). Compound **4c** (179 mg, 0.732 mmol) and **19b** (289 mg, 0.608 mmol) were dissolved in THF (4.0 mL) and then Et_3N (0.17 mL, 1.22 mmol) was added. To the solution was added DEPC (149 μL, 0.913 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for additional 14 h. After saturated $NaHCO_3$ aqueous solution was added, the organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered and evaporated. The oil residue was purified by column chromatography with a gradient elution system, a 4:1–2:1 mixture of hexane and EtOAc used as eluents to give **20c** (425 mg, 0.605 mmol, 99%) as a colorless oil. ^{1}H

NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 2/1)] δ ppm: 0.80–0.97 (m, 15H), 1.07* (d, 1H, J = 6.6 Hz), 1.10-1.20 (m, 1H), 1.22–1.40 (m, 18H), 1.41–1.53 (m, 3H), 1.58–1.75 (m, 1H), 1.77–1.85 (m, 5/3H), 1.94–2.00 (m, 4/3H), 2.69–2.77 (m, 2/3H), 2.80* (s, 1H), 2.84–2.91* (m, 1/3H), 2.95 (s, 2H), 3.25* (br s, 1/3H), 3.60–3.64 (m, 2/3H), 3.68 (dd, 2/3H, J = 3.3, 9.5 Hz), 3.69* (dd, 1/3H, J = 3.1, 9.4 Hz), 3.70–3.77 (br, 1H), 3.93 (dd, 1H, J = 3.0, 9.5 Hz), 4.44–4.57 (m, 4/3H), 4.48 and 4.55 (AB type d's, each 1H, J = 12.2 Hz), 4.59–4.68 (m, 2H), 4.73–4.78 (m, 1H), 5.10 (dd, 2/3H, J = 5.7, 10.1 Hz), 5.24 (dd, 1H, J = 1.2, 8.6 Hz), 5.31 (dd, 1H, J = 1.3, 14.1 Hz), 5.82–5.92 (m, 1H), 6.64 (d, 2/3H, J = 8.2 Hz), 6.80–6.85 (m, 1H), 7.24–7.37 (m, 5H), 7.63* (d, 1/3H, J = 9.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.7, 14.1, 14.2, 14.4, 14.8, 14.9, 21.71, 21.75, 22.7, 23.2, 23.4, 24.3, 24.5, 24.7, 26.0, 26.3, 26.4, 29.3, 29.55, 29.59, 29.66, 29.72, 31.1, 31.9, 34.3, 35.6, 35.7, 36.8, 37.5, 37.7, 40.8, 41.3, 52.6, 54.8, 56.1, 56.6, 59.2, 66.18, 66.21, 69.5, 73.4, 73.5, 74.4, 75.6, 118.8, 118.9, 127.7, 127.91, 127.93, 128.2, 128.5, 128.6, 131.3, 131.4, 136.8, 137.3, 169.3, 169.6, 170.71, 170.75, 170.8, 171.5, 176.8, 178.1; IR ($CHCl_3$) cm^{-1}: 3431, 2961, 2929, 2856, 1746, 1672, 1622, 1511, 1503, 1466; HRMS calcd for $C_{40}H_{68}N_3O_7$ $(M+H)^+$ calcd 702.5057, found 702.5071; $[\alpha]_D^{24} = -63.0$ (c 1.25, $CHCl_3$).

4.1.32. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-*N*-Me-L-Leu-L-Ile-L-Ser(Bn)-OAllyl (20d). 94%, a colorless amorphous foam, ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 2/1)] δ ppm: 0.86–0.97 (m, 15H), 1.07* (d, 1H, J = 6.6 Hz), 1.08–1.17 (m, 1H), 1.23 (d, 2H, J = 6.9 Hz), 1.27–1.36 (m, 7H), 1.37–1.54 (m, 4H), 1.57–1.64 (m, 1H), 1.66–2.00 (m, 3H), 2.69–2.76 (m, 2/3H), 2.80* (s, 1H), 2.83–2.87* (m, 1/3H), 2.95 (s, 2H), 3.30* (br s, 1/3H), 3.62* (br, 1H), 3.67 (dd, 2/3H, J = 3.4, 9.5 Hz), 3.68* (dd, 1/3H, J = 3.0, 9.5 Hz), 3.70–3.84 (br, 1H), 3.93 (dd, 1H, J = 3.0, 9.5 Hz), 4.31 (dd, 2/3H, J = 5.9, 8.4 Hz), 4.42* (dd, 1/3H, J = 5.9, 9.2 Hz), 4.44–4.56* (m, 2/3H), 4.48 and 4.56 (AB type d's, each 2/3H, J = 12.1 Hz), 4.59–4.68 (m, 2H), 4.72–4.78 (m, 1H), 5.10 (dd, 2/3H, J = 5.5, 10.2 Hz), 5.22–5.26 (m, 1H), 5.28–5.33 (m, 1H), 5.81–5.91 (m, 1H), 6.60 (d, 2/3H, J = 8.2 Hz), 6.75–6.81 (m, 1H), 7.24–7.38 (m, 5H), 7.73* (d, 1/3H, J = 9.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.27, 11.32, 14.1, 14.7, 14.8, 15.4, 15.6, 21.67, 21.73, 22.6, 23.3, 23.4, 24.3, 24.48, 24.53, 24.7, 25.9, 29.3, 29.5, 31.1, 31.7, 31.8, 34.3, 35.6, 35.76, 35.80, 37.4, 37.5, 40.8, 41.4, 52.6, 57.4, 57.9, 59.1, 66.2, 69.5, 73.4, 73.5, 74.4, 75.6, 118.8, 118.9, 127.7, 127.8, 127.9, 128.1, 128.5, 128.6, 131.3, 131.5, 136.9, 137.3, 169.3, 169.5, 170.48, 170.51, 170.6, 171.2, 176.8, 178.0; IR (KBr) cm^{-1}: 3274, 2957, 2931, 2875, 1742, 1642, 1618, 1540, 1455, 1115; HRMS calcd for $C_{36}H_{60}O_7N_3$ $(M+H)^+$ calcd 646.4431, found 646.4436. Anal. calcd for $C_{36}H_{59}N_3O_7$: C, 66.95; H, 9.21; N, 6.51; Found: C, 66.75; H, 9.24; N, 6.40; $[\alpha]_D^{23}$ −72.6 (c 1.10, $CHCl_3$).

4.1.33. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Me)-OBn (20i). 100%, a slightly yellow oil, ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/mino = 2.0/1)] δ ppm: 0.77* (d, 1H, J = 6.8 Hz), 0.82 (d, 2H, J = 7.0 Hz), 0.84–1.00 (m, 10H), 0.96 (d, 2H, J = 6.6 Hz), 1.04–1.20 (m, 1H), 1.08* (d, 1H, J = 6.6 Hz), 1.23 (d, 2H, J = 7.0 Hz), 1.22–1.46 (m, 10H), 1.59–1.70 (m, 1H), 1.77–1.84 (m, 3H), 1.89–2.00 (m, 1H), 2.69–2.76 (m, 2/3H), 2.80* (s, 1H), 2.86–2.92* (m, 1/3H), 2.95 (s, 2H), 3.30 (s, 3H), 3.59–3.64 (m, 5/3H), 3.80 (br, 1H), 3.80–3.87 (m, 1H), 4.47 (dd, 2/3H, J = 4.4, 8.7 Hz), 4.58* (dd, 1/3H, J = 4.3, 9.5 Hz), 4.67* (dd, 1/3H, J = 4.3, 10.4 Hz), 4.74–4.79 (m, 1H), 5.09 (dd, 1H, J = 5.6, 10.0 Hz), 5.13 and 5.25 (AB type d's, each 2/3H, J = 12.3 Hz), 5.16* and 5.21* (AB type d's, each 1/3H, J = 12.3 Hz), 6.63 (d, 2/3H), 6.82–6.85 (m, 1H), 7.31–7.40 (m, 5H), 7.63* (d, 1/3H, J = 9.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers): δ ppm: 11.7, 14.06, 14.12, 14.3, 14.78, 14.85, 21.7, 21.8, 22.6, 23.2, 23.4, 24.3, 24.5, 24.7, 25.9, 26.3, 26.4, 29.3, 29.7, 31.2, 31.7, 31.8, 34.3, 35.6, 35.8, 36.8, 37.5, 37.6, 40.9, 41.4, 52.6, 56.1, 56.6, 59.1, 59.18, 59.21, 67.3, 67.4, 72.0, 74.4, 75.7, 128.05, 128.12, 128.4, 128.51, 128.55, 128.61, 135.1, 135.2, 169.6, 169.8, 170.7, 170.79, 170.83, 171.5, 176.9, 178.1; IR ($CHCl_3$) cm^{-1}: 3431, 2962, 2931, 1746, 1672, 1624, 1502, 1460, 1118; HRMS calcd for $C_{34}H_{58}N_3O_7$ $(M+H)^+$ 620.4275, found 620.4270; $[\alpha]_D^{24}$ −70.5 (c 1.05, $CHCl_3$).

4.1.34. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20j). 92%, a colorless solid (mp, 152–153 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.86–0.95 (m, 15H), 1.10–1.30 (m, 8H), 1.22 (d, 3H, J = 7.0 Hz), 1.36–1.51 (m, 4H), 1.54–1.73 (m, 3H), 1.90–1.99 (m, 1H), 2.29–2.36 (m, 1H), 3.23 (br, 1H), 3.55–3.64 (m, 1H), 3.67 (dd, 1H, J = 3.2, 9.6 Hz), 3.94 (dd, 1H, J = 3.6, 9.6 Hz), 4.43–4.48 (m, 1H), 4.46 and 4.55 (AB type d's, each 1H, J = 12.3 Hz), 4.50–4.56 (m, 1H), 4.58–4.68 (m, 2H), 4.78 (dt, 1H, J = 3.2, 8.4 Hz), 5.23 (dt, 1H, J = 1.2, 10.2 Hz), 5.31 (dt, 1H, J = 1.3, 18.8 Hz), 5.81–5.91 (m, 1H), 6.23 (d, 1H, J = 7.8 Hz), 6.79 (d, 1H, J = 8.1 Hz), 6.99 (d, 1H, J = 8.9 Hz), 7.23–7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.8, 14.1, 14.3, 15.4, 21.8, 22.6, 23.0, 24.9, 25.8, 26.1, 29.3, 31.8, 35.5, 37.8, 40.5, 46.6, 52.2, 52.5, 56.5, 66.2, 69.5, 73.3, 74.2, 118.8, 127.8, 128.0, 128.5, 131.5, 137.2, 169.5, 171.1, 172.2, 176.0; IR (KBr) cm^{-1}: 3284, 2958, 2930, 2973, 1745, 1640, 1547, 1397, 1212, 1114; HRMS calcd for $C_{35}H_{58}N_3O_7$ $(M+H)^+$ calcd 632.4275, found; 632.4274. Anal. calcd for $C_{35}H_{57}N_3O_7{\cdot}1/4H_2O$: C, 66.06; H, 9.11; N, 6.60, found: C, 66.07; H, 9.05; N, 6.68; $[\alpha]_D^{24}$ −25.9 (c 1.07, $CHCl_3$).

4.1.35. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-*N*-Et-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20k). 28%, a slightly yellow oil, ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 2.8/1)] δ ppm: 0.80 (d, 3/4H, J = 6.7 Hz), 0.86–0.99 (m, 45/4H), 0.95 (d, 9/4H, J = 6.6 Hz), 0.98* (d, 3/4H, J = 6.6 Hz), 1.06* (d, 3/4H, J = 6.6 Hz), 1.12–1.44 (m, 69/4H), 1.47–1.65 (m, 2H), 1.79–1.90 (m, 1H), 1.93–1.99 (m, 1H), 2.66–2.74 (m, 3/4H), 2.83–2.86* (m, 1/4H), 3.27–3.36 (m, 1H), 3.48–3.57 (m, 1H), 3.65–3.81 (m, 3H), 3.92 (dd, 1H, J = 3.2, 9.5 Hz), 4.43–4.69 (m, 4H), 4.47 and 4.56 (AB type d's, each 1H, J = 12.3 Hz), 4.74–4.79 (m, 1H), 5.23 (dd, 1H, J = 1.4, 9.8 Hz), 5.29 (dd, 1H, J = 1.4, 18.8 Hz), 5.81–5.92 (m, 1H), 6.67 (d, 3/4H, J = 8.2 Hz), 6.83* (d, 1/4H, J = 7.9 Hz), 7.23–7.36

(m, 5H), 7.50–7.55 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.75, 11.80, 14.09, 14.12, 14.2, 14.3, 14.5, 15.1, 15.47, 15.52, 21.8, 22.3, 22.57, 22.64, 22.9, 23.3, 24.1, 24.3, 25.0, 25.5, 25.6, 26.4, 29.1, 29.36, 29.44, 31.6, 31.69, 31.74, 31.8, 32.7, 34.4, 35.3, 37.5, 37.6, 37.8, 39.7, 41.3, 42.0, 52.6, 56.3, 56.6, 59.7, 66.17, 66.21, 69.58, 69.63, 73.4, 73.6, 74.5, 75.4, 77.5, 118.7, 118.9, 127.7, 127.9, 128.0, 128.2, 128.5, 128.6, 131.4, 131.5, 136.8, 137.3, 169.3, 169.6, 171.1, 171.2, 171.4, 172.1, 176.2, 178.6; IR ($CHCl_3$) cm^{-1}: 3432, 2961, 2932, 2873, 1746, 1671, 1614, 1503, 1385, 1252; HRMS calcd for $C_{37}H_{61}N_3O_7Na$ $(M+Na)^+$ 682.4407, found 682.4400; $[\alpha]_D^{24}$ −32.4 (*c* 1.28, $CHCl_3$).

4.1.36. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-L-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20l). 96%, a colorless solid (mp, 81–82 °C), ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 2/1)] δ ppm: 0.86–0.94 (m, 9H), 1.10–1.20 (m, 1H), 1.23 (d, 3H, *J* = 7.1 Hz), 1.28–1.41 (m, 8H), 1.41–1.55 (m, 3H), 1.70–1.95 (m, 2H), 1.96–2.06 (m, 2H), 2.09–2.16 (m, 1H), 2.29–2.34* (m, 1/3H), 2.37–2.45 (m, 1H), 2.61 (qu, 2/3H, *J* = 7.0 Hz), 3.51–3.61 (m, 2H), 3.63–3.71 (m, 2H), 3.77* (br t, 1/3H, *J* = 9.1 Hz), 3.92 (dd, 2/3H, *J* = 3.4, 9.5 Hz), 3.93–3.97* (m, 1/3H), 4.35–4.45 (m, 1H), 4.45 (dd, 2/3H, *J* = 4.2, 8.3 Hz), 4.48 and 4.55 (AB type d's, each 2/3H, *J* = 12.2 Hz), 4.55–4.59 (m, 2/3H), 4.60–4.67 (m, 2H), 4.68–4.71 (m, 1H), 4.73–4.79 (m, 1H), 5.21–5.26 (m, 1H), 5.31 (dq, 1H, *J* = 1.3, 16.9 Hz), 5.81–5.92 (m, 1H), 6.75 (d, 2/3H, *J* = 8.3 Hz), 6.78* (d, 1/3H, *J* = 8.7 Hz), 7.14* (d, 1/3H, *J* = 9.1 Hz), 7.27–7.37 (m, 5H), 7.50 (d, 2/3H, *J* = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.4, 11.7, 14.06, 14.2, 14.6, 15.1, 22.59, 22.62, 25.1, 25.2, 25.8, 26.3, 27.0, 29.3, 31.7, 31.8, 33.8, 35.3, 37.0, 37.1, 43.0, 46.1, 46.4, 47.5, 52.60, 52.67, 52.68, 56.7, 57.2, 59.5, 61.4, 66.1, 66.2, 69.4, 69.6, 73.3, 73.4, 73.9, 74.4, 76.5, 118.7, 118.9, 127.68, 127.78, 127.82, 128.0, 128.5, 131.3, 131.5, 137.1, 137.4, 169.3, 169.7, 171.0, 171.8, 172.1, 176.2, 177.1; IR (KBr) cm^{-1}: 3385, 3296, 2959, 2927, 1734, 1643, 1626, 1552, 1454, 1203; HRMS calcd for $C_{34}H_{53}N_3O_7Na$ $(M+Na)^+$ calcd 638.3781, found 638.3765. Anal. calcd for $C_{34}H_{53}N_3O_7$: C, 66.31; H, 8.68; N, 6.82, found: C, 65.95; H, 8.42; N, 6.74; $[\alpha]_D^{25}$ −64.9 (*c* 1.07, $CHCl_3$).

4.1.37. (2*R*,3*R*)-3-Hydroxy-2-methylnonanoyl-L-homo-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20m). 91%, a colorless oil, ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 3/2)] δ ppm: 0.82–0.96 (m, 9H), 1.07* (d, 6/5H, *J* = 6.9 Hz), 1.10–1.55 (m, 15H), 1.23 (d, 9/5H, *J* = 7.2 Hz), 1.65–1.86 (m, 2H), 1.91–2.02 (m, 1H), 2.26 (br d, 3/5H, *J* = 13.4 Hz), 2.49–2.58 (m, 1H), 2.69–2.80 (m, 1H), 3.07–3.14* (m, 2/5H), 3.66–3.69 (m, 8/5H), 3.76* (dt, 2/5H, *J* = 2.2, 8.3 Hz), 3.83 (br d, 3/5H, *J* = 13.4 Hz), 3.90–3.95 (m, 7/5H), 4.44–4.58 (m, 3H), 4.58–4.67 (m, 3H), 4.73–4.80 (m, 1H), 5.22–5.27 (m, 2H), 5.31 (dd, 1H, *J* = 1.3, 15.6 Hz), 5.81–5.92 (m, 1H), 6.60 (d, 3/5H, *J* = 8.2 Hz), 6.75 (d, 3/5H, *J* = 8.5 Hz), 6.89* (d, 2/5H, *J* = 8.1 Hz), 7.24–7.38 (m, 27/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.6, 11.8, 14.09, 14.12, 14.4, 14.6, 14.8, 15.0, 20.3, 21.1, 22.62, 22.66, 24.8, 25.0, 25.3, 25.5, 26.0, 26.4, 26.56, 26.64, 29.3, 29.4, 31.6, 31.77, 31.85, 34.3, 35.3, 37.4, 37.7, 39.9, 40.7, 41.7, 43.7, 51.8, 52.6, 56.3, 56.7, 57.4, 66.21, 66.23, 69.5, 69.6, 73.4, 73.5, 74.1, 75.2, 118.8, 118.9, 127.7, 127.9, 128.1, 128.5, 128.6, 131.4, 131.5, 136.9, 137.3, 169.4, 169.6, 170.1, 170.76, 170.78, 171.6, 175.7, 177.0; IR ($CHCl_3$) cm^{-1}: 3431, 2959, 2932, 2873, 1746, 1671, 1641, 1502, 1457, 1255; HRMS calcd for $C_{34}H_{53}N_3O_7Na$ $(M+Na)^+$ calcd 652.3938, found 652.3925; $[\alpha]_D^{24}$ −57.2 (*c* 1.04, $CHCl_3$).

4.1.38. (3*R*)-Hydroxynonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20n). 100%, a colorless oil, ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 2.6/1)] δ ppm: 0.80* (d, 6/7H, *J* = 6.8 Hz), 0.85 (d, 15/7H, *J* = 6.8 Hz), 0.84–0.97 (m, 9H), 0.95 (d, 3H, *J* = 6.8 Hz), 1.07–1.50 (m, 13H), 1.55–1.76 (m, 2H), 1.94–2.00 (m, 1H), 2.30* (d, 2/7H, *J* = 13.7 Hz), 2.37 (dd, 5/7H, *J* = 8.8, 16.6 Hz), 2.52 (dd, 5/7H, *J* = 2.9, 16.6 Hz), 2.68* (dd, 2/7H, *J* = 9.8, 13.7 Hz), 2.81* (s, 6/7H), 2.91 (s, 15/7H), 3.68 (dd, 5/7H, *J* = 2.9, 9.8 Hz), 3.76* (dd, 2/7H, *J* = 2.9, 9.8 Hz), 3.93 (dd, 5/7H, *J* = 2.9, 9.8 Hz), 3.95* (dd, 2/7H, *J* = 2.9, 9.8 Hz), 3.98–4.07 (m, 1H), 4.18–4.31 (m, 1H), 4.43–4.44 (m, 1H), 4.44 and 4.51* (AB type d's, each 2/7H, *J* = 11.7 Hz), 4.48 and 4.56 (AB type d's, each 5/7H, *J* = 11.7 Hz), 4.59–4.69 (m, 2H), 4.73–4.77 (m, 1H), 5.14 (dd, 1H, *J* = 6.8, 9.8 Hz), 5.23–5.33 (m, 2H), 5.82–5.91 (m, 1H), 6.64 (d, 5/7H, *J* = 7.8 Hz), 6.75 (d, 5/7H, *J* = 8.8 Hz), 6.97* (d, 2/7H, *J* = 7.8 Hz), 7.23–7.37 (m, 5H), 7.42* (d, 2/7H, *J* = 9.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.67, 11.74, 14.05, 14.09, 14.31, 14.34, 21.9, 22.1, 22.59, 22.63, 23.0, 23.3, 24.4, 24.9, 25.2, 25.6, 26.3, 26.5, 29.2, 29.6, 31.1, 31.6, 31.7, 31.8, 36.1, 36.4, 36.9, 37.5, 37.6, 37.9, 40.0, 52.6, 54.8, 56.3, 59.9, 66.19, 66.22, 68.1, 69.5, 69.7, 71.4, 73.4, 73.7, 118.78, 118.84, 127.7, 127.9, 128.2, 128.4, 128.5, 128.7, 131.3, 131.4, 137.3, 169.3, 169.5, 170.4, 170.7, 170.8, 171.1, 172.8, 174.0; IR ($CHCl_3$) cm^{-1}: 3431, 2961, 2931, 2873, 1746, 1673, 1627, 1502, 1273, 1103; HRMS calcd for $C_{35}H_{57}N_3O_7Na$ $(M+Na)^+$ 654.4094, found 654.4089; $[\alpha]_D^{25}$ −57.9 (*c* 1.26, $CHCl_3$).

4.1.39. (2*R*,3*R*)-3-Boc-amino-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20o). 85%, a colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.83 (d, 3H, *J* = 7.0 Hz), 0.83–0.92 (m, 9H), 0.95 (d, 3H, *J* = 6.7 Hz), 1.06–1.14 (m, 1H), 1.18 (d, 3H, *J* = 7.0 Hz), 1.17–1.49 (m, 11H), 1.44 (s, 9H), 1.54–1.61 (m, 1H), 1.67–1.81 (m, 2H), 1.92–1.98 (m, 1H), 2.93 (s, 3H), 2.93–2.99 (m, 1H), 3.63–3.69 (m, 1H), 3.67 (dd, 1H, *J* = 3.1, 9.5 Hz), 3.93 (dd, 1H, *J* = 3.1, 9.4 Hz), 4.46 (dt, 1H, *J* = 2.9, 8.1 Hz), 4.48 and 4.57 (AB type d's, each 1H, *J* = 12.3 Hz), 4.59–4.69 (m, 2H), 4.75 (m, 1H), 5.18–5.21 (m, 1H), 5.24 (d, 1H, *J* = 10.0 Hz), 5.30 (d, 1H, *J* = 17.4 Hz), 5.81–5.91 (m, 1H), 5.94 (d, 1H, *J* = 9.6 Hz), 6.58 (d, 1H, *J* = 8.1 Hz), 6.69 (d, 1H, *J* = 8.7 Hz), 7.28–7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.7, 14.0, 14.2, 14.5, 21.6, 22.58, 22.63, 23.3, 24.6, 26.3, 26.6, 28.3, 28.4, 29.2, 30.5, 31.6, 31.8, 34.1, 35.5, 37.6, 38.4, 52.6, 53.56, 53.63, 56.1, 66.2, 69.5, 73.3, 78.7, 118.8, 127.6, 127.7, 128.0, 128.5, 131.4, 137.3, 156.3, 169.6, 170.68, 170.73, 177.2; IR ($CHCl_3$) cm^{-1}: 3430, 2962, 2931, 2873, 1745, 1697, 1675, 1626, 1500, 1165; HRMS calcd for $C_{41}H_{68}N_4O_8Na$ $(M+Na)^+$ 767.4935, found 767.4934; $[\alpha]_D^{24}$ −73.4 (*c* 1.13, $CHCl_3$).

4.1.40. (2*R*,3*S*)-3-Hydroxy-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (20p). 80%, a colorless oil, ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 5.7/1)] δ ppm: 0.80* (d, 3/7H, J = 6.8 Hz), 0.83 (d, 18/7H, J = 6.8 Hz), 0.86–0.93 (m, 10H), 0.95 (d, 18/7H, J = 6.8 Hz), 0.96* (d, 3/7H, J = 6.8 Hz), 1.09 (d, 3/7H, J = 6.8 Hz), 1.15 (d, 18/7H, J = 6.8 Hz), 1.23–1.35 (m, 9H), 1.43–1.59 (m, 3H), 1.68–1.73 (m, 2H), 1.93–2.01 (m, 1H), 2.64 (dq, 6/7H, J = 2.9, 6.8 Hz), 2.78* (s, 3/7H), 2.94 (s, 18/7H), 3.15–3.20* (m, 1/7H), 3.43–3.48* (m, 1/7H), 3.67 (dd, 6/7H, J = 3.4, 9.3 Hz), 3.74* (dd, 1/7H, J = 2.9, 9.8 Hz), 3.81–3.85 (m, 1H), 3.93 (dd, 1H, J = 3.4, 9.3 Hz), 4.10–4.13 (m, 6/7H), 4.44–4.49 (m, 1H), 4.47 and 4.56 (AB type d's, each 1H, J = 12.7 Hz), 4.62–4.67 (m, 2H), 4.74–4.77 (m, 1H), 5.11 (dd, 1H, J = 6.8, 8.8 Hz), 5.23 (dd, 1H, J = 2.0, 8.8 Hz), 5.30 (dd, 1H, J = 2.0, 17.6 Hz), 5.82–5.91 (m, 1H), 6.63 (d, 6/7H, J = 7.8 Hz), 6.73 (d, 6/7H, J = 8.8 Hz), 6.77* (d, 1/7H, J = 8.8 Hz), 7.25–7.37 (m, 5H), 7.64* (d, 1/7H, J = 9.8 Hz), ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 9.9, 11.7, 14.1, 14.2, 22.0, 22.6, 23.0, 24.9, 26.0, 26.3, 29.3, 30.8, 31.8, 34.0, 35.8, 37.4, 39.9, 52.6, 54.4, 56.1, 66.2, 69.5, 71.7, 73.4, 118.8, 127.7, 127.9, 128.5, 128.6, 131.5, 137.3, 169.6, 170.5, 170.7, 178.8; IR ($CHCl_3$) cm^{-1}: 3432, 2961, 2933, 2873, 1746, 1673, 1616, 1502, 1466, 1106; HRMS calcd for $C_{36}H_{60}N_3O_7$ $(M+H)^+$ 646.4431, found 646.4429; $[\alpha]_D^{25}$ −78.3 (*c* 1.00, $CHCl_3$).

4.1.41. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-2-methyltridecanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21c). To a solution of **20c** (202 mg, 0.287 mmol) and **15a** (136 mg, 0.348 mmol) in CH_2Cl_2 (1.5 mL), were added DMAP (38 mg, 0.31 mmol), CSA (33 mg, 0.14 mmol) followed by DIPC (68 μL, 0.43 mmol) at room temperature. The reaction mixture was stirred at the same temperature. Moreover, **15a** and other reagents were sometimes added in order to finish the reaction. The mixture was concentrated and diluted with hexane and EtOAc. The mixture was filtered and the filtrate was washed with 10% aqueous citric acid, saturated $NaHCO_3$, aqueous solution and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography with a gradient elution system, a 3:1–2:1 mixture of hexane and EtOAc used as eluents to give **21c** (299 mg, 0.278 mmol, 97%) as a colorless amorphous foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.81–0.93 (m, 21H), 0.95 (d, 3H, J = 6.7 Hz), 1.10 (d, 3H, J = 6.8 Hz), 1.18 (d, 3H, J = 6.0 Hz), 1.19–1.39 (m, 18H), 1.38–1.50 (m, 1H), 1.44 (s, 9H), 1.46–1.65 (m, 3H), 1.71–1.80 (m, 1H), 1.95–2.01 (m, 1H), 2.99 (s, 3H), 3.08 (qu, 1H, J = 6.9 Hz), 3.67 (dd, 1H, J = 3.0, 9.5 Hz), 3.78 (dd, 1H, J = 4.1, 8.5 Hz), 3.92 (dd, 1H, J = 3.0, 9.5 Hz), 4.08–4.42 (m, 3H), 4.42–4.45 (m, 1H), 4.47 and 4.56 (AB type d's, each 1H, J = 12.0 Hz), 4.58–4.68 (m, 2H), 4.74 (dt, 1H, J = 3.1, 8.1 Hz), 5.08–5.16 (m, 3H), 5.23 (dt, 1H, J = 1.3, 10.2 Hz), 5.31 (dt, 1H, J = 1.3, 17.6 Hz), 5.81–5.91 (m, 1H), 6.66–6.72 (m, 3H), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.7, 11.6, 12.2, 14.1, 14.2, 17.9, 19.5, 21.8, 22.6, 23.2, 24.8, 25.1, 25.5, 25.7, 26.3, 28.3, 29.3, 29.5, 29.6, 29.9, 30.5, 31.9, 35.8, 37.2, 39.9, 41.1, 52.6, 54.3, 56.2, 60.8, 66.2, 68.7, 69.5, 73.3, 76.4, 80.2, 118.7, 127.7, 127.9, 128.4, 131.5, 137.3, 155.7, 169.0, 169.6, 170.3, 170.7, 170.8, 174.4; IR ($CHCl_3$) cm^{-1}: 3430, 2959, 2930, 2858, 1744, 1677, 1636, 1499, 1471, 1256; HRMS calcd for $C_{57}H_{99}N_5O_{12}SiNa$ $(M+Na)^+$ calcd 1096.6941, found 1096.6949. Anal. calcd for $C_{57}H_{99}N_5O_{12}Si\cdot H_2O$: C, 62.66; H, 9.32; N, 6.41, found: C, 62.89; H, 9.28; N, 6.59; $[\alpha]_D^{24}$ −51.9 (*c* 1.02, $CHCl_3$).

4.1.42. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-Ile-L-Ser(Bn)-OAllyl (21d). 95%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.81–0.92 (m, 21H), 0.94 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.8 Hz), 1.18 (d, 3H, J = 6.4 Hz), 1.05–1.35 (m, 7H), 1.37–1.48 (m, 4H), 1.44 (s, 9H), 1.55–1.65 (m, 3H), 1.71–1.79 (m, 1H), 1.88–1.94 (m, 1H), 2.99 (s, 3H), 3.08 (qu, 1H, J = 6.8 Hz), 3.66 (dd, 1H, J = 3.1, 9.5 Hz), 3.77 (dd, 1H, J = 4.2, 8.4 Hz), 3.92 (dd, 1H, J = 3.0, 9.5 Hz), 4.08–4.19 (m, 3H), 4.27 (dd, 1H, J = 6.0, 8.3 Hz), 4.47 and 4.56 (AB type d's, each 1H, J = 12.1 Hz), 4.60–4.68 (m, 2H), 4.74 (dt, 1H, J = 3.1, 8.1 Hz), 5.08 (d, 1H, J = 7.4 Hz), 5.11–5.16 (m, 2H), 5.23 (dd, 1H, J = 1.2, 10.4 Hz), 5.30 (dt, 1H, J = 1.2, 17.0 Hz), 5.81–5.90 (m, 1H), 6.63 (d, 1H, J = 8.3 Hz), 6.68–6.71 (m, 2H), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.2, 12.3, 14.0, 15.5, 17.9, 19.5, 21.8, 22.5, 23.2, 23.5, 24.5, 24.8, 25.0, 25.7, 28.3, 29.1, 29.9, 30.5, 31.6, 35.8, 37.0, 39.9, 41.1, 52.6, 54.3, 57.5, 66.2, 68.8, 69.5, 73.3, 76.3, 80.2, 118.7, 127.7, 127.8, 128.4, 131.5, 137.3, 155.7, 169.0, 169.5, 170.3, 170.5, 170.6, 174.4; IR (KBr) cm^{-1}: 3315, 2959, 2931, 2859, 1749, 1655, 1526, 1464, 1388, 1196; HRMS calcd for $C_{53}H_{92}N_5O_{12}Si$ $(M+H)^+$ calcd 1018.6512, found 1018.6509. Anal. calcd for $C_{53}H_{91}N_5O_{12}Si\cdot H_2O$: C, 61.42; H, 9.04; N, 6.76; Found: C, 61.65; H, 9.04; N, 6.95; $[\alpha]_D^{24}$ −55.3 (*c* 1.11, $CHCl_3$).

4.1.43. (2*R*,3*R*)-3-[Boc-L-Thr(TBS)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21e). 94%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.06 (s, 3H), 0.09 (s, 3H), 0.81–0.90 (m, 21H), 0.94 (d, 3H, J = 6.6 Hz), 1.06–1.14 (m, 7H), 1.18–1.35 (m, 9H), 1.39–1.50 (m, 1H), 1.47 (s, 9H), 1.54–1.65 (m, 3H), 1.70–1.77 (m, 1H), 1.95–2.01 (m, 1H), 2.99 (s, 3H), 3.08 (qu, 1H, J = 7.0 Hz), 3.66 (dd, 1H, J = 3.1, 9.5 Hz), 3.88–3.95 (br m, 1H), 3.92 (dd, 1H, J = 3.0, 9.5 Hz), 4.05 (dd, 1H, J = 5.0, 18.7 Hz), 4.13 (br d, 1H, J = 6.1 Hz), 4.44 (dd, 2H, J = 4.5, 8.7 Hz), 4.47 and 4.56 (AB type d's, each 1H, J = 12.1 Hz), 4.58–4.68 (m, 2H), 4.74 (dt, 1H, J = 3.0, 8.1 Hz), 5.13–5.18 (br m, 2H), 5.23 (dt, 1H, J = 1.3, 10.3 Hz), 5.30 (dq, 1H, J = 1.3, 17.6 Hz), 5.37 (br d, 1H, J = 7.2 Hz), 5.81–5.89 (m, 1H), 6.65 (d, 1H, J = 8.3 Hz), 6.69 (br s, 1H), 7.11 (br t, 1H, J = 4.5 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: −5.1, −4.7, 11.7, 12.3, 14.0, 14.3, 17.9, 19.3, 21.8, 22.6, 23.2, 24.8, 25.1, 25.7, 26.3, 28.3, 29.1, 30.0, 30.4, 31.7, 35.8, 37.2, 40.0, 41.3, 52.7, 54.2, 56.2, 59.6, 66.2, 68.2, 69.5, 73.3, 76.3, 77.5, 80.1, 118.8, 127.7, 127.9, 128.5, 131.5, 137.4, 155.9, 169.0, 169.6, 170.4, 170.8, 174.5; IR (KBr) cm^{-1}: 3317, 2958, 2932, 2860, 1748, 1719, 1654, 1522, 1199, 1170; HRMS calcd for $C_{53}H_{92}N_5O_{12}Si$ $(M+H)^+$ calcd 1018.6512, found 1018.6515. Anal. calcd for $C_{53}H_{91}N_5O_{12}Si\cdot H_2O$: C,

61.42; H, 9.04; N, 6.76; Found: C, 61.23; H, 8.94; N, 7.13; $[\alpha]_D^{24}$ −55.4 (*c* 1.08, $CHCl_3$).

4.1.44. (2*R*,3*R*)-3-[Boc-L-Thr(TBS)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-Ile-L-Ser(Bn)-OAllyl (21f). 96%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.06 (s, 3H), 0.09 (s, 3H), 0.83–0.90 (m, 21H), 0.94 (d, 3H, *J* = 6.3 Hz), 1.10–1.14 (m, 7H), 1.18–1.37 (m, 9H), 1.38–1.54 (m, 2H), 1.46 (s, 9H), 1.55–1.66 (m, 2H), 1.70–1.78 (m, 1H), 1.88–1.94 (m, 1H), 2.99 (s, 3H), 3.07 (qu, 1H, *J* = 6.9 Hz), 3.66 (dd, 1H, *J* = 3.1, 9.5 Hz), 3.87–3.94 (br m, 1H), 3.92 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.01–4.13 (m, 2H), 4.28 (dd, 1H, *J* = 6.2, 8.5 Hz), 4.41–4.44 (m, 1H), 4.47 and 4.55 (AB type d's, each 1H, *J* = 12.2 Hz), 4.59–4.66 (m, 2H), 4.74 (dt, 1H, *J* = 3.1, 8.2 Hz), 5.13–5.16 (m, 2H), 5.23 (dd, 1H, *J* = 1.3, 10.2 Hz), 5.30 (dq, 1H, *J* = 1.3, 15.2 Hz), 5.37 (br d, 1H, *J* = 7.4 Hz), 5.81–5.90 (m, 1H), 6.65 (d, 1H, *J* = 8.2 Hz), 6.68 (br d, 1H, *J* = 8.4 Hz), 7.10 (br t, 1H, *J* = 4.5 Hz), 7.25–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.1, −4.7, 11.2, 12.3, 14.0, 15.5, 17.8, 19.3, 21.8, 22.6, 23.2, 24.5, 24.8, 25.0, 25.7, 28.3, 29.1, 30.4, 31.7, 35.8, 37.0, 39.9, 41.3, 52.6, 54.1, 57.5, 59.6, 66.2, 68.2, 69.5, 73.3, 76.3, 77.5, 80.1, 118.8, 127.7, 127.9, 128.4, 131.5, 137.3, 155.8, 169.0, 169.5, 170.4, 170.5, 170.6, 174.5; IR ($CHCl_3$) cm^{-1}: 3426, 2959, 2931, 2860, 1745, 1713, 1674, 1495, 1368, 1257; HRMS calcd for $C_{53}H_{92}N_5O_{12}Si$ $(M+H)^+$ calcd 1018.6512, found 1018.6502. Anal. calcd for $C_{53}H_{91}N_5O_{12}Si{\cdot}1/2H_2O$: C, 61.96; H, 9.03; N, 6.82; Found: C, 61.97; H, 8.91; N, 7.14; $[\alpha]_D^{24}$ −55.6 (*c* 1.14, $CHCl_3$).

4.1.45. (2*R*,3*R*)-3-(Boc-L-Abu-GlyO)-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21g). 90%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$, major conformer) δ ppm: 0.83–0.96 (m, 19H), 1.11 (d, 3H, *J* = 6.8 Hz), 1.15 (t, 3H, *J* = 6.6 Hz), 1.20–1.40 (m, 5H), 1.42–1.47 (m, 3H), 1.45 (s, 9H), 1.58–1.68 (m, 2H), 1.72–1.84 (m, 2H), 1.86–1.92 (m, 1H), 1.95–1.99 (m, 1H), 2.99 (s, 3H), 3.03–3.10 (m, 1H), 3.67 (dd, 1H, *J* = 3.0, 9.5 Hz), 3.84–3.87 (m, 1H), 3.92 (dd, 1H, *J* = 3.2, 9.5 Hz), 4.06–4.11 (m, 2H), 4.42–4.44 (m, 1H), 4.46 and 4.57 (AB type d's, each 1H, *J* = 12.0 Hz), 4.62–4.64 (m, 2H), 4.72–4.76 (m, 1H), 5.02 (d, 1H, *J* = 8.1 Hz), 5.10 (dd, 1H, *J* = 6.0, 9.5 Hz), 5.18 (dt, 1H, *J* = 2.9, 7.8 Hz), 5.23 (dd, 1H, *J* = 1.4, 10.3 Hz), 5.30 (dd, 1H, *J* = 1.4, 16.9 Hz), 5.81–5.91 (m, 1H), 6.61 (br s, 1H), 6.66 (d, 1H, *J* = 8.2 Hz), 6.70 (br d, 1H, *J* = 7.2 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 9.9, 11.7, 12.5, 14.0, 14.3, 21.8, 22.6, 23.2, 23.5, 24.8, 25.0, 25.8, 26.3, 28.3, 29.1, 30.2, 30.7, 31.6, 35.9, 37.2, 40.0, 41.3, 42.3, 52.7, 54.6, 55.7, 56.2, 66.2, 69.5, 73.3, 76.4, 76.6, 80.1, 118.8, 127.7, 127.9, 128.5, 131.5, 137.4, 155.6, 169.2, 169.6, 170.6, 172.1, 174.6; IR ($CHCl_3$) cm^{-1}: 3433, 2964, 2933, 2874, 1744, 1677, 1500, 1369, 1255, 1163; HRMS calcd for $C_{47}H_{78}N_5O_{11}$ $(M+H)^+$ 888.5698, found 888.5708; $[\alpha]_D^{24}$ −68.7 (*c* 1.51, $CHCl_3$).

4.1.46. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(Me)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21h). 86%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.81–0.91 (m, 12H), 0.95 (d, 3H, *J* = 6.6 Hz), 1.11 (d, 3H, *J* = 6.8 Hz), 1.15 (d, 3H, *J* = 6.5 Hz), 1.20 (d, 3H, *J* = 6.3 Hz), 1.22–1.33 (m, 9H), 1.45 (s, 9H), 1.58–1.65 (m, 2H), 1.71–1.79 (m, 1H), 1.94–2.01 (m, 1H), 2.99 (s, 3H), 3.08 (qu, 1H, *J* = 6.9 Hz), 3.35 (s, 3H), 3.61–3.68 (m, 2H), 3.81–3.93 (m, 2H), 4.11–4.13 (m, 1H), 4.27 (br t, 1H, *J* = 6.7 Hz), 4.42–4.44 (m, 1H), 4.47 and 4.56 (AB type d's, each 1H, *J* = 12.0 Hz), 4.59–4.68 (m, 2H), 4.72–4.76 (m, 1H), 5.11–5.20 (m, 3H), 5.23 (dd, 1H, *J* = 1.3, 11.4 Hz), 5.30 (dd, 1H, *J* = 1.3, 17.6 Hz), 5.81–5.91 (m, 1H), 6.66 (d, 1H, *J* = 8.1 Hz), 6.71 (br d, 1H, *J* = 6.3 Hz), 6.84 (br t, 1H, *J* = 4.8 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.6, 12.5, 14.0, 14.2, 15.3, 21.8, 22.5, 23.2, 23.4, 24.8, 25.0, 26.3, 28.3, 29.1, 30.1, 30.6, 31.6, 35.8, 37.2, 39.9, 41.3, 42.3, 52.6, 54.4, 56.2, 56.7, 66.2, 69.5, 73.3, 76.3, 77.5, 118.7, 127.7, 127.9, 128.4, 131.5, 137.3, 169.6, 170.5, 170.8, 174.5; IR ($CHCl_3$) cm^{-1}: 3433, 2963, 2933, 2873, 1745, 1674, 1500, 1369, 1252, 1164; HRMS calcd for $C_{48}H_{80}N_5O_{12}$ $(M+H)^+$ 918.5803, found 918.5811; $[\alpha]_D^{25}$ −64.1 (*c* 1.21, $CHCl_3$).

4.1.47. (2*R*,3*R*)-3-[Boc-L-Thr(TBS)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Me)-OBn (21i). 91%, a slightly yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.80 (d, 3H, *J* = 7.1 Hz), 0.83–0.92 (m, 9H), 0.87 (s, 9H), 0.95 (d, 3H, *J* = 6.6 Hz), 1.10 (d, 3H, *J* = 6.8 Hz), 1.18 (d, 3H, *J* = 6.1 Hz), 1.20–1.31 (m, 10H), 1.40–1.48 (m, 2H), 1.44 (s, 9H), 1.59–1.66 (m, 2H), 1.70–1.77 (m, 1H), 1.92–1.99 (m, 1H), 2.99 (s, 3H), 3.08 (t, 1H, *J* = 6.9 Hz), 3.29 (s, 3H), 3.59 (dd, 1H, *J* = 3.2, 9.4 Hz), 3.78 (dd, 1H, *J* = 4.5, 19.0 Hz), 3.83 (dd, 1H, *J* = 3.2, 9.4 Hz), 4.08–4.19 (m, 3H), 4.44 (dd, 1H, *J* = 4.5, 8.6 Hz), 4.73–4.77 (m, 1H), 5.08–5.15 (m, 3H), 5.14 and 5.25 (AB type d's, each 1H, *J* = 12.3 Hz), 6.63 (d, 1H, *J* = 8.2 Hz), 6.70–6.71 (m, 2H), 7.30–7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.6. 12.3, 14.0, 14.1, 14.2, 17.9, 19.5, 21.9, 22.5, 22.6, 23.2, 24.8, 25.0, 25.7, 26.3, 28.3, 29.1, 29.9, 30.5, 31.6, 35.8, 37.2, 39.9, 41.1, 52.6, 54.3, 56.1, 59.2, 67.3, 68.7, 72.0, 76.3, 76.5, 80.2, 128.1, 128.4, 128.5, 135.3, 155.7, 169.0, 169.8, 170.3, 170.7, 170.8, 174.4; IR ($CHCl_3$) cm^{-1}: 3431, 2959, 2931, 2859, 1744, 1676, 1500, 1257, 1163, 1118; HRMS calcd for $C_{51}H_{90}N_5O_{12}Si$ $(M+H)^+$ 992.6355, found 992.6365; $[\alpha]_D^{25}$ −56.8 (*c* 1.07, $CHCl_3$).

4.1.48. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-2-methylnonanoyl-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21j). 100%, a colorless solid (mp 128–130 °C), ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.07 (s, 3H), 0.85–0.94 (m, 24H), 1.13 (d, 3H, *J* = 7.2 Hz), 1.18 (d, 3H, *J* = 6.1 Hz), 1.15–1.29 (m, 10H), 1.39–1.47 (m, 1H), 1.43 (s, 9H), 1.55–1.67 (m, 4H), 1.90–1.96 (m, 1H), 2.60 (qu, 1H, *J* = 6.9 Hz), 3.67 (dd, 1H, *J* = 3.1, 9.5 Hz), 3.76 (dd, 1H, *J* = 4.0, 17.9 Hz), 3.93 (dd, 1H, *J* = 3.1, 9.5 Hz), 4.14–4.20 (m, 2H), 4.24 (dd, 1H, *J* = 6.5, 17.9 Hz), 4.46–4.53 (m, 2H), 4.47 and 4.56 (AB type d's, each 1H, *J* = 12.3 Hz), 4.59–4.68 (m, 2H), 4.75 (dt, 1H, *J* = 3.1, 8.2 Hz), 5.03 (q, 1H, *J* = 5.7 Hz), 5.21 (br, 1H), 5.23 (dd, 1H, *J* = 1.3, 10.3 Hz), 5.28–5.33 (m, 1H), 5.81–5.91 (m, 1H), 6.34 (br s, 1H), 6.67 (br, 2H), 7.13 (br, 1H), 7.25–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.8, 14.0, 14.2, 17.9, 19.6, 19.8, 21.9, 22.6, 23.0,

24.8, 25.1, 25.7, 26.1, 28.3, 29.1, 31.3, 31.6, 38.0, 40.6, 41.4, 44.7, 51.9, 52.7, 56.5, 66.2, 68.7, 69.5, 73.3, 77.5, 77.6, 80.2, 118.8, 127.7, 127.9, 128.5, 131.5, 137.3, 155.7, 169.1, 169.5, 170.6, 170.9, 172.3, 173.0; IR ($CHCl_3$) cm^{-1}: 3294, 2959, 2932, 2860, 1744, 1642, 1540, 1367, 1201, 1115; HRMS calcd for $C_{52}H_{90}N_5O_{12}Si$ $(M+H)^+$ calcd 1004.6356, found 1004.6356. Anal. calcd for $C_{52}H_{89}N_5O_{12}Si$: C, 62.18; H, 8.93; N, 6.97, found: C, 61.84; H, 8.69; N, 7.05; $[\alpha]_D^{24}$ −7.2 (*c* 1.06, $CHCl_3$).

4.1.49. (2*R*,3*R*)-3-(Boc-L-*allo*-Thr(TBS)-GlyO)-2-methyl-nonanoyl-*N*-Et-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21k). 94%, colorless amorphous foam, ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.84–0.94 (m, 12H), 0.87 (s, 9H), 0.93 (d, 3H, *J* = 6.6 Hz), 1.13 (d, 3H, *J* = 6.9 Hz), 1.17 (d, 3H, *J* = 6.2 Hz), 1.17–1.32 (m, 12H), 1.38–1.44 (m, 3H), 1.44 (s, 9H), 1.59–1.79 (m, 3H), 1.96–2.03 (m, 1H), 3.00–3.07 (m, 1H), 3.26–3.35 (m, 1H), 3.53–3.60 (m, 1H), 3.67 (dd, 1H, *J* = 3.4, 9.5 Hz), 3.77 (dd, 1H, *J* = 4.0, 18.4 Hz), 3.90 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.09–4.20 (m, 3H), 4.40 (dd, 1H, *J* = 4.4, 8.2 Hz), 4.46 and 4.56 (AB type d's, each 1H, *J* = 12.2 Hz), 4.61–4.64 (m, 2H), 4.72–4.75 (m, 1H), 4.95–5.00 (m, 1H), 5.06–5.09 (m, 1H), 5.11–5.16 (m, 1H), 5.23 (dd, 1H, *J* = 1.3, 10.3 Hz), 5.30 (dd, 1H, *J* = 1.3, 17.7 Hz), 5.81–5.91 (m, 1H), 6.69 (d, 1H, *J* = 8.1 Hz), 6.73 (t, 1H, *J* = 4.9 Hz), 6.96 (d, 1H, *J* = 8.3 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.7, 13.3, 13.7, 14.01, 14.04, 14.4, 16.0, 17.9, 19.5, 19.6, 22.3, 22.5, 22.6, 22.9, 24.8, 24.9, 25.2, 25.69, 25.72, 26.4, 28.3, 28.8, 29.1, 30.2, 31.56, 31.64, 31.9, 36.7, 36.9, 41.0, 41.1, 52.7, 56.5, 65.5, 66.2, 68.8, 69.5, 73.3, 76.9, 118.7, 127.7, 127.8, 128.4, 131.5, 137.4, 168.9, 169.6, 170.3, 170.9, 171.7, 175.2; IR ($CHCl_3$) cm^{-1}: 3431, 2960, 2931, 2860, 1745, 1676, 1500, 1385, 1257, 1163; HRMS calcd for $C_{54}H_{93}N_5O_{12}SiNa$ $(M+Na)^+$ 1054.6488, found 1054.6432; $[\alpha]_D^{24}$ −50.2 (*c* 1.06, $CHCl_3$).

4.1.50. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-2-methyl-nonanoyl-L-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21l). 95%, a colorless amorphous foam, ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.85–0.90 (m, 18H), 1.12 (d, 3H, *J* = 7.1 Hz), 1.18 (d, 3H, *J* = 6.3 Hz), 1.21–1.42 (m, 9H), 1.44 (s, 9H), 1.50–1.61 (m, 1H), 1.71–1.77 (m, 1H), 1.80–1.90 (m, 2H), 1.98–2.04 (m, 2H), 2.08–2.21 (m, 1H), 2.38–2.42 (m, 1H), 2.93 (qu, 1H, *J* = 7.2 Hz), 3.57 (dt, 1H, *J* = 3.0, 8.5 Hz), 3.61–3.68 (m, 1H), 3.68 (dd, 1H, *J* = 3.4, 9.5 Hz), 3.76 (dd, 1H, *J* = 4.2, 18.4 Hz), 3.90 (dd, 1H, *J* = 3.1, 9.5 Hz), 4.08–4.18 (m, 3H), 4.40 (dd, 1H, *J* = 4.6, 8.3 Hz), 4.47 and 4.55 (AB type d's, each 1H, *J* = 12.2 Hz), 4.58–4.68 (m, 3H), 4.74 (dt, 1H, *J* = 3.2, 8.1 Hz), 5.07 (br d, 1H, *J* = 6.6 Hz), 5.16 (dt, 1H, *J* = 2.8, 8.2 Hz), 5.22 (dt, 1H, *J* = 1.3, 10.4 Hz), 5.30 (dq, 1H, *J* = 1.4, 17.4 Hz), 5.81–5.91 (m, 1H), 6.70 (t, 1H, *J* = 4.2 Hz), 6.74 (d, 1H, *J* = 8.1 Hz), 7.26–7.36 (m, 5H), 7.45 (d, 1H, *J* = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.7, 13.0, 14.1, 14.3, 17.9, 19.6, 22.6, 24.8, 25.1, 25.7, 26.3, 27.1, 28.3, 29.1, 30.4, 31.7, 37.0, 41.2, 41.5, 47.5, 52.7, 56.9, 59.6, 66.1, 68.8, 69.6, 73.3, 76.6, 77.5, 118.7, 127.7, 127.8, 128.4, 131.5, 137.5, 155.7, 168.8, 169.7, 170.4, 171.0, 171.3, 173.7; IR ($CHCl_3$) cm^{-1}: 3431, 2959, 2931, 2860, 1745, 1714, 1676, 1500, 1256, 1162; HRMS calcd for $C_{51}H_{85}N_5O_{12}SiNa$ $(M+Na)^+$ calcd 1010.5861, found 1010.5862. Anal. calcd for $C_{51}H_{85}N_5O_{12}Si{\cdot}1/2H_2O$: C, 61.42; H, 8.69; N, 7.02, found: C, 61.31; H, 8.74; N, 7.16; $[\alpha]_D^{25}$ −38.4 (*c* 1.07, $CHCl_3$).

4.1.51. (2*R*,3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-2-methyl-nonanoyl-L-homo-Pro-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21m). 97%, a colorless amorphous foam, ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.84 (d, 3H, *J* = 7.1 Hz), 0.85–0.93 (m, 15H), 1.12 (d, 3H, *J* = 7.0 Hz), 1.18 (d, 3H, *J* = 6.0 Hz), 1.19–1.39 (m, 10H), 1.45 (s, 9H), 1.40–1.52 (m, 2H), 1.57–1.72 (m, 2H), 1.74–1.85 (m, 3H), 1.92–1.98 (m, 1H), 2.23 (br d, 1H, *J* = 13.2 Hz), 3.09–3.16 (m, 2H), 3.66 (dd, 1H, *J* = 3.1, 9.5 Hz), 3.83 (dd, 1H, *J* = 4.2, 18.4 Hz), 3.92 (dd, 1H, *J* = 3.0, 9.5 Hz), 4.02 (br d, 1H, *J* = 13.2 Hz), 4.08–4.20 (m, 3H), 4.42 (dd, 1H, *J* = 4.5, 8.4 Hz), 4.47 and 4.54 (AB type d's, each 1H, *J* = 12.1 Hz), 4.60–4.68 (m, 2H), 4.74 (dt, 1H, *J* = 3.1, 8.2 Hz), 5.07–5.15 (m, 2H), 5.20 (br d, 1H, *J* = 4.8 Hz), 5.24 (dd, 1H, *J* = 1.3, 10.5 Hz), 5.30 (dq, 1H, *J* = 1.4, 16.7 Hz), 5.81–5.91 (m, 1H), 6.63 (d, 1H, *J* = 8.2 Hz), 6.71 (d, 1H, *J* = 5.4 Hz), 6.74 (d, 1H, *J* = 8.3 Hz), 7.26–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.0, −4.6, 11.8, 12.1, 14.0, 14.1, 14.4, 17.9, 19.6, 20.3, 22.6, 22.7, 25.2, 25.6, 25.7, 25.9, 26.4, 28.3, 29.0, 29.8, 31.6, 37.4, 39.4, 41.2, 43.6, 52.2, 52.6, 56.4, 66.2, 68.8, 69.5, 73.3, 76.4, 118.8, 127.7, 127.9, 128.5, 131.5, 137.4, 155.7, 169.1, 169.6, 170.4, 170.8, 171.0, 173.6; IR (KBr) cm^{-1}: 3317, 2957, 2931, 2858, 1747, 1657, 1525, 1366, 1196, 835; HRMS calcd for $C_{52}H_{87}N_5O_{12}SiNa$ $(M+Na)^+$ calcd 1024.6018, found 1024.6019. Anal. calcd for $C_{52}H_{87}N_5O_{12}Si{\cdot}1/2H_2O$: C, 61.75; H, 8.77; N, 6.92, found: C, 61.57; H, 8.43; N, 6.83; $[\alpha]_D^{24}$ −50.5 (*c* 1.06, $CHCl_3$).

4.1.52. (3*R*)-3-[Boc-L-*allo*-Thr(TBS)-GlyO]-nonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21n). 90%, a colorless amorphous foam, ^1H NMR (400 MHz, $CDCl_3$, major conformer) δ ppm: 0.03 (s, 3H), 0.06 (s, 3H), 0.81–1.00 (m, 21H), 0.92 (d, 3H, *J* = 6.6 Hz), 1.14 (d, 3H, *J* = 6.2 Hz), 1.18–1.42 (m, 10H), 1.42 (s, 9H), 1.58–1.77 (m, 5H), 1.98–2.05 (m, 1H), 2.55 (dd, 1H, *J* = 5.1, 15.1 Hz), 2.65 (dd, 1H, *J* = 8.0, 15.1 Hz), 2.90 (s, 3H), 3.66 (dd, 1H, *J* = 3.0, 9.5 Hz), 3.77 (dd, 1H, *J* = 4.0, 18.4 Hz), 3.93 (dd, 1H, *J* = 2.9, 9.5 Hz), 4.11–4.21 (m, 2H), 4.25 (dd, 1H, *J* = 6.6, 18.4 Hz), 4.40 (dd, 1H, *J* = 5.9, 8.8 Hz), 4.46 and 4.57 (AB type d's, each 1H, *J* = 12.2 Hz), 4.59–4.68 (m, 2H), 4.78–4.81 (m, 1H), 5.16 (dd, 1H, *J* = 6.0, 9.5 Hz), 5.22 (dd, 1H, *J* = 1.3, 10.3 Hz), 5.20–5.36 (m, 3H), 5.80–5.90 (m, 1H), 6.68 (d, 1H, *J* = 8.3 Hz), 6.77 (d, 1H, *J* = 8.8 Hz), 6.97 (dd, 1H, *J* = 4.1, 5.8 Hz), 7.25–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: −5.0, −4.7, 11.5, 14.0, 14.5, 17.9, 19.6, 21.9, 22.6, 23.2, 24.9, 25.2, 25.6, 25.7, 26.2, 28.2, 28.3, 29.0, 31.0, 31.6, 34.3, 36.1, 36.9, 38.7, 41.2, 52.7, 54.6, 56.8, 66.2, 68.9, 69.6, 72.2, 73.4, 77.5, 118.7, 127.7, 127.9, 128.5, 131.5, 137.4, 155.6, 169.6, 169.7, 170.5, 170.75, 170.81, 170.9; IR ($CHCl_3$) cm^{-1}: 3431, 3365, 2959, 2931, 1743, 1676, 1499, 1368, 1256, 1163; HRMS calcd for $C_{52}H_{89}N_5O_{12}SiNa$ $(M+Na)^+$ 1026.6175, found 1026.6206; anal. calcd for $C_{52}H_{89}N_5O_{12}Si{\cdot}3/2H_2O$: C, 60.55; H, 8.99; N, 6.79, found: C 60.31; H, 8.68; N, 6.97; $[\alpha]_D^{26}$ −33.1 (*c* 1.06, $CHCl_3$).

4.1.53. (2*R*,3*R*)-3-[Boc-*N*-Me-L-*allo*-Thr(TBS)-GlyNH]-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21o). 99%, a colorless amorphous foam, ^{1}H NMR [400 MHz, CD_3OD, two rotamers (major/minor = 4.5/1)] δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.85–0.98 (m, 21H), 0.96 (d, 3H, J = 6.5 Hz), 1.05–1.45 (m, 14H), 1.08 (d, 3H, J = 6.8 Hz), 1.17 (d, 3H, J = 5.9 Hz), 1.45 (s, 9H), 1.78–1.88 (m, 1H), 1.90–1.93 (m, 1H), 2.95* (s, 1/2H), 3.04 (s, 5/2H), 3.04–3.16 (m, 1H), 3.68–3.74 (m, 1H), 3.74 (dd, 1H, J = 3.8, 9.8 Hz), 3.89 (dd, 1H, J = 4.5, 9.8 Hz), 3.95–4.00 (m, 2H), 4.03–4.05 (m, 1H), 4.09–4.20 (m, 1H), 4.45–4.48 (m, 1H), 4.49 and 4.57 (AB type d's, each 5/6H, J = 12.1 Hz), 4.50* and 4.58* (AB type d's, each 1/6H, J = 11.9 Hz), 4.62–4.64 (m, 2H), 4.70 (t, 5/6H, J = 4.5 Hz), 4.73* (t, 1/6H, J = 4.3 Hz), 5.20 (dd, 1H, J = 2.7, 11.6 Hz), 5.24–5.26 (m, 1H), 5.31 (dd, 1H, J = 2.7, 18.9 Hz), 5.85–5.96 (m, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (125 MHz, CD_3OD, both rotamers) δ ppm: −4.8, −4.4, 12.0, 12.1, 13.5, 14.4, 14.9, 15.1, 18.8, 20.3, 22.1, 23.3, 23.65, 23.71, 23.8, 25.9, 26.0, 26.3, 27.4, 27.5, 28.8, 30.1, 30.3, 31.5, 32.2, 32.9, 37.4, 38.9, 40.5, 43.8, 53.2, 54.3, 57.6, 58.1, 62.4, 67.0, 69.1, 69.7, 70.4, 70.5, 74.2, 80.8, 118.7, 128.8, 128.9, 129.4, 132.4, 133.2, 139.1, 170.9, 171.1, 172.9, 173.5, 178.1; IR ($CHCl_3$) cm^{-1}: 3429, 3347, 2960, 2931, 2859, 1668, 1501, 1368, 1257, 1162; HRMS calcd for $C_{53}H_{92}N_6O_{11}SiNa$ $(M+Na)^+$ 1039.6491, found 1039.6516. Anal. calcd for $C_{53}H_{92}N_6O_{11}Si$: C, 62.57; H, 9.11; N, 8.26, found: C 62.46; H, 8.84; N, 8.09; $[\alpha]_D^{24}$ −50.7 (*c* 1.29, $CHCl_3$).

4.1.54. (2*R*,3S)-3-(Boc-L-Thr(TBS)-GlyO)-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21p). 82%, a yellow amorphous foam, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 0.05 (s, 3H), 0.08 (s, 3H), 0.83 (d, 3H, J = 6.8 Hz), 0.85–0.90 (m, 9H), 0.87 (s, 9H), 0.96 (d, 3H, J = 6.8 Hz), 1.12 (d, 3H, J = 6.8 Hz), 1.17–1.33 (m, 10H), 1.20 (d, 3H, J = 5.9 Hz), 1.42–1.64 (m, 4H), 1.44 (s, 9H), 1.72–1.78 (m, 1H), 1.95–2.00 (m, 1H), 2.91–2.95 (m, 1H), 2.94 (s, 3H), 3.67 (dd, 1H, J = 2.9, 9.8 Hz), 3.90–3.95 (m, 2H), 4.07–4.16 (m, 3H), 4.44 (dd, 1H, J = 4.9, 8.8 Hz) 4.47 and 4.56 (AB type d's, each 1H, J = 12.2 Hz), 4.60–4.67 (m, 2H), 4.75 (dt, 1H, J = 2.9, 7.8 Hz), 5.09 (d, 1H, J = 7.8 Hz), 5.16 (dd, 1H, J = 5.9, 9.8 Hz), 5.23 (dd, 1H, J = 2.0, 10.8 Hz), 5.25–5.27 (m, 1H), 5.30 (dd, 1H, J = 2.0, 17.6 Hz), 5.82–5.90 (m, 1H), 6.66 (d, 1H, J = 7.8 Hz), 6.71–6.77 (m, 2H), 7.27–7.36 (m, 5H), ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: −5.1, −4.6, 11.7, 14.0, 14.1, 14.2, 17.9, 19.7, 21.8, 22.5, 23.2, 24.7, 25.2, 25.7, 26.3, 28.3, 29.0, 30.5, 31.6, 32.4, 35.7, 37.2, 40.4, 41.3, 52.6, 54.0, 56.2, 66.2, 68.8, 69.5, 73.3, 77.5, 118.8, 127.7, 127.9, 128.4, 131.5, 137.3, 169.0, 169.6, 170.5, 170.7, 170.8, 175.0; IR (KBr) cm^{-1}: 3312, 2958, 2931, 2859, 1747, 1653, 1525, 1389, 1198, 1111; HRMS calcd for $C_{53}H_{92}N_5O_{12}Si$ $(M+H)^+$ 1018.6512, found 1018.6519; $[\alpha]_D^{24}$ −52.6 (*c* 1.41, $CHCl_3$).

4.1.55. (2*R*,3*R*)-3-[Boc-*N*-Me-L-*allo*-Thr(TBS)-GlyO]-2-methylnonanoyl-*N*-Me-L-Leu-L-*allo*-Ile-L-Ser(Bn)-OAllyl (21q). 100%, a colorless amorphous foam, ^{1}H NMR (400 MHz, $CDCl_3$, major conformer) δ ppm: −0.04 (s, 3H), 0.04 (s, 3H), 0.80–0.90 (m, 21H), 0.92–0.95 (m, 3H), 1.08 (d, 3H, J = 6.8 Hz), 1.20–1.30 (m, 11H), 1.22 (d, 3H, J = 6.1 Hz), 1.42 (s, 9H), 1.56–1.70 (m, 2H), 1.71–1.78 (m, 2H), 1.93–2.01 (m, 1H), 3.00 (s, 3H), 3.11 (qu, 1H, J = 6.4 Hz), 3.19 (s, 3H), 3.53 (d, 1H, J = 17.2 Hz), 3.66 (dd, 1H, J = 3.0, 9.5 Hz), 3.85 (dd, 1H, J = 6.2, 8.1 Hz), 3.91 (dd, 1H, J = 3.3, 9.5 Hz), 4.43 (dd, 1H, J = 4.5, 8.7 Hz), 4.46 and 4.55 (AB type d's, each 1H, J = 12.1 Hz), 4.53–4.58 (m, 1H), 4.58–4.67 (m, 3H), 4.73 (dt, 1H, J = 3.1, 8.2 Hz), 5.03 (br q, 1H, J = 5.7 Hz), 5.15 (dd, 1H, J = 6.0, 9.7 Hz), 5.21–5.24 (m, 2H), 5.30 (dq, 1H, J = 1.3, 16.7 Hz), 5.80–5.90 (m, 1H), 6.64 (d, 1H, J = 8.2 Hz), 6.70 (d, 1H, J = 8.7 Hz), 7.25–7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: −5.1, −5.0, −4.9, −4.8, 11.5, 11.7, 14.0, 14.1, 14.2, 17.8, 20.6, 20.9, 21.88, 21.94, 22.55, 22.64, 23.1, 23.2, 24.7, 25.4, 25.7, 26.3, 26.9, 28.27, 28.32, 29.1, 29.4, 30.4, 31.56, 31.63, 35.1, 35.7, 35.8, 37.1, 37.2, 39.9, 49.7, 52.6, 54.2, 55.3, 56.2, 66.2, 69.5, 71.1, 73.3, 75.7, 77.5, 79.6, 118.7, 127.7, 127.9, 128.4, 131.5, 137.4, 155.1, 168.5, 169.6, 170.76, 170.79, 172.6, 174.4; IR ($CHCl_3$) cm^{-1}: 3433, 2960, 2931, 2860, 1746, 1710, 1650, 1501, 1258, 1164; HRMS calcd for $C_{54}H_{94}N_5O_{12}Si$ $(M+H)^+$ calcd 1032.6669, found 1032.6680. Anal. calcd for $C_{54}H_{93}N_5O_{12}Si\cdot 1/5H_2O$: C, 62.60; H, 9.09; N, 6.76, found: C, 62.33; H, 8.64; N, 6.82; $[\alpha]_D^{27}$ −52.8 (*c* 1.17, $CHCl_3$).

4.1.56. General procedure of deprotections and macrolactamization: compound 22c. To a solution of **21c** (287 mg, 0.267 mmol) in THF (2.0 mL) was added a mixture of AcOH (110 μL, 1.92 mmol) and TBAF (1.0 M THF solution, 1.35 mL, 1.35 mmol) at 0 °C. The solution was stirred at the same temperature for 2 h and at room temperature for an additional 16 h. This reaction mixture was diluted with EtOAc and washed with 5% aqueous $KHSO_4$ solution, saturated $NaHCO_3$ aqueous solution and brine. The resulting organic layer was dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography with a gradient elution system, a 2:1–1:1 mixture of hexane and EtOAc used as eluents to give a alcohol (233 mg, 0.242 mmol, 91%) as a colorless amorphous foam. This compound (231 mg, 0.241 mmol) and morpholine (63 μL, 0.72 mmol) were dissolved in THF (2.5 mL). To this solution was added $Pd(PPh_3)_4$ (14.2 mg) and the reaction mixture was stirred at room temperature for 18 h. The mixture was concentrated and purified by column chromatography with EtOAc and then a 10:1 mixture of EtOAc and CH_3OH used as an eluents to give a acid (208 mg, 0.226 mmol, 94%) as a slightly yellow amorphous foam. To a solution of the acid (150.4 mg, 163 μmol) in CH_2Cl_2 (2.0 mL) was added TFA (0.4 mL) at room temperature. After being stirred at the same temperature, the solvents were removed in vacuo. The residue was dissolved in CH_2Cl_2 and reconcentrated repeatedly to remove excess TFA. The crude products was dried under reduced pressure to afford a TFA salt (169 mg) and which was used for macrocyclization without further purification. This salt (51.0 mg, 49.3 μmol) was dissolved in THF (27 mL) and the solution was slowly added to a suspension of HATU (208 mg, 0.547 mmol) and DIEA (185 μL) in THF (27.6 mL) for over 10 h at 0 °C with a syringe pump under high dilution condition. After being stirred at the same temperature for an additional 7 h and at room temperature for 1

day, the mixture was evaporated, diluted with 3:1 mixture of CH_3OH and EtOAc and filtered. The filtrate was concentrated, dissolved in EtOAc and washed with 1% aqueous HCl solution, saturated $NaHCO_3$ aqueous solution and then brine. The organic layer was dried over Na_2SO_4, filtered and evaporated. The residue was purified by preparative HPLC (column: Develosil ODS-HG5 (10 mm×250 mm); wavelength: 210 nm; flow rate: 4.0 mL/min) with an 89:11 mixture of CH_3OH and 1% aqueous triethylammmonium acetate as an eluent to give **22c** [13.0 mg, 16.2 μmol, 33% (two steps)] as a colorless solid (mp 72–74 °C). ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 3.5/1)] δ ppm: 0.85–0.98 (m, 15H), 1.10 (d, 12/5H, J = 6.9 Hz), 1.16* (d, 3/5H, J = 7.0 Hz), 1.18–1.67 (m, 24H), 1.72–1.76 (m, 1H), 1.82–1.92 (m, 1H), 1.99–2.04 (m, 1H), 2.08–2.16 (m, 1H), 2.79* (s, 3/5H), 3.08–3.14 (m, 1H), 3.17 (s, 12/5H), 3.62 (dd, 4/5H, J = 3.9, 17.2 Hz), 3.68 (br s, 4/5H), 3.80* (dd, 1/5H, J = 3.7, 18.5 Hz), 3.84 (dd, 1H, J = 4.7, 10.0 Hz), 3.89 (dd, 4/5H, J = 5.5, 10.0 Hz), 3.93* (dd, 1/5H, J = 5.9, 10.0 Hz), 4.01* (q, 1/5H, J = 6.0 Hz), 4.11–4.22 (m, 9/5H), 4.29 (dd, 4/5H, J = 4.9, 9.7 Hz), 4.34* (dd, 1/5H, J = 4.6, 9.1 Hz), 4.37–4.42 (m, 4/5H), 4.45* (t, 1/5H, J = 7.0 Hz), 4.54 and 4.55 (AB type d's, each 1H, J = 11.8 Hz), 4.77* (dd, 1/5H, J = 3.8, 9.5 Hz), 4.84* (d, 1/5H, J = 10.8 Hz), 5.10–5.14 (m, 4/5H), 6.75* (d, 1/5H, J = 4.3 Hz), 6.81–6.88 (m, 9/5H), 7.17* (d, 1/5H, J = 8.6 Hz), 7.24* (dd, 1/5H, J = 3.9, 7.3 Hz), 7.31–7.38 (m, 5H), 7.62 (br d, 4/5H, J = 4.7 Hz), 7.87 (br s, 4/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.69, 11.74, 11.78, 14.1, 14.6, 14.8, 15.1, 19.8, 19.9, 21.8, 22.5, 22.6, 23.04, 23.11, 24.2, 24.7, 25.2, 26.3, 26.9, 27.1, 28.8, 29.27, 29.35, 29.41, 29.51, 29.54, 29.57, 31.2, 31.9, 36.8, 37.5, 38.1, 38.4, 39.4, 40.4, 40.7, 55.4, 55.7, 56.2, 56.8, 57.3, 58.0, 59.2, 67.65, 67.69, 68.0, 73.4, 73.8, 78.1, 127.9, 128.2, 128.4, 128.6, 128.7, 136.6, 137.0, 169.0, 169.2, 169.8, 170.0, 170.8, 170.9, 171.5, 172.3, 172.8, 173.8, 174.3, 176.7; IR (KBr) cm^{-1}: 3328, 2958, 2926, 2856, 1738, 1656, 1542, 1466, 1377, 1201; HRMS calcd for $C_{43}H_{71}N_5O_9Na$ $(M+Na)^+$ calcd 824.5150, found 824.5142. Anal. calcd for $C_{43}H_{71}N_5O_9\cdot 1/2H_2O$: C, 63.68; H, 8.95; N, 8.63, found: C, 63.54; H, 8.79; N, 8.63; $[\alpha]_D^{24} = +8.0$ (c 1.18, $CHCl_3$).

4.1.57. 25-*epi*-24-*O*Bn-globomycin (22d). 40% (two steps), a colorless solid (mp 72–74 °C), ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 3.0/1)] δ ppm: 0.88 (t, 9/4H, J = 6.7 Hz), 0.90–0.96 (m, 42/4H), 1.00 (d, 9/4H, J = 6.8 Hz), 1.10 (d, 9/4H, J = 7.0 Hz), 1.16* (d, 3/4H, J = 7.0 Hz), 1.18–1.43 (m, 39/4H), 1.22 (d, 9/4H, J = 6.0 Hz), 1.47–1.58 (m, 1H), 1.57–1.70 (m, 2H), 1.72–1.76 (m, 2H), 1.87–1.99* (m, 2/4H), 2.02–2.09 (m, 3/4H), 2.10–2.15 (m, 3/4H), 2.80* (s, 3/4H), 3.07–3.12 (m, 1H), 3.17 (s, 9/4H), 3.60* (d, 1/4H, J = 3.5 Hz), 3.69 (dd, 6/4H, J = 4.3, 17.2 Hz), 3.81* (dd, 1/4H, J = 3.9, 18.3 Hz), 3.85–3.93* (m, 2/4H), 3.89 (t, 6/4H, J = 5.4 Hz), 3.99* (d, 1/4H, J = 4.6 Hz), 4.13–4.23 (m, 12/4H), 4.27 (q, 3/4H, J = 5.3 Hz), 4.30–4.35 (m, 5/4H), 4.41* (dd, 1/4H, J = 5.4, 8.5 Hz), 4.45* (t, 1/4H, J = 7.1 Hz), 4.54 and 4.56 (AB type d's, each 1H, J = 11.7 Hz), 4.62* (dd, 1/4H, J = 4.8, 9.3 Hz), 4.85* (d, 1/4H, J = 10.8 Hz), 5.07–5.11 (m, 3/4H), 6.78* (d, 1/4H, J = 4.7 Hz), 6.86* (d, 1/4H, J = 9.3 Hz), 6.97 (d, 3/4H, J = 7.7 Hz), 7.04 (s, 3/4H), 7.23* (d, 1/4H, J = 8.7 Hz), 7.30–7.37 (m, 21/4H), 7.59 (dd, 3/4H, J = 4.1, 8.0 Hz), 7.74 (br d, 3/4H, J = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, both rotamers) δ ppm: 11.87, 11.91, 14.2, 15.1, 16.3, 16.4, 19.7, 19.9, 21.9, 22.68, 22.70, 23.2, 24.3, 24.85, 24.89, 25.0, 25.3, 26.4, 28.9, 29.1, 29.3, 29.5, 29.8, 31.4, 31.7, 31.8, 36.6, 37.7, 38.1, 38.5, 39.5, 39.6, 40.7, 41.0, 41.1, 55.4, 57.2, 57.9, 58.0, 58.9, 59.2, 67.5, 67.65, 67.70, 68.0, 73.4, 73.9, 77.1, 77.2, 78.1, 127.7, 128.0, 128.3, 128.5, 128.6, 136.9, 168.7, 169.1, 169.5, 169.8, 170.8, 171.2, 171.7, 172.5, 173.4, 173.6, 176.2; IR (KBr) cm^{-1}: 3326, 2959, 2929, 2872, 1738, 1656, 1540, 1465, 1202, 1115; HRMS calcd for $C_{39}H_{64}N_5O_9$ $(M+H)^+$ calcd 746.4704, found 746.4704.. Anal. calcd for $C_{39}H_{63}N_5O_9\cdot H_2O$: C, 61.31; H, 8.58; N, 9.17, found: C, 61.69; H, 8.47; N, 9.05; $[\alpha]_D^{26}$ −6.6 (c 1.02, $CHCl_3$).

4.1.58. 22-*epi*-24-*O*Bn-globomycin (22e). 50% (2 steps), a colorless solid (mp, 77–79 °C), ^{1}H NMR (500 MHz, $CDCl_3$, major confomer (major/minor = 5.2/1)) δ ppm: 0.87–0.98 (m, 15H), 1.12 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.4 Hz), 1.26–1.31 (m, 8H), 1.36–1.52 (m, 3H), 1.63–1.75 (m, 2H), 1.91–2.08 (m, 3H), 2.19–2.24 (m, 1H), 3.01–3.07 (m, 1H), 3.07–3.13 (m, 1H), 3.19 (s, 3H), 3.53 (dd, 1H, J = 3.6, 17.0 Hz), 3.67 (br s, 1H), 3.80 (dd, 1H, J = 4.0, 10.0 Hz), 3.90 (dd, 1H, J = 4.9, 10.0 Hz), 4.24 (dd, 1H, J = 4.1, 7.5 Hz), 4.37 (d, 1H, J = 8.8 Hz), 4.50-4.61 (m, 1H), 4.54 and 4.57 (AB type d's, each 1H, J = 11.9 Hz), 4.70 (q, 1H, J = 6.4 Hz), 5.32–5.36 (m, 1H), 6.35 (d, 1H, J = 2.8 Hz), 6.71 (d, 1H, J = 8.8 Hz), 7.30–7.39 (m, 5H), 7.93 (dd, 1H, J = 3.6, 9.1 Hz), 8.36 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, both rotamers) δ ppm: 11.8, 12.0, 12.2, 14.16, 14.25, 14.6, 15.0, 15.2, 19.4, 19.5, 21.8, 22.6, 22.7, 22.8, 23.2, 23.4, 24.0, 25.1, 25.3, 26.5, 27.0, 27.2, 27.3, 29.16, 29.29, 29.36, 29.42, 29.8, 31.5, 31.7, 31.8, 37.6, 38.0, 38.3, 38.5, 39.9, 40.0, 40.7, 41.9, 56.1, 56.2, 56.3, 57.1, 57.8, 58.7, 59.3, 66.0, 66.5, 67.8, 68.1, 69.2, 73.2, 73.4, 73.7, 76.5, 76.6, 78.3, 127.8, 128.0, 128.2, 128.3, 128.5, 136.4, 136.7, 169.1, 169.3, 169.78, 169.82, 170.3, 170.8, 171.3, 172.8, 172.9, 174.3, 174.6, 177.0; IR (KBr) cm^{-1}: 3324, 2959, 2930, 2872, 1742, 1655, 1543, 1467, 1203, 1116; HRMS calcd for $C_{39}H_{64}N_5O_9$ $(M+H)^+$ calcd 746.4704, found 764.4690. Anal. calcd for $C_{39}H_{63}N_5O_9\cdot H_2O$: C, 61.31; H, 8.58; N, 9.17, found: C, 61.44; H, 8.77; N, 8.94; $[\alpha]_D^{25}$ +41.3 (c 0.53, $CHCl_3$).

4.1.59. Compound 22f. 41% (two steps), a colorless solid (mp 91–93 °C), ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 3.8/1)] δ ppm: 0.87–0.97 (m, 12H), 1.00* (d, 3/5H, J = 6.8 Hz), 1.05 (d, 12/5H, J = 6.8 Hz), 1.11–1.14 (m, 27/5H), 1.17* (d, 3/5H, J = 6.8 Hz), 1.19–1.36 (m, 10H), 1.40–1.56 (m, 12/5H), 1.57–1.75 (m, 6/5H), 1.86–1.99 (m, 6/5H), 2.10–2.16* (m, 1/5H), 2.21–2.29 (m, 1H), 2.78* (s, 3/5H), 2.83 (br s, 1H), 2.99–3.07 (m, 4/5H), 3.09–3.13* (m, 1/5H), 3.18 (s, 12/5H), 3.55 (dd, 4/5H, J = 3.4, 17.1 Hz), 3.70 (br s, 4/5H), 3.75* (dd, 1/5H, J = 2.0, 18.6 Hz), 3.83 (dd, 4/5H, J = 3.9, 9.8 Hz), 3.90 (dd, 1H, J = 4.9, 9.8 Hz), 3.95* (dd, 1/5H, J = 3.9, 9.8 Hz), 4.21–4.24 (m, 4/5H), 4.29–4.32* (m, 1/5H), 4.35–4.44 (m, 2H), 4.50 (dd, 4/5H, J = 8.8, 17.1 Hz), 4.54–4.56* (m, 1/5H), 4.59 and 4.55 (AB type d's each 1H, J = 11.7 Hz), 4.64–4.69 (m, 6/5H), 4.88* (d, 1/5H,

$J = 10.7$ Hz), 5.30–5.34 (m, 4/5H), 6.39 (d, 4/5H, $J = 2.9$ Hz), 6.57* (d, 1/5H, $J = 2.9$ Hz), 6.70 (d, 4/5H, $J = 8.8$ Hz), 6.90* (d, 1/5H, $J = 8.8$ Hz), 7.06* (d, 1/5H, $J = 8.8$ Hz), 7.31–7.39 (m, 26/5H), 7.92 (dd, 4/5H, $J = 3.4$, 9.3 Hz), 8.24 (br s, 4/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.8, 12.0, 12.2, 14.00, 14.03, 15.1, 16.3, 16.4, 19.2, 19.4, 21.6, 22.50, 22.54, 22.57, 23.1, 23.2, 23.9, 24.6, 24.9, 25.1, 26.3, 29.1, 29.2, 29.3, 31.4, 31.6, 31.7, 37.5, 37.8, 38.1, 38.4, 39.8, 40.68, 40.73, 41.8, 56.1, 56.9, 57.7, 57.9, 58.2, 58.7, 59.2, 65.9, 66.4, 67.8, 68.1, 73.4, 73.7, 76.4, 76.6, 78.3, 127.8, 128.1, 128.2, 128.4, 128.7, 136.6, 136.9, 169.3, 169.5, 169.8, 170.1, 170.7, 171.0, 171.5, 172.6, 173.0, 174.2, 174.3, 177.1; HRMS calcd for $C_{39}H_{64}N_5O_9$ $(M+H)^+$ calcd 746.4704, found 746.4707. Anal. calcd for $C_{39}H_{63}N_5O_9 \cdot 1/3H_2O$: C, 62.29; H, 8.53; N, 9.31; Found: C, 62.26; H, 8.60; N, 9.25; $[\alpha]_D^{27}$, + 34.9 (*c* 1.02, $CHCl_3$).

4.1.60. 22-Deoxy-24-*O*Bn-globomycin (22g). 41% (2 steps), a colorless amorphous foam, ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 2.3/1)] δ ppm: 0.77–1.07 (m, 17H), 1.12* (d, 2H, $J = 7.0$ Hz), 1.16* (d, 1H, $J = 7.0$ Hz), 1.27–1.39 (m, 9H), 1.42–1.58 (m, 3H), 1.60–1.77 (m, 3H), 1.92–2.09 (m, 3H), 2.11–2.22 (m, 1H), 2.78* (s, 1H), 3.01–3.07 (m, 2/3H), 3.10–3.16* (m, 1/3H), 3.16 (s, 2H), 3.55 (dd, 2/3H, $J = 3.4$, 17.2 Hz), 3.79–3.97 (m, 8/3H), 3.96 (dd, 1H, $J = 4.5$, 7.9 Hz), 4.21 (dd, 2/3H, $J = 4.1$, 8.2 Hz), 4.30* (dd, 1/3H, $J = 4.1$, 8.2 Hz), 4.41–4.51 (m, 3H), 4.54 and 4.57 (AB type d's, each 1H, $J = 11.7$ Hz), 4.81* (dd, 1/3H, $J = 3.4$, 9.3 Hz), 4.85* (d, 1/3H, $J = 10.7$ Hz), 5.24–5.29 (m, 2/3H), 6.24 (d, 2/3H, $J = 8.4$ Hz), 6.53* (d, 1/3H, $J = 8.4$ Hz), 6.70 (br s, 1H), 6.89* (d, 1/3H, $J = 9.4$ Hz), 7.13* (dd, 1/3H, $J = 2.9$, 6.8 Hz), 7.27–7.39 (m, 5H), 7.63 (dd, 2/3H, $J = 3.9$, 8.8 Hz), 8.14 (br s, 2/3H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 10.0, 10.2, 10.80, 10.84, 14.0, 14.9, 15.0, 15.1, 21.7, 22.5, 22.57, 22.60, 22.7, 23.1, 23.2, 23.9, 24.0, 24.1, 24.9, 25.2, 26.4, 27.0, 27.1, 29.0, 29.2, 29.4, 31.5, 31.6, 31.7, 37.4, 37.7, 38.1, 38.5, 39.7, 40.5, 40.7, 54.6, 54.7, 55.8, 56.2, 56.3, 56.5, 59.3, 67.8, 68.1, 73.5, 73.8, 76.3, 77.5, 78.2, 127.9, 128.1, 128.3, 128.5, 128.7, 128.8, 136.6, 137.0, 168.9, 169.5, 169.90, 169.94, 171.1, 171.9, 172.8, 173.1, 174.2, 174.3, 177.1; IR ($CHCl_3$) cm^{-1}: 3429, 3360, 2963, 2932, 2873, 1667, 1543, 1503, 1467, 1101; HRMS calcd for C39H64N5O8 $(M+H)^+$ 730.4755, found 730.4752. Anal. calcd for $C_{39}H_{63}N_5O_8 \cdot H_2O$: C, 62.63; H, 8.76; N, 9.36, found: C, 62.66; H, 8.44; N, 9.26; $[\alpha]_D^{24}$ + 15.3 (*c* 2.86, $CHCl_3$).

4.1.61. 22-*O*Me-24-*O*Bn-globomycin (22h). 37% (2 steps), a colorless amorphous foam, ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 2.0/1)] δ ppm: 0.87–0.99 (m, 12H), 1.12 (d, 2H, $J = 6.8$ Hz), 1.15* (d, 1H, $J = 6.8$ Hz), 1.17 (d, 2H, $J = 6.8$ Hz), 1.19* (d, 1H, $J = 6.8$ Hz), 1.22–1.39 (m, 8H), 1.43–1.57 (m, 2H), 1.60–1.75 (m, 20/3H), 1.88–1.97 (m, 1H), 2.05–2.09* (m, 1/3H), 2.10–2.16* (m, 1/3H), 2.19–2.24 (m, 2/3H), 2.77 (s, 1H), 2.99–3.05 (m, 2/3H), 3.10–3.14* (m, 1/3H), 3.17 (s, 2H), 3.30 (s, 2H), 3.31 (s, 1H), 3.56 (dd, 2/3H, $J = 3.9$, 17.6 Hz), 3.69 (dd, 2/3H, $J = 5.9$, 18.6 Hz), 3.79–3.83* (m, 1/3H), 3.85–3.89 (m, 4/3H), 3.96* (dd, 1/3H, $J = 3.9$, 10.8 Hz), 4.01–4.06 (m, 4/3H), 4.23 (dd, 2/3H, $J = 4.9$, 7.8 Hz), 4.35–4.63 (m, 8/3H), 4.52* and 4.59* (AB type d's, each 1/3H, $J = 11.7$ Hz), 4.55 and 4.60 (AB type d's, each 2/3H, $J = 11.7$ Hz), 4.80 (dd, 2/3H, $J = 3.9$, 9.8 Hz), 4.85 (dd, 2/3H, $J = 3.9$, 7.8 Hz), 5.28–5.32 (m, 2/3H), 6.47-6.49 (m, 4/3H), 6.86–6.91 (m, 1H), 6.94–6.96* (m, 1/3H), 7.28–7.39 (m, 14/3H), 7.71 (dd, 2/3H, $J = 3.9$, 8.8 Hz), 8.28 (br s, 1H), ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.6, 11.8, 14.00, 14.03, 14.75, 14.80, 15.07, 15.10, 21.6, 22.4, 22.57, 22.62, 23.1, 23.2, 24.0, 24.8, 25.1, 26.5, 27.0, 27.1, 28.8, 29.0, 29.2, 29.3, 31.4, 31.6, 31.70, 31.73, 37.4, 37.5, 38.1, 38.5, 39.5, 40.1, 54.8, 55.5, 56.1, 56.2, 56.3, 56.4, 56.67, 56.74, 59.3, 68.0, 73.4, 73.9, 74.9, 75.3, 76.1, 77.5, 78.1, 127.9, 128.18, 128.23, 128.5, 128.60, 128.64, 128.7, 136.6, 136.9, 168.7, 169.0, 169.3, 169.5, 169.66, 169.72, 171.9, 172.6, 173.1, 174.0, 174.6; IR ($CHCl_3$) cm^{-1}: 3349, 2962, 2932, 2872, 1752, 1666, 1545, 1501, 1252, 1102. Anal. calcd for $C_{40}H_{65}N_5O_9 \cdot 2/3H_2O$: C, 62.23; H, 8.66; N, 9.07, found: C 62.00; H, 8.51; N, 9.03; HRMS calcd for $C_{40}H_{65}N_5O_9Na$ $(M+Na)^+$ 782.4680, found 782.4680; $[\alpha]_D^{26}$ + 12.1 (*c* 1.01, $CHCl_3$).

4.1.62. 1-*N*-Demethyl-24-*O*Bn-globomycin (22j). The reaction was carried out in THF as a solvent. 42% (two steps), a colorless solid (mp 197–199 °C), ^{1}H NMR (500 MHz, CD_3OD) δ ppm: 0.88–0.96 (m, 15H), 1.16 (d, 3H, $J = 7.3$ Hz), 1.21 (d, 3H, $J = 6.5$ Hz), 1.25–1.31 (m, 9H), 1.46–1.53 (m, 2H), 1.63–1.74 (m, 4H), 2.00–2.08 (m, 1H), 2.61 (qu, 1H, $J = 7.5$ Hz), 3.68 (d, 1H, $J = 17.2$ Hz), 3.79 (dd, 1H, $J = 4.4$, 9.9 Hz), 3.95 (dd, 1H, $J = 5.3$, 9.9 Hz), 4.11–4.13 (m, 1H), 4.20 (t, 1H, $J = 4.8$ Hz), 4.26–4.29 (m, 1H), 4.29 (d, 1H, $J = 4.2$ Hz), 4.38 (d, 1H, $J = 17.2$ Hz), 4.40 (d, 1H, $J = 4.9$ Hz), 4.54 and 4.55 (AB type d's, each 1H, $J = 11.9$ Hz), 5.21 (dt, 1H, $J = 3.9$, 8.1 Hz), 7.27–7.35 (m, 5H); ^{13}C NMR (100 MHz, CD_3OD) δ ppm: 12.1, 14.5, 15.5, 15.6, 19.5, 21.4, 23.70, 23.73, 26.07, 26.12, 27.5, 30.2, 32.8, 33.5, 37.9, 41.9, 42.0, 47.4, 54.7, 57.9, 59.2, 60.5, 68.5, 69.0, 74.3, 76.7, 128.7, 128.9, 129.3, 138.7, 170.8, 171.5, 172.2, 174.8, 175.7 176.7; IR (KBr) cm^{-1}: 3322, 2959, 2930, 2873, 1739, 1664, 1525, 1456, 1210, 1101; HRMS calcd for $C_{38}H_{62}N_5O_9$ $(M+H)^+$ calcd 732.4548, found 732.4561. Anal. calcd for $C_{38}H_{61}N_5O_9 \cdot 1/2H_2O$: C, 61.60; H, 8.43; N, 9.45; Found: C, 61.42; H, 8.59; N, 9.21; $[\alpha]_D^{24}$ + 9.9 (*c* 0.54, CH_3OH).

4.1.63. 1-*N*-Et derivative (22k). 54% (two steps), a colorless solid (mp, 78 °C), ^{1}H NMR [500 MHz, $CDCl_3$, major conformer (major/minor > 20/1)] δ ppm: 0.88 (t, 3H, $J = 6.8$ Hz), 0.92–0.98 (m, 12H), 1.12 (d, 3H, $J = 7.0$ Hz), 1.21–1.33 (m, 14H), 1.36–1.55 (m, 4H), 1.59–1.68 (m, 1H), 1.84–2.05 (m, 3H), 2.94–3.01 (m, 1H), 3.41–3.49 (m, 2H), 3.53 (dd, 1H, $J = 3.2$, 17.0 Hz), 3.56–3.60 (m, 2H), 3.79 (dd, 1H, $J = 4.3$, 10.0 Hz), 3.89 (dd, 1H, $J = 5.2$, 10.0 Hz), 4.01–4.09 (m, 1H), 4.22 (q, 1H, $J = 4.1$ Hz), 4.32 (dd, 1H, $J = 3.7$, 7.8 Hz), 4.41 (dd, 1H, $J = 3.7$, 7.8 Hz), 4.48 (dd, 1H, $J = 9.0$, 17.0 Hz), 4.52 and 4.56 (AB type d's, each 1H, $J = 11.9$ Hz), 5.30–5.35 (m, 1H), 6.59 (d, 1H, $J = 2.7$ Hz), 6.66 (d, 1H, $J = 8.4$ Hz), 7.30–7.39 (m, 5H), 7.77 (dd,1H, $J = 3.2$, 9.0 Hz), 8.43 (d, 1H, $J = 7.8$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$, major conformer) δ ppm: 11.8, 14.0, 14.56, 14.62, 15.6, 20.0, 22.3, 22.6, 22.8, 24.1, 25.2, 27.2, 29.2, 31.5, 31.6, 37.3, 39.0,

40.5, 41.5, 47.0, 56.5, 56.6, 58.0, 67.1, 68.05, 68.09, 73.4, 76.6, 127.9, 128.3, 128.7, 137.0, 168.9, 169.2, 170.3, 173.5, 174.8, 177.1; IR ($CHCl_3$) cm^{-1}: 3421, 3339, 2963, 2933, 2873, 1754, 1686, 1665, 1545, 1502; HRMS calcd for $C_{40}H_{66}N_5O_9$ $(M+H)^+$ 760.4861, found 760.4832. Anal. calcd for $C_{40}H_{65}N_5O_9 \cdot 1/2H_2O$: C, 62.48; H, 8.65; N, 9.11, found: C, 62.40; H, 8.91; N, 8.94; $[\alpha]_D^{25}$ +56.4 (*c* 1.33, $CHCl_3$).

4.1.64. Proline-substituted derivative (22l). 52% (two steps), a colorless solid (mp, 99–101 °C), ^1H NMR (500 MHz, $CDCl_3$, major conformer) δ ppm: 0.77 (d, 3H, *J* = 6.8 Hz), 0.88 (t, 3H, *J* = 6.8 Hz), 0.94 (t, 3H, *J* = 7.3 Hz), 1.13 (d, 3H, *J* = 6.8 Hz), 1.23–1.34 (m, 14H), 1.48–1.56 (m, 1H), 2.00–2.12 (m, 3H), 2.18–2.25 (m, 1H), 2.31–2.40 (m, 1H), 2.89 (qu, 1H, *J* = 6.8 Hz), 3.66–3.73 (m, 3H), 3.82 (dd, 2H, *J* = 4.9, 9.8 Hz), 4.02 (dd, 1H, *J* = 4.9, 16.6 Hz), 3.95 (dd, 1H, *J* = 4.9, 16.6 Hz), 4.33–4.38 (m, 2H), 4.40–4.45 (m, 2H), 4.52 and 4.53 (AB type d's, each 1H, *J* = 11.7 Hz), 4.82–4.88 (m, 1H), 5.04–5.08 (m, 1H), 5.78 (d, 1H, *J* = 6.8 Hz), 7.26–7.40 (m, 5H), 7.51 (br s, 1H), 7.56 (br d, 1H, *J* = 6.8 Hz), 7.69 (br d, 1H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.7, 11.8, 13.67, 13.72, 14.0, 14.3, 15.4, 19.6, 22.5, 22.6, 25.1, 25.2, 25.4, 27.0, 29.0, 29.1, 29.4, 29.7, 31.6, 33.0, 35.2, 41.9, 42.1, 48.1, 52.1, 57.9, 59.6, 62.6, 66.8, 69.4, 73.4, 73.6, 75.2, 76.1, 76.4, 127.88, 127.98, 128.03, 128.1, 128.4, 128.5, 137.2, 168.4, 170.4, 170.7, 171.5, 172.0, 172.3, 174.6; IR (KBr) cm^{-1}: 3338, 2961, 2931, 2873, 1741, 1658, 1525, 1456, 1261, 1099; HRMS calcd for $C_{37}H_{57}N_5O_9Na$ $(M+Na)^+$ calcd 738.4054, found 738.4055. Anal. calcd for $C_{37}H_{57}N_5O_9 \cdot 1/2H_2O$: C, 61.31; H, 8.06; N, 9.66, found: C, 61.13; H, 7.93; N, 9.64; $[\alpha]_D^{27}$ −34.3 (*c* 1.14, $CHCl_3$).

4.1.65. Homo-proline-substituted derivative (22m). 16% (two steps), a colorless solid (mp, 86 °C), ^1H NMR (400 MHz, $CDCl_3$, major conformer) δ ppm: 0.86–0.92 (m, 6H), 0.91 (d, 3H, *J* = 6.8 Hz), 0.98 (t, 3H, *J* = 6.8 Hz), 1.14 (d, 3H, *J* = 6.8 Hz), 1.21 (d, 3H, *J* = 5.9 Hz), 1.24–1.45 (m, 11H), 1.48–1.67 (br m, 2H), 1.67–1.75 (br m, 1H), 1.82–1.92 (br m, 1H), 1.97–2.05 (br m, 1H), 2.45–2.53 (br m, 2H), 2.94–3.02 (br m, 1H), 3.79–3.87 (m, 2H), 3.94 (br s, 1H), 3.98–4.08 (br m, 1H), 4.16 (dd, 1H, *J* = 7.3, 18.1 Hz), 4.27–4.33 (m, 2H), 4.45–4.67 (m, 4H), 4.75 (dd, 1H, *J* = 3.9, 8.8 Hz), 5.09 (br d, 1H, *J* = 8.8 Hz), 6.53 (d, 1H, *J* = 8.8 Hz), 6.83 (br s, 1H), 7.08 (d, 1H, *J* = 8.8 Hz), 7.28–7.37 (m, 5H), 7.46 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.9, 13.0, 14.2, 15.0, 19.9, 21.2, 22.7, 25.0, 25.6, 26.9, 27.1, 29.2, 29.8, 30.0, 31.7, 31.8, 37.8, 39.7, 40.3, 41.2, 54.8, 56.2, 57.2, 57.4, 67.7, 67.9, 73.5, 73.7, 76.8, 76.9, 127.6, 128.0, 128.3, 128.4, 128.6,136.4, 169.4, 169.5, 169.8, 171.1, 172.5, 173.7; IR ($CHCl_3$) cm^{-1}: 3690, 3422, 3361, 2931, 2861, 1737, 1676, 1503, 1425, 1429; HRMS calcd for $C_{38}H_{59}N_5O_9Na$ $(M+Na)^+$ 752.4210, found 752.4221. Anal. calcd for $C_{38}H_{59}N_5O_9 \cdot 2/3H_2O$: C, 61.52; H, 8.20; N, 9.44, found: C, 61.48; H, 8.07; N, 9.32; $[\alpha]_D^{26}$ −42.6 (*c* 1.86, $CHCl_3$).

4.1.66. 3-Demethyl-24-*O*Bn-globomycin (22n). 55% (2 steps), a colorless amorphous foam, ^1H NMR (400 MHz, $CDCl_3$, major conformer) δ ppm: 0.86–1.02 (m, 9H), 0.92 (d, 3H, *J* = 6.7 Hz), 0.97 (d, 3H, *J* = 6.8 Hz), 1.22 (d, 3H, *J* = 6.4 Hz), 1.26–1.54 (m, 11H), 1.56–1.73 (m, 3H), 1.88–1.98 (m, 2H), 2.50 (dd, 1H, *J* = 12.0, 13.3 Hz), 2.78 (dd, 1H, *J* = 1.7, 13.3 Hz), 2.94 (s, 3H), 3.11 (br, 1H), 3.69 (dd, 1H, *J* = 2.9, 18.1 Hz), 3.79 (dd, 1H, *J* = 4.4, 9.9 Hz), 3.91 (dd, 1H, *J* = 4.9, 9.9 Hz), 3.98–4.04 (m, 1H), 4.21–4.24 (m, 1H), 4.47 (dd, 1H, *J* = 6.7, 9.3 Hz), 4.53 and 4.60 (AB type d's, each 1H, *J* = 11.8 Hz), 4.58–4.61 (m, 1H), 4.87 (dd, 1H, *J* = 3.4, 9.1 Hz), 5.17–5.19 (m, 1H), 5.28–5.30 (m, 1H), 6.52–6.55 (m, 2H), 7.06 (d, 1H, *J* = 9.1 Hz), 7.27–7.40 (m, 5H), 7.55 (dd, 3H, *J* = 2.4, 8.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.9, 14.0, 14.7, 15.4, 19.8, 21.4, 21.9, 22.5, 23.3, 23.4, 24.7, 25.2, 27.1, 27.3, 28.9, 29.7, 31.5, 31.6, 32.4, 35.1, 36.4, 38.2, 39.8, 40.4, 56.0, 56.5, 56.6, 67.8, 68.2, 71.4, 73.5, 73.7, 127.97, 128.04, 128.4, 128.7, 136.8, 169.2, 171.1, 171.4, 172.1, 173.7; IR ($CHCl_3$) cm^{-1}: 3428, 3367, 2961, 2931, 2873, 1740, 1666, 1512, 1386, 1251; HRMS calcd for $C_{38}H_{61}N_5O_9Na$ $(M+Na)^+$ 754.4367, found 754.4380. Anal. calcd for $C_{38}H_{61}N_5O_9 \cdot 1/2H_2O$: C, 61.60; H, 8.43; N, 9.45, found: C 61.75; H, 8.10; N, 9.23; $[\alpha]_D^{26}$ −59.6 (*c* 1.09, $CHCl_3$).

4.1.67. 5-Aza-24-*O*Bn-globomycine (22o). 61% (two steps), a colorless sold (mp 88 °C), ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.86–0.89 (m, 6H), 0.95 (t, 3H, *J* = 7.3 Hz), 1.00–1.14 (m, 9H), 1.18 (d, 3H, *J* = 6.3 Hz), 1.21–1.43 (m, 10H), 1.58–1.69 (m, 2H), 1.82–2.04 (m, 3H), 2.30–2.37 (m, 1H), 3.01 (br s, 1H), 3.23 (s, 3H), 3.40 (br s, 2H), 3.48 (dd, 1H, *J* = 4.0, 17.0 Hz), 3.61 (br s, 1H), 3.95 (d, 2H, *J* = 7.0 Hz), 4.24–4.25 (m, 1H), 4.35 (dd, 1H, *J* = 8.7, 17.0 Hz), 4.50–4.51 (m, 1H), 4.55 and 4.59 (AB type d's, each 1H, *J* = 11.8 Hz), 4.71 (q, 1H, *J* = 7.0 Hz), 4.77 (br s, 1H), 5.95 (d, 1H, *J* = 7.0 Hz), 6.70 (br s, 1H), 7.07 (br d, 1H, *J* = 5.8 Hz), 7.29–7.36 (m, 5H), 8.12 (br s, 1H), 8.23 (br d, 1H, *J* = 7.0 Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 11.8, 14.1, 14.6, 16.0, 19.4, 22.3, 22.7, 23.2, 25.4, 26.3, 26.9, 28.8, 29.7, 31.7, 35.1, 37.9, 38.8, 43.1, 52.0, 57.3, 59.1, 63.4, 65.7, 67.1, 73.4, 127.5, 127.7, 128.3, 137.9, 168.8, 171.2, 171.7, 171.9, 173.3, 176.4; IR ($CHCl_3$) cm^{-1}: 3374, 3302, 2962, 2932, 2873, 1665, 1621, 1544, 1287, 1110; HRMS calcd for $C_{39}H_{64}N_6O_8Na$ $(M+Na)^+$ 767.4683, found 767.4683. Anal. calcd for $C_{39}H_{64}N_6O_8 \cdot H_2O$: C, 61.39; H, 8.72; N, 11.01, found: C 61.48; H, 8.50; N, 10.77; $[\alpha]_D^{24}$ −153.5 (*c* 1.30, $CHCl_3$).

4.1.68. 4-*epi*-24-*O*Bn-Globomycin (22p). 39% (two steps), a colorless solid (mp 82 °C), ^1H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 1.4/1)] δ ppm: 0.73* (d, 6/5H, *J* = 6.8 Hz), 0.82–0.95 (m, 51/5H), 0.97 (d, 9/5H, *J* = 6.5 Hz), 1.00 (d, 9/5H, *J* = 6.4 Hz), 1.13–1.32 (m, 16H), 1.39–1.45 (m, 7/5H), 1.57–1.66 (m, 2H), 1.79–1.86 (m, 3/5H), 1.96–2.03 (m, 3/5H), 2.18–2.20* (m, 2/5H), 2.35–2.37* (m, 2/5H), 2.49–2.52 (m, 3/5H), 2.84 (s, 6/5H), 2.89–2.92 (m, 3/5H), 3.06–3.10* (m, 2/5H), 3.19 (s, 9/5H), 3.22* (d, 2/5H, *J* = 9.4 Hz), 3.28 (d, 3/5H, *J* = 8.7 Hz), 3.61 (dd, 1H, *J* = 5.3, 9.6 Hz), 3.67 (dd, 1H, *J* = 4.9, 9.6 Hz), 3.85–3.96 (m, 13/5H), 4.15* (dd, 2/5H, *J* = 4.1, 7.5 Hz), 4.18–4.28 (m, 8/5H), 4.33–4.46 (m, 8/5H), 4.51 and 4.72* (AB type d's, each 2/5H, *J* = 11.8 Hz), 4.53–4.60 (m, 8/5H), 5.01* (br s, 2/5H), 5.16–5.20 (m, 3/5H), 5.21–5.26* (m, 2/5H), 6.30* (d, 2/

5H, $J = 8.7$ Hz), 6.84–6.86* (m, 2/5H), 6.94–6.95 (m, 3/5H), 7.28–7.38 (m, 33/5H), 7.89* (d, 2/5H, $J = 9.6$ Hz), 8.36 (br s, 3/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.4, 11.7, 14.0, 14.5, 15.3, 15.7, 19.5, 20.3, 21.9, 22.4, 22.5, 22.6, 23.1, 25.0, 25.3, 25.8, 25.9, 26.4, 27.0, 28.92, 28.94, 29.7, 31.3, 31.6, 31.7, 33.7, 34.6, 35.2, 37.59, 37.64, 39.5, 40.0, 41.3, 41.5, 41.9, 51.4, 54.9, 56.6, 56.8, 57.8, 60.1, 66.4, 67.6, 67.8, 68.1, 68.3, 73.6, 74.1, 77.9, 127.8, 127.9, 128.2, 128.4, 128.5, 128.7, 136.4, 137.2, 167.2, 169.6, 170.2, 170.4, 170.5, 170.6, 172.4, 172.9, 174.6, 175.7; IR ($CHCl_3$) cm^{-1}: 3394, 2963, 2931, 2873, 1727, 1663, 1535, 1498, 1261, 1100; HRMS calcd for $C_{39}H_{63}N_5O_9Na$ $(M+Na)^+$ 768.4523; Found 768.4547. Anal. calcd for $C_{39}H_{63}N_5O_9 \cdot 1/3H_2O$: C, 62.29; H, 8.53; N, 9.31, found: C 62.18; H, 8.24; N, 8.91; $[\alpha]_D^{24}$ +15.4 (*c* 1.65, $CHCl_3$).

4.1.69. 8-*N*-Me-24-*O*Bn-globomycin (22q). 41% (2 steps), a colorless solid (mp 63–65 °C), ^{1}H NMR (500 MHz, $CDCl_3$, major conformer) δ ppm: 0.83 (d, 3H, $J = 6.8$ Hz), 0.86–0.98 (m, 12H), 1.18 (d, 3H, $J = 6.8$ Hz), 1.20 (d, 3H, $J = 6.8$ Hz), 1.23–1.46 (m, 7H), 1.47–1.59 (m, 2H), 1.63–1.79 (m, 4H), 1.81–1.99 (m, 2H), 2.15–2.27 (m, 2H), 3.04 (s, 3H), 3.17–3.21 (m, 1H), 3.27 (s, 3H), 3.59 (d, 1H, $J = 8.8$ Hz), 3.62 (d, 1H, $J = 8.8$ Hz), 3.86 (dd, 1H, $J = 5.9$, 8.8 Hz), 4.05–4.09 (m, 1H), 4.33 (br d, 1H, $J = 6.8$ Hz), 4.38–4.42 (m, 1H), 4.45 (dd, 1H, $J = 2.9$, 8.8 Hz), 4.53 (d, 1H, $J = 11.2$ Hz), 4.56 (d, 1H, $J = 8.8$ Hz), 4.66 (d, 1H, $J = 11.2$ Hz), 4.76–4.81 (m, 1H), 5.11–5.15 (m, 1H), 7.11 (br d, 1H, $J = 4.8$ Hz), 7.27–7.42 (m, 6H), 8.03 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 10.9, 11.7, 11.9, 12.3, 14.0, 14.1, 15.3, 19.47, 19.50, 21.9, 22.51, 22.55, 22.59, 22.9, 23.0, 24.3, 25.3, 25.5, 26.3, 26.9, 27.4, 28.1, 28.9, 29.0, 30.9, 31.6, 31.8, 35.5, 36.0, 37.0, 37.2, 38.2, 38.3, 38.5, 40.6, 41.7, 50.0, 51.9, 52.2, 54.0, 55.7, 56.4, 59.0, 68.4, 68.6, 68.8, 69.2, 73.4, 76.3, 78.5, 127.7, 127.8, 128.1, 128.19, 128.25, 128.33, 128.6, 137.5, 168.0, 169.92, 169.99, 170.01, 170.2, 170.8, 171.4, 172.2, 172.6, 177.5; IR (KBr) cm^{-1}: 3380, 2958, 2930, 2873, 1745, 1681, 1657, 1530, 1496, 1204; HRMS calcd for $C_{40}H_{65}N_5O_9Na$ $(M+Na)^+$ calcd 782.4680, found 782.4671. Anal. calcd for $C_{40}H_{65}N_5O_9 \cdot 1/5H_2O$: C, 62.92; H, 8.63; N, 9.17, found: C, 62.51; H, 8.01; N, 9.03; $[\alpha]_D^{26}$ −21.6 (*c* 1.01, $CHCl_3$).

4.2. Globomycin analogues

Compound **22c** (28.2 mg, 35.2 μmol) was dissolved in CH_3OH (1.5 mL). To this solution, $Pd(OH)_2$ (23.6 mg) was added and the resulting mixture was stirred at room temperature for 11 h under H_2 atmosphere. $Pd(OH)_2$ was removed by filtration and the filtrate was evaporated. The residue was purified by column chromatography with a gradient elution system, 30:1–20:1 mixture of CH_2Cl_2 and CH_3OH as eluents to give **1c**[1f] (22.6 mg, 31.7 μmol, 90%) as a colorless solid (mp 92–94 °C).

4.2.1. 25-*epi*-Globomycin (1d). 97%, a colorless solid (mp 108–110 °C), ^{1}H NMR [500 MHz, $CDCl_3$, 16 mM, two rotamers (major/minor = 4.5/1)] δ ppm: 0.88 (t, 3H, $J = 6.7$ Hz), 0.90–1.05 (m, 39/4H), 1.01 (d, 9/4H, $J = 6.8$ Hz), 1.09 (d, 9/4H, $J = 6.9$ Hz), 1.14* (d, 3/4H, $J = 6.9$ Hz), 1.16–1.47 (m, 13H), 1.49–1.73 (m, 15/4H), 1.82–1.87* (m, 1/4H), 1.92–2.07* (m, 2/4H), 2.10–2.16 (m, 6/4H), 2.79* (s, 3/4H), 2.86 (br, 2H), 3.12–3.19 (m, 1H), 3.21 (s, 9/4H), 3.63 (br s, 3/4H), 3.81 (dd, 3/4H, $J = 3.8$, 17.3 Hz), 3.87* (dd, 1/4H, $J = 3.7$, 18.0 Hz), 3.93–4.03 (m, 10/4H), 4.08 (t, 3/4H, $J = 6.6$ Hz), 4.17–4.20* (m, 1/4H), 4.24 (dd, 3/4H, $J = 7.2$, 17.3 Hz), 4.30 (d, 3/4H, $J = 6.8$ Hz), 4.36–4.41 (m, 7/4H), 4.52* (t, 1/4H, $J = 7.0$ Hz), 4.59* (dd, 1/4H, $J = 5.8$, 9.1 Hz), 4.95* (d, 1/4H, $J = 9.3$ Hz), 5.03 (dt, 3/4H, $J = 3.1$, 8.6 Hz), 6.90* (d, 1/4H, $J = 9.1$ Hz), 7.18 (d, 3/4H, $J = 7.5$ Hz), 7.35 (br s, 3/4H), 7.51–7.53* (br, 2/4H), 7.65–7.68 (br m, 7/4H); ^{13}C NMR (100 MHz, $CDCl_3$, 33 mM, both rotamers) δ ppm: 11.6, 12.0, 12.7, 14.2, 15.1, 16.0, 16.5, 18.9, 19.1, 22.0, 22.7, 22.9, 23.1, 23.2, 24.5, 24.9, 25.0, 25.4, 25.7, 29.18, 29.23, 29.5, 29.8, 31.5, 31.7, 31.8, 36.5, 37.4, 38.1, 38.6, 39.0, 40.2, 40.8, 41.0, 41.5, 57.1, 57.5, 57.6, 57.8, 58.6, 59.0, 59.1, 60.7, 61.6, 66.7, 67.1, 76.5, 76.9, 77.7, 168.7, 170.38, 170.44, 170.58, 170.66, 170.9, 172.7, 173.7, 174.4, 176.4; IR (KBr) cm^{-1}: 3327, 2960, 2931, 2873, 1739, 1656, 1543, 1466, 1378, 1199; HRMS calcd for $C_{32}H_{58}N_5O_9$ $(M+H)^+$ calcd 656.4235, found 656.4227. Anal. calcd for $C_{32}H_{57}N_5O_9 \cdot 3/4H_2O$: C, 57.42; H, 8.81; N, 10.46, found: C, 57.44; H, 8.67; N, 10.27; $[\alpha]_D^{24}$ +3.1 (*c* 0.50, CH_3OH).

4.2.2. 22-*epi*-Globomycin (1e). 90%, a colorless solid (mp 110–112 °C), ^{1}H NMR [500 MHz, $CDCl_3$, 16 mM, major conformer (major/minor = 8.8/1)] δ ppm: 0.87–0.97 (m, 15H), 1.12 (d, 3H, $J = 6.8$ Hz), 1.20 (d, 3H, $J = 5.9$ Hz), 1.30–1.42 (m, 10H), 1.44–1.57 (m, 2H), 1.60–1.68 (m, 1H), 1.69–1.74 (m, 1H), 2.13–2.21 (m, 2H), 2.30 (br s, 2H), 3.03–3.09 (m, 1H), 3.22 (s, 3H), 3.62 (s, 1H), 3.65 (s, 1H), 3.86 (dd, 1H, $J = 5.9$, 11.7 Hz), 4.00 (dd, 1H, $J = 3.9$, 11.7 Hz), 4.18 (s, 1H), 4.35 (d, 1H, $J = 8.8$ Hz), 4.42–4.45 (m, 1H), 4.64 (dd, 1H, $J = 3.9$, 7.8 Hz), 4.69 (q, 1H, $J = 5.9$ Hz), 5.31–5.35 (m, 1H), 6.74 (d, 1H, $J = 8.8$ Hz), 7.55 (s, 1H), 8.02 (d, 1H, $J = 3.9$ Hz), 8.43 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, both rotamers) δ ppm: 11.76, 11.85, 13.0, 14.2, 14.5, 14.9, 15.1, 19.6, 19.8, 22.0, 22.7, 23.1, 23.3, 24.1, 25.2, 25.3, 25.6, 26,9, 27.4, 29.3, 29.8, 31.6, 31.7, 31.8, 37.2, 37.7, 38.4, 38.9, 39.4, 40.3, 40.8, 41.6, 56.6, 57.8, 58.9, 59.1, 60.9, 61.8, 65.9, 66.3, 69.1, 76.5, 77.6, 169.3, 169.7, 170.50, 170.56, 170.62, 170.9, 173.3, 173.6, 174.8, 175.2, 177.1; IR (KBr) cm^{-1}: 3330, 2959, 2931, 2873, 1740, 1657, 1543, 1467, 1379, 1204; HRMS calcd for $C_{32}H_{58}N_5O_9$ $(M+H)^+$ calcd 656.4235, found 656.4232; $[\alpha]_D^{24}$ +34.4 (*c* 0.50, CH_3OH).

4.2.3. Stereoisomer at the C(22) and C(25) positions of globomycin (1f). 95%, a colorless solid (mp, 118–120 °C), ^{1}H NMR [500 MHz, $CDCl_3$, 16 mM, two rotamers (major/minor = 5.2/1)] δ ppm: 0.88 (t, 3H, $J = 6.9$ Hz), 0.92–0.97 (m, 9H), 1.03 (d, 3H, $J = 6.7$ Hz), 1.10 (d, 3H, $J = 6.9$ Hz), 1.19 (d, 3H, $J = 6.5$ Hz), 1.20–1.33 (m, 10H), 1.34–1.42 (m, 1H), 1.46–1.60 (m, 1H), 1.60 (br s, 2H), 1.66–1.73 (m, 1H), 1.92–1.98* (m, 1/6H), 2.04–2.11 (m, 1H), 2.16–2.22 (m, 5/6H), 2.79* (s, 3/6H), 2.98 (br s, 1H), 3.05 (qu, 5/6H, $J = 7.3$ Hz), 3.16–3.21* (m, 1/6H), 3.22 (s, 15/6H), 3.48* (d, 1/6H, $J = 4.1$ Hz), 3.64 (br s, 5/6H), 3.81 (dd, 5/6H, $J = 7.8$, 18.0 Hz),

3.83–3.93 (m, 1H), 3.97–4.13 (m, 9/6H), 4.24–4.35 (m, 15/6H), 4.39* (d, 1/6H, J = 8.1 Hz), 4.48 (dd, 5/6H, J = 5.2, 8.0 Hz), 4.52* (t, 1/6H, J = 6.3, 9.3 Hz), 4.59* (dd, 1/6H, J = 6.3, 9.3 Hz), 4.62–4.68 (m, 5/6H), 5.05* (d, 1/6H, J = 9.5 Hz), 5.26–5.30 (m, 5/6H), 6.75 (d, 5/6H, J = 8.6 Hz), 6.78* (m, 1/6H), 7.41 (d, 5/6H, J = 3.1 Hz), 7.57* (d, 1/6H, J = 8.4 Hz), 7.62* (br s, 1/6H), 7.78* (br t, 1/6H, J = 2.4 Hz), 7.95 (br s, 5/6H), 8.16 (br s, 5/6H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 10.9, 11.8, 13.4, 14.02, 14.05, 14.09, 15.0, 15.6, 16.3, 19.6, 19.7, 21.8, 22.4, 22.56, 22.62, 23.0, 23.2, 24.1, 24.2, 24.5, 24.8, 25.3, 25.5, 29.1, 29.2, 29.7, 29.9, 31.5, 31.56, 31.60, 31.7, 36.7, 37.4, 38.2, 38.6, 39.2, 40.2, 40.8, 41.2, 42.2, 56.9, 57.1, 58.0, 58.4, 58.6, 58.9, 60.6, 61.9, 65.7, 66.3, 68.4, 76.4, 169.4, 169.9, 170.2, 170.85, 170.9, 171.2, 171.4, 172.7, 173.4, 174.4, 175.1, 177.2; IR (KBr) cm^{-1}: 3327, 2959, 2931, 2873, 1738, 1656, 1543, 1520, 1466, 1203; HRMS calcd for $C_{32}H_{57}N_5O_9Na$ $(M+Na)^+$ calcd 678.4054, found 678.4044. Anal. calcd for $C_{32}H_{57}N_5O_9\cdot H_2O$: C, 57.04; H, 8.83; N, 10.39, found: C, 57.23; H, 8.54; N, 10.32; $[\alpha]_D^{27}$ +16.1 (c 0.50, CH_3OH).

4.2.4. 22-Deoxyglobomycin (1g). 93%, a colorless solid (mp, 95 °C), ^{1}H NMR [400 MHz, $CDCl_3$, two rotamers (major/minor = 4.0/1)] δ ppm: 0.77–1.07 (m, 14H), 0.88 (t, 3H, J = 6.5 Hz), 1.11 (d, 12/5H, J = 6.9 Hz), 1.15* (d, 3/5H, J = 6.9 Hz), 1.26–1.55 (m, 15H), 1.67–1.87 (m, 2H), 1.98–2.07 (m, 1H), 2.09–2.20 (m, 1H), 2.78* (s, 3/5H), 3.02–3.10 (m, 4/5H), 3.15–3.20* (s, 1/5H), 3.21 (s, 12/5H), 3.55–3.72 (m, 4H), 3.86 (dd, 1H, J = 5.9, 11.5 Hz), 3.90–3.91* (m, 1/5H), 3.96 (dd, 4/5H, J = 3.9, 11.5 Hz), 4.05–4.07* (m, 1/5H), 4.19–4.24 (m, 4/5H), 4.27–4.37 (m, 9/5H), 4.52* (t, 1/5H, J = 6.9 Hz), 4.66 (dd, 4/5H, J = 3.7, 7.7 Hz), 4.75* (dd, 1/5H, J = 4.6, 9.3 Hz), 4.96* (br d, 1/5H, J = 10.0 Hz), 5.24–5.29 (m, 4/5H), 6.46 (d, 4/5H, J = 7.8 Hz), 6.86* (d, 1/5H, J = 9.3 Hz), 7.06* (d, 1/5H, J = 7.8 Hz), 7.53–7.55* (m, 1/5H), 7.65* (br s, 1/5H), 7.78 (d, 4/5H, J = 2.9 Hz), 7.80–7.85 (br, 4/5H), 8.13–8.20 (br, 4/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 10.2, 10.3, 11.60, 11.63, 12.3, 14.0, 14.7, 14.8, 14.9, 21.8, 22.5, 23.0, 23.1, 23.7, 23.9, 24.3, 25.0, 25.2, 25.7, 26.8, 27.1, 29.06, 29.11, 29.2, 29.6, 29.7, 31.5, 31.6, 31.7, 36.8, 37.4, 38.1, 38.6, 39.2, 40.5, 41.3, 41.5, 54.9, 55.1, 56.5, 57.5, 57.8,59.2, 60.8, 61.9, 76.1, 77.7, 168.9, 170.0, 170.7, 170.9, 171.3, 171.4, 173.3, 174.6, 177.2; IR ($CHCl_3$) cm^{-1}: 3355, 2963, 2932, 2874, 1733, 1671, 1545, 1503, 1465, 1379; HRMS calcd for $C_{32}H_{57}N_5O_8Na$ $(M+Na)^+$ 662.4105, found 662.4114; $[\alpha]_D^{26}$ −2.8 (c 2.05, $CHCl_3$).

4.2.5. 22-*O*Me-globomycin (1h). 99%, a colorless solid (mp, 89 °C), ^{1}H NMR [500 MHz, $CDCl_3$, 16 mM, two rotamers (major/minor = 4.3/1)] δ ppm: 0.88 (d, 3H, J = 6.8 Hz), 0.90–0.97 (m, 9H), 1.11 (d, 3H, J = 6.8 Hz), 1.16* (d, 3/5H, J = 6.8 Hz), 1.19 (d, 12/5H, J = 6.8 Hz), 1.28–1.38 (m, 12H), 1.41–1.52 (m, 2H), 1.55–1.63 (m, 2H), 1.64–1.72 (m, 1H), 2.07–2.12 (m, 1H), 2.16–2.21 (m, 1H), 2.78* (s, 3/5H), 3.01–3.08 (m, 1H), 3.21 (s, 12/5H), 3.34 (s, 12/5H), 3.35* (s, 3/5H), 3.62–3.77 (m, 9/5H), 3.90–4.01 (m, 9/5H), 4.05–4.10 (m, 1H), 4.17–4.25 (m, 1H), 4.30 (dd, 1H, J = 7.8, 16.6 Hz), 4.49* (t, 1/5H, J = 6.8 Hz), 4.62 (dd, 4/5H, J = 3.9, 7.8 Hz), 4.74* (dd, 1/5H, J = 3.9, 7.8 Hz), 4.80 (dd, 1/5H, J = 3.9, 8.8 Hz), 4.83 (dd, 4/5H, J = 3.9, 8.8 Hz), 4.94 (d, 1/5H, J = 10.7 Hz), 5.27–5.31 (m, 1H), 6.46 (d, 4/5H, J = 7.8 Hz), 6.89* (d, 1/5H, J = 9.8 Hz), 7.06* (d, 1/5H, J = 7.8 Hz), 7.28-7.30 (m, 4/5H), 7.47 (d, 1H, J = 3.9 Hz), 7.84–7.95 (br s, 1H), 8.09 (br s, 1H); ^{13}C NMR (125 MHz, $CHCl_3$, both rotamers) δ ppm: 11.8, 12.6, 14.2, 14.9, 15.0, 15.1, 15.2, 21.9, 22.7, 23.2, 23.3, 24.3, 25.2, 25.3, 25.9, 27.0, 27.3, 29.3, 29.6, 29.7, 29.8, 31.6, 31.7, 31.8, 37.0, 37.5, 38.3, 38.7, 39.4, 40.3, 41.3, 41.6, 55.1, 55.7, 56.3, 56.4, 56.57, 56.63, 57.8, 58.6, 59.3, 61.1, 61.8, 68.5, 74.9, 75.3, 76.0, 76.5, 77.2, 77.7, 168.5, 169.0, 169.1, 169.9, 170.2, 170.7, 173.4, 174.7, 174.9, 177.1; IR ($CHCl_3$) cm^{-1}: 3347, 2962, 2932, 1668, 1546, 1501, 1467, 1380, 1249, 1187; HRMS calcd for $C_{33}H_{60}N_5O_9$ $(M+H)^+$ 670.4391, found 670.4403. Anal. calcd for $C_{33}H_{59}N_5O_9\cdot H_2O$: C, 57.62; H, 8.94; N, 10.18, found: C 57.91; H, 8.94; N, 10.03; $[\alpha]_D^{25}$ +20.9 (c 2.69, $CHCl_3$).

4.2.6. 24-*O*Me-Globomycin (1i). 27%, a colorless amorphous foam, ^{1}H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 3.7/1)] δ ppm: 0.82–0.99 (m, 14H), 1.12 (d, 12/5H, J = 6.8 Hz), 1.17* (d, 3/5H, J = 6.8 Hz), 1.33 (d, 3H, J = 6.8 Hz), 1.52–2.00 (m, 15H), 2.00–2.09 (m, 1H), 2.10–2.17 (m, 1H), 2.79* (s, 3/5H), 3.07–3.16 (m, 1H), 3.19 (s, 12/5H), 3.39 (s, 12/5H), 3.42* (s, 3/5H), 3.61 (dd, 4/5H, J = 3.9, 17.6 Hz), 3.70 (br s, 1H), 3.67–3.83 (m, 16/5H), 4.02–4.04* (m, 1/5H), 4.10–4.15 (m, 4/5H), 4.25–4.32 (m, 8/5H), 4.43 and 4.46 (AB type d's, each 1H, J = 8.8 Hz), 4.50–4.53* (m, 1/5H), 4.80 (dd, 1H, J = 3.9, 8.8 Hz), 4.90 (d, 1H, J = 10.7 Hz), 5.16–5.20* (m, 1/5H), 6.70* (br d, 1/5H, J = 3.9 Hz), 6.81–6.85 (m, 9/5H), 7.18* (d, 1/5H, J = 7.8 Hz), 7.34* (d, 1/5H, J = 8.8 Hz), 7.69 (dd, 4/5H, J = 2.9, 7.8 Hz), 8.00 (br s, 4/5H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.9, 14.2, 14.8, 15.2, 20.0, 20.1, 21.9, 22.7, 23.2, 23.3, 24.3, 24.9, 25.3, 26.3, 27.1, 27.3, 28.4, 29.1, 29.3, 29.6, 29.8, 31.4, 31.7, 31.8, 37.0, 37.7, 38.2, 38.5, 39.7, 40.8, 41.5, 45.3, 55.5, 55.7, 56.3, 56.6, 56.8, 57.9, 59.1, 59.3, 67.9, 68.0, 70.1, 70.4, 76.6, 76.9, 77.2, 78.2, 94.4, 123.9, 129.3, 168.96, 169.00, 169.8, 170.0, 170.5, 171.0, 171.1, 172.4, 172.6, 173.9, 174.2, 176.6; IR ($CHCl_3$) cm^{-1}: 3422, 3342, 2962, 2932, 1737, 1666, 1542, 1511, 1118; HRMS calcd for $C_{33}H_{59}N_5O_9Na$ $(M+Na)^+$ 692.4210, found 692.4210. Anal. calcd for $C_{33}H_{59}N_5O_9\cdot 9/10H_2O$: C, 57.77; H, 8.76; N, 9.84, found: C, 58.06; H, 8.76; N, 9.84; $[\alpha]_D^{25}$ = +13.7 (c 1.19, $CHCl_3$).

4.2.7. 1-*N*-Demethylglobomycin (1j). 100%, a colorless solid (mp 122–124 °C), ^{1}H NMR (500 MHz, CD_3OD, single isomer) δ ppm: 0.89 (t, 3H, J = 7.1 Hz), 0.93–0.99 (m, 9H), 1.00 (d, 3H, J = 7.0 Hz), 1.18 (d, 3H, J = 7.3 Hz), 1.23 (d, 3H, J = 6.5 Hz), 1.25–1.35 (m, 9H), 1.48–1.58 (m, 2H), 1.64–1.78 (m, 4H), 2.07–2.11 (m, 1H), 2.61 (qu, 1H, J = 7.5 Hz), 3.68 (d, 1H, J = 17.2 Hz), 3.87 (dd, 1H, J = 4.5, 11.2 Hz), 3.97 (dd, 1H, J = 4.6, 11.2 Hz), 4.07 (t, 1H, J = 4.5 Hz), 4.18–4.21 (m, 1H), 4.28 (dd, 1H, J = 3.9, 10.9 Hz), 4.33 (d, 1H, J = 4.1 Hz), 4.39 (d, 1H, J = 17.2 Hz), 4.44 (d, 1H, J = 4.6 Hz), 5.24 (dt, 1H, J = 4.5, 8.3 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ ppm: 12.0, 14.4, 15.5, 19.3, 21.4, 23.61, 23.62, 26.0, 26.1, 27.6, 30.1, 32.8, 33.3, 37.8, 41.9, 42.0, 47.6, 48.3, 54.8, 59.3,

59.7, 60.5, 61.6, 68.4, 76.8, 171.2, 171.8, 173.0, 175.3 176.3, 177.1; IR (KBr) cm^{-1}: 3305, 2960, 2931, 2873, 1719, 1656, 1528, 1465, 1381, 1210; HRMS calcd for $C_{31}H_{55}N_5O_9Na$ $(M+Na)^+$ calcd 664.3898, found 664.3902. Anal. calcd for $C_{31}H_{55}N_5O_9 \cdot 11/10H_2O$: C, 56.28; H, 8.71; N, 10.59, found: C, 56.64; H, 8.46; N, 10.19; $[\alpha]_D^{26}$ +6.8 (*c* 0.50, CH_3OH).

4.2.8. 1-*N*-Et-globomycin (1k). 85% a colorless solid (mp, 86°), ^1H NMR [500 MHz, $CDCl_3$, major conformer (major/minor > 20/1)] δ ppm: 0.88 (t, 3H, *J* = 6.8 Hz), 0.90–0.96 (m, 12H), 1.12 (d, 3H, *J* = 6.8 Hz), 1.24–1.32 (m, 15H), 1.35–1.43 (m, 2H), 1.47–1.57 (m, 2H), 1.88–1.99 (m, 2H), 2.13–2.18 (m, 1H), 2.99 (qu, 1H, *J* = 6.8 Hz), 3.48 (q, 2H, *J* = 6.8 Hz), 3.56–3.60 (m, 2H), 3.85–3.95 (m, 2H), 3.98–4.04 (br, 2H), 4.14 (d, 1H, *J* = 2.9 Hz), 4.28–4.33 (m, 2H), 4.44 (dd, 1H, *J* = 9.3, 17.1 Hz), 4.49 (dd, 1H, *J* = 3.4, 7.3 Hz), 5.29 (dt, 1H, *J* = 2.9, 8.8 Hz), 6.90 (d, 1H, *J* = 6.8 Hz), 7.59 (s, 1H), 7.79 (br d, 1H, *J* = 7.8 Hz), 8.46 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, major conformer) δ ppm: 11.6, 14.0, 14.4, 14.5, 15.5, 18.5, 22.3, 22.5, 22.7, 24.0, 25.1, 27.2, 29.2, 31.4, 31.5, 37.0, 39.1, 40.1, 41.5, 47.1, 56.5, 58.9, 59.1, 61.0, 66.8, 67.2, 76.2, 168.4, 169.7, 171.1, 174.3, 175.2, 177.3; IR (KBr) cm^{-1}: 3325, 2960, 2931, 2873, 1759, 1656, 1547, 1464, 1380, 1193; HRMS calcd for $C_{33}H_{59}N_5O_9Na$ $(M+Na)^+$ 692.4210, found 692.4178. Anal. calcd for $C_{33}H_{59}N_5O_9 \cdot 3/5H_2O$: C, 58.23; H, 8.91; N, 10.29. Found: C, 57.93; H, 8.57; N, 9.99; $[\alpha]_D^{26}$ +56.0 (*c* 2.08, $CHCl_3$).

4.2.9. Proline-substituted globomycin (1l). 98%, a colorless solid (mp 134–136 °C), ^1H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 5.2/1)] δ ppm: 0.83 (d, 3H, *J* = 7.0 Hz), 0.87 (t, 3H, *J* = 7.1 Hz), 0.95 (t, 3H, *J* = 7.4 Hz), 1.09* (d, 1H, *J* = 6.9 Hz), 1.13* (d, 1H, *J* = 6.1 Hz), 1.22–1.38 (m, 15H), 1.49–1.59 (m, 1H), 1.62–1.66 (m, 1H), 1.89–1.93* (m, 1/6H), 1.95–2.02 (m, 5/6H), 2.02–2.22 (m, 17/6H), 2.23–2.32* (m, 1/6H), 2.43–2.49 (m, 5/6H), 2.51–2.53* (m, 1/6H), 2.86–2.95 (m, 2H), 3.49–3.54 (m, 5/6H), 3.57–3.62 (m, 1H), 3.64–3.79 (m, 13/6H), 3.92 (dd, 5/6H, *J* = 5.9, 14.8 Hz), 3.96 (dd, 5/6H, *J* = 5.4, 14.8 Hz), 4.07–4.13* (m, 1/6H), 4.21-4.32 (m, 14/6H), 4.37 (t, 5/6H, *J* = 7.8 Hz), 4.54–4.56 (m, 10/6H), 4.74 (d, 5/6H, *J* = 8.2 Hz), 4.93* (dd, 1/6H, *J* = 4.8, 8.2 Hz), 5.05–5.13 (m, 1H), 5.20–5.21* (m, 1/6H), 5.41* (br d, 1/6H, *J* = 10.2 Hz), 5.55* (d, 1/6H, *J* = 9.2 Hz), 5.76 (d, 5/6H, *J* = 5.8 Hz), 7.07* (d, 1/6H, *J* = 3.8 Hz), 7.52 (br s, 5/6H), 7.56 (d, 5/6H, *J* = 7.0 Hz), 7.78 (d, 5/6H, *J* = 6.8 Hz), 8.34* (br, 1/6H), 8.75* (br d, 1/6H, *J* = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, 33 mM, both rotamers) δ ppm: 11.6, 11.9, 13.6, 13.9, 14.0, 14.4, 15.2, 18.0, 19.7, 22.4, 22.5, 24.7, 24.9, 25.1, 25.4, 26.4, 27.0, 28.87, 28.90, 29.0, 29.6, 31.5, 31.6, 31.9, 32.5, 34.6, 35.1, 40.9, 41.4, 42.3, 42.8, 48.0, 48.7, 53.9, 55.8, 56.6, 58.3, 58.9, 59.3, 61.7, 62.2, 62.8, 66.2, 66.4, 75.6, 76.4, 169.3, 169.5, 170.3, 170.7, 171.3, 171.4, 172.3, 172.8, 173.0, 173.8, 175.1; IR (KBr) cm^{-1}: 3339, 2961, 2931, 2875, 1739, 1658, 1528, 1463, 1266, 1077; HRMS calcd for $C_{30}H_{51}N_5O_9Na$ $(M+Na)^+$ calcd 648.3584, found 648.3589. Anal. calcd for $C_{30}H_{51}N_5O_9 \cdot H_2O$: C, 55.97; H, 8.30; N, 10.88, found: C, 56.12; H, 8.11; N, 10.87; $[\alpha]_D^{25}$ −40.4 (*c* 1.14, $CHCl_3$).

4.2.10. Homo-proline substituted globomycin (1m). 89%, a colorless solid (mp 104 °C), ^1H NMR (400 MHz, $CDCl_3$, 16 mM, major conformer) δ ppm: 0.81–0.99 (m, 12H), 1.14 (d, 3H, *J* = 6.8 Hz), 1.20–1.54 (m, 12H), 1.23 (d, 3H, *J* = 5.9 Hz), 1.55–1.83 (br m, 3H), 2.02–2.12 (br m, 1H), 2.43–2.56 (br m, 2H), 3.03–3.09 (m, 1H), 3.58–4.54 (br m, 8H), 4.58–4.72 (br m, 2H), 4.77–4.83 (br m, 1H), 5.07–5.21 (br m, 1H), 6.61 (d, 1H, *J* = 8.8 Hz), 7.41 (br d, 1H, *J* = 5.9 Hz), 7.66 (br s, 1H), 7.71 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 29 mM, both rotamers) δ ppm: 11.7, 11.9, 13.3, 14.2, 14.3, 14.8, 15.0, 18.9, 21.2, 22.7, 22.8, 24.9, 25.3, 26.9, 27.1, 29.1, 29.2, 29.4, 29.8, 30.1, 31.7, 31.8, 31.9, 32.0, 37.5, 39.7, 40.2, 41.7, 56.5, 57.4, 58.3, 60.9, 66.9, 76.5, 76.8, 77.2, 169.4, 170.4, 170.7, 170.8, 171.0, 171.1, 171.9, 173.4, 174.1; IR ($CHCl_3$) cm^{-1}: 3690, 3347, 2932, 2861, 1739, 1658, 1512, 1461, 1381, 1249; HRMS calcd for $C_{31}H_{53}N_5O_9Na$ $(M+Na)^+$ 662.3741, found 662.3758. Anal. calcd for $C_{31}H_{53}N_5O_9 \cdot H_2O$: C, 56.60; H, 8.43; N, 10.65; found: C, 56.89; H, 8.31; N, 10.37; $[\alpha]_D^{26}$ −56.9 (*c* 1.93, $CHCl_3$).

4.2.11. 3-Demethylglobomycin (1n). 94%, a coloreless powder (mp 107 °C), ^1H NMR [500 MHz, $CDCl_3$, two rotamers (major/minor = 4.2/1)] δ ppm: 0.87–0.90 (m, 5H), 0.92–1.00 (m, 9H), 1.19 (d, 3H, *J* = 6.8 Hz), 1.23–1.48 (m, 11H), 1.54–1.78 (m, 3H), 1.90–2.00 (m, 2H), 2.11–2.19 (m, 1H), 2.38* (dd, 1/5H, *J* = 3.9, 16.6 Hz), 2.50 (t, 4/5H, *J* = 12.7 Hz), 2.76 (d, 4/5H, *J* = 12.7 Hz), 2.81* (s, 3/5H), 2.92* (d, 1/5H, *J* = 6.8 Hz), 2.95 (s, 12/5H), 3.00* (dd, 1/5H, *J* = 4.9, 16.6 Hz), 3.74 (dd, 4/5H, *J* = 2.9, 18.6 Hz), 3.88–4.00 (m, 2H), 4.03–4.14 (m, 6/5H), 4.24–4.35 (m, 9/5H), 4.32–4.35 (m, 1H), 4.42–4.47 (m, 1H), 4.45 (dd, 1H, *J* = 5.4, 8.3 Hz), 4.71* (dd, 1/5H, *J* = 4.4, 9.4 Hz), 4.91 (dd, 4/5H, *J* = 3.4, 9.4 Hz), 5.11 (d, 4/5H, *J* = 7.8 Hz), 5.20–5.24 (m, 1H), 5.30–5.34* (m, 1/5H), 6.64* (d, 1/5H, *J* = 8.8 Hz), 6.99 (d, 4/5H, *J* = 7.8 Hz), 7.12 (d, 4/5H, *J* = 9.8 Hz), 7.24 (s, 4/5H), 7.45–7.47* (m, 1/5H), 7.54* (t, 1/5H, *J* = 5.4 Hz), 7.57–7.61* (br, 1/5H, *J* = 3.9 Hz), 7.65 (d, 4/5H, *J* = 7.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.6, 11.8, 13.98, 14.04, 14.8, 15.3, 18.4, 21.3, 21.8, 22.48, 22.53, 23.4, 24.5, 24.7, 24.9, 25.2, 27.4, 28.9, 29.0, 29.5, 31.5, 31.6, 32.5, 35.1, 36.4, 37.6, 40.1, 40.5, 56.0, 58.0, 59.0, 60.9, 66.9, 71.5, 170.4, 170.9, 171.2, 171.5, 171.7, 172.1, 174.5; IR (KBr) cm^{-1}: 3371, 2959, 2931, 2872, 1742, 1657, 1518, 1466, 1385, 1204; HRMS calcd for $C_{31}H_{56}N_5O_9$ $(M+H)^+$ 642.4078, found 642.4086. Anal. calcd for $C_{31}H_{55}N_5O_9 \cdot 27/50H_2O$: C, 57.15; H, 8.68; N, 10.75; Found: C 57.54; H, 8.69; N, 10.35; $[\alpha]_D^{25}$ −61.8 (*c* 1.13, $CHCl_3$).

4.2.12. 5-Aza-globomycin (1o). 94%, a colorless solid (mp 212–213.5 °C), ^1H NMR (500 MHz, CD_3OD, major conformer) δ ppm: 0.86–1.04 (m, 17H), 1.07 (d, 3H, *J* = 6.8 Hz), 1.24 (d, 3H, *J* = 6.8 Hz), 1.11–1.46 (m, 9H), 1.56–1.60 (m, 1H), 1.61–1.70 (m, 1H), 1.73–1.78 (m, 1H), 1.93–1.99 (m, 1H), 2.25–2.30 (m, 1H), 3.14–3.17 (m, 1H), 3.25 (s, 3H), 3.82 and 3.88 (AB type d's, each 1H, *J* = 17.1 Hz), 3.86 (dd, 1H, *J* = 3.9, 11.0 Hz), 3.95–4.02 (m, 1H), 4.07 (dd, 1H, *J* = 3.9, 11.0 Hz), 4.09–4.12 (m, 1H), 4.13–4.18 (m, 1H), 4.22 (d, 1H, *J* = 5.9 Hz), 4.35 (br d, 1H, *J* = 5.9 Hz), 4.60 (t, 1H, *J* = 3.9 Hz),

^{13}C NMR (125 MHz, CD_3OD, both rotamers) δ ppm: 8.8, 11.5, 12.4, 12.5, 16.5, 19.0, 20.7, 20.8, 23.5, 24.4, 24.8, 27.0, 29.9, 33.3, 35.0, 37.5, 40.6, 45.5, 45.9, 46.1, 46.3, 50.4, 53.2, 58.3, 61.0, 64.7, 168.9, 169.7, 169.9, 170.38, 180.39, 170.7, 175.7; IR (KBr) cm^{-1}: 3342, 2959, 2930, 2873, 1657, 1520, 1467, 1408, 1271, 1076; HRMS calcd for $C_{32}H_{58}N_6O_8Na$ $(M+Na)^+$ 677.4214, foundd 677.4211. Anal. calcd for $C_{32}H_{58}N_6O_8{\cdot}1/3H_2O$: C, 58.16; H, 8.95; N, 12.72; Found: C 58.00; H, 8.81; N, 12.57; $[\alpha]_D^{24}$ −65.5 (*c* 1.05, CH_3OH).

4.2.13. 4-*epi*-Globomycin (1p). 95%, a colorless solid, (mp, 81 °C), ^{1}H NMR [500 MHz, $CDCl_3$, 16 mM, two rotamers (major/minor = 2.6/1)] δ ppm: 0.77 (d, 6/7H, *J* = 6.8 Hz), 0.83–1.01 (m, 99/7H), 1.13–1.40 (m, 114/7H), 1.46-1.53 (m, 5/7H), 1.55-1.64 (m, 9/7H), 1.68–1.74 (m, 5/7H), 1.77–1.88 (m, 1H), 1.94–1.99 (m, 5/7H), 2.13–2.17* (m, 2/7H), 2.24–2.27 (m, 1H), 2.84 (s, 6/7H), 2.94–2.98 (m, 5/7H), 3.12–3.18* (m, 2/7H), 3.18 (s, 15/7H), 3.39 (br s, 5/7H), 3.51–3.56* (m, 2/7H), 3.61 (t, 5/7H, *J* = 7.8 Hz), 3.78–3.83 (m, 1H), 3.89–4.03 (m, 19/7H), 4.10–4.19 (m, 2H), 4.27–4.31 (m, 1H), 4.41–4.44 (m, 9/7H), 4.54* (dd, 2/7H, *J* = 3.9, 9.8 Hz), 4.60* (dd, 2/7H, *J* = 3.9, 9.8 Hz), 4.77 (br s, 5/7H), 5.22* (t, 2/7H, *J* = 9.3 Hz), 5.27–5.29 (m, 5/7H), 6.36* (d, 2/7H, *J* = 8.8 Hz), 7.23–7.25* (m, 2/7H), 7.42–7.45 (m, 1H), 7.50 (br s, 5/7H), 7.82–7.84 (m, 12/7H); ^{13}C NMR (125 MHz, $CDCl_3$, both rotamers) δ ppm: 11.3, 11.5, 11.6, 13.9, 14.0, 14.4, 15.3, 19.4, 19.7, 22.2, 22.4, 22.47, 22.50, 22.6, 23.0, 25.0, 25.3, 25.7, 25.9, 26.8, 26.9, 28.8, 29.0, 29.6, 29.7, 31.5, 31.6, 33.1, 35.4, 37.1, 37.7, 38.4, 39.6, 39.8, 40.9, 41.2, 41.4, 54.3, 56.5, 56.8, 57.0, 59.0, 59.6, 59.9, 61.4, 66.7, 67.0, 68.4, 73.9, 77.9, 168.6, 169.5, 170.5, 170.9, 171.0, 171.2, 171.3, 173.1, 174.4, 175.2, 176.1; IR ($CHCl_3$) cm^{-1}: 3390, 3336, 2963, 2932, 2874, 1737, 1674, 1531, 1501, 1263; HRMS calcd for $C_{32}H_{57}N_5O_9Na$ $(M+Na)^+$ 678.4054, found 678.4055. Anal. calcd for $C_{32}H_{57}N_5O_9{\cdot}H_2O$: C, 57.04; H, 8.83; N, 10.39, found: C 56.77; H, 8.91; N, 10.24; $[\alpha]_D^{24}$ −1.23 (*c* 1.02, $CHCl_3$).

4.2.14. 8-*N*-Me-globomycin (1q). 94%, a colorless solid (94–96 °C), ^{1}H NMR (500 MHz, $CDCl_3$, 16 mM, major conformer) δ ppm: 0.86–0.99 (m, 15H), 1.16–1.20 (m, 6H), 1.22–1.38 (m, 10H), 1.47–1.60 (m, 2H), 1.67–1.74 (m, 1H), 1.81–1.87 (m, 1H), 2.12–2.18 (m, 1H), 2.25-2.31 (m, 1H), 3.00 (s, 3H), 3.16–3.19 (m, 2H), 3.24 (br s, 1H), 3.28 (s, 3H), 3.57–3.60 (m, 1H), 3.70 (d, 1H, *J* = 18.5 Hz), 3.72-3.77 (m, 1H), 3.93-3.98 (m, 1H), 4.14–4.18 (d, 2H, *J* = 4.9 Hz), 4.36–4.41 (m, 2H), 4.55 (d, 1H, *J* = 18.5 Hz), 5.11–5.15 (m, 1H), 7.21 (d, 1H, *J* = 6.8 Hz), 7.47–7.53 (br m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, 30 mM, major conformer) δ ppm: 11.8, 12.6, 14.0, 14.1, 19.5, 22.0, 22.6, 23.0, 25.2, 25.4, 27.0, 29.1, 31.0, 31.7, 35.5, 35.9, 38.1, 40.6, 41.4, 51.9, 54.5, 54.8, 56.8, 62.0, 67.8, 68.0, 77.3, 168.7, 170.2, 171.4, 172.2, 172.6, 177.1; IR (KBr) cm^{-1}: 3370, 2958, 2930, 2873, 1739, 1654, 1530, 1504, 1468, 1206; HRMS calcd for $C_{33}H_{59}N_5O_9Na$ $(M+Na)^+$ calcd 692.4211, found 692.4185. Anal. calcd for $C_{33}H_{59}N_5O_9{\cdot}H_2O$: C, 57.62; H, 8.94; N, 10.18, found: C, 57.71; H, 8.94; N, 10.04; $[\alpha]_D^{26}$ −44.5 (*c* 0.50, CH_3OH).

References and notes

1. (a) Taxonomy of producing organism and fermentation. Inukai, M.; Enokita, R.; Torikata, A.; Nakahara, M.; Iwado, S.; Arai, M. *J. Antibiot*. **1978**, *31*, 410. (b) Isolation and physico-chemical and biological characterization: Inukai, M.; Nakajima, M.; Osawa, M.; Haneishi, T.; Arai, M. *J. Antibiot*. **1978**, *31*, 421. (c) Structual determination of **1a**: Nakajima, M.; Inukai, M.; Haneishi, T.; Terahara, A.; Arai, M. *J. Antibiot*. **1978**, *31*, 426. (d) Kogen, H.; Kiho, T.; Nakayama, M.; Furukawa, Y.; Kinoshita, T.; Inukai, M. *J. Am. Chem. Soc*. **2000**, *122*, 10214. (e) Kiho, T.; Nakayama, M.; Kogen, H. *Tetrahedron* **2003**, *59*, 1685. (f) Kiho, T.; Nakayama, M.; Yasuda, K.; Miyakoshi, S.; Inukai, M.; Kogen, H. *Bioorg. Med. Chem. Lett*. **2003**, *13*, 2315.
2. (a) Omoto, S.; Suzuki, H.; Inouye, S. *J. Antibiot*. **1979**, *32*, 83. (b) Omoto, S.; Ogino, H.; Inouye, S. *J. Antibiot*. **1981**, *34*, 1416.
3. Pugsley, A. P. *Microbiol. Rev*. **1993**, *57*, 50.
4. (a) Inukai, M.; Takeuchi, M.; Shimizu, K.; Arai, M. *J. Antibiot*. **1978**, *31*, 1203. (b) Hussain, M.; Ichihara, S.; Mizushima, S. *J. Biol. Chem*. **1980**, *255*, 3707. (c) Dev, I. K.; Harvey, R. J.; Ray, P. H. *J. Biol. Chem*. **1985**, *260*, 5891. (d) Ichihara, S.; Hussain, M.; Mizushima, S. *J. Biol. Chem*. **1981**, *256*, 3125. (e) Witke, C.; Götz, F. *FEMS Microl. Lett*. **1995**, *126*, 233. (f) Braun, B., Wu, H. C. In *Bacterial Cell Wall*; Ghuysen, J. M., Hakenbeck, R., Eds.; Elsevier: Amsterdam, 1994; Chapter 14.
5. (a) Cavard, D. *Arch. Microbiol*. **1998**, *171*, 50. (b) Ochsner, U. A.; Vasil, A. I.; Johnson, Z.; Vasil, M. L. *J. Bacteriol*. **1999**, *181*, 1099. (c) Paitan, Y.; Orr, E.; Ron, E. Z.; Rosenberg, E. *J. Bacteriol*. **1999**, *181*, 5644. (d) Tibor, A.; Decelle, B.; Letteson, J.-J. *Infect. Immun*. **1999**, *67*, 4960.
6. Abiko, A.; Liu, J.-F.; Masamune, S. *J. Am. Chem. Soc*. **1997**, *119*, 2586.
7. (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc*. **1981**, *103*, 2127. (b) Evans, D. A.; Dow, R. L. *Tetrahedron Lett*. **1986**, *27*, 1007. (c) Rychnovsky, S. D.; Buckmelter, A. J.; Dahanukar, V. H.; Skalitzky, D. J. *J. Org. Chem*. **1999**, *64*, 6849.
8. Samuelsen, B.; Odham, G. *Acta Chem. Scand*. **1970**, *24*, 468.
9. Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Org. Syn*. **1992**, *71*, 1.
10. Coste, J.; Le-Nguyen, D.; Castro, B. *Tetrahedron Lett*. **1990**, *31*, 205.
11. Shioiri, T.; Yokoyama, Y.; Kasai, Y.; Yamada, S. *Tetrahedron* **1976**, *32*, 2211.
12. Boden, E. P.; Keck, G. E. *J. Org. Chem*. **1985**, *50*, 2394.
13. (a) Carpino, L. A.; El-Faham, A. *J. Org. Chem*. **1994**, *59*, 695. (b) Carpino, L. A. *J. Am. Chem. Soc*. **1993**, *115*, 4397. (c) Carpino, L. A.; El-Faham, A. *J. Org. Chem*. **1995**, *60*, 3561. (d) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev*. **1997**, *97*, 2243.
14. The cyclization yield for **1m** was very low.
15. Compound **1j** and **1o** are insoluble in $CDCl_3$.
16. *O*-Bn globomycin derivative in L-Ser residue was also inactive against *Escherichia coli* SANK 70569 (>50 μg/mL). Diacetylation of **1a** in L-Ser and L-*allo*-Thr residue diminished the activity.[2b]
17. Kiho, T.; Iwata, Y.; Kogen, H.; Miyamoto, S. Conformational analysis of globomycin with a signal peptidase II inhibitory activity using molecular dynamics simulation. *Drug Des. Discov*., in press.
18. National Committee for Clinical Laboratory Standards. *Standard Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard (M7-A5)*; NCCLS: Villanova, 2000; p 7.