JOC*Article*

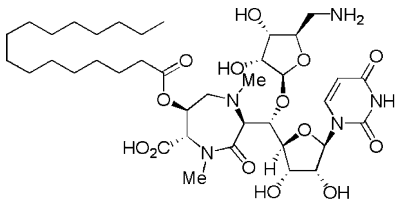
Synthesis of Caprazamycin Analogues and Their Structure−Activity Relationship for Antibacterial Activity

Shinpei Hirano, Satoshi Ichikawa,* and Akira Matsuda*

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan

matuda@pharm.hokudai.ac.jp; ichikawa@pharm.hokudai.ac.jp

Received October 19, 2007



palmitoylcaprazol

	MIC (μg/mL)
S. aureus MS16526 (MRSA)	6.25
E. faecalis NCTC 12201 (VRE)	12.5

Synthesis of palmitoyl caprazol **7**, which possesses a simple fatty acyl side chain at the 3‴-position of the diazepanone moiety, was carried out and their antibacterial activity was evaluated. The key elements of our approach include the improved synthesis of the key 5′-*β*-*O*-aminoribosyl-glycyluridine derivative, installation of the palmitoyl side chain to the cyclization precursor, and the construction of the diazepanone by an intramolecular reductive amination. The second generation synthesis of (+)-caprazol was also established. Palmitoyl caprazol **7** exhibited antibacterial activity against *Mycobacterium smegmatis* ATCC607 (MIC = 6.25 *μ*g/mL) with potency similar to that of the caprazamycins (CPZs). Palmitoyl caprazol **7** and $N^{6'}$-desmethyl palmitoyl caprazol **28** also exhibited antibacterial activity against drug-resistant bacteria including methyciline-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) strains (MIC = 3.13−12.5 *μ*g/mL).

Introduction

Tuberculosis (TB) is a disease primarily of the respiratory system from which two million people die each year.[1] With resistant strains continuing to emerge,[2] the need for better anti-TB agents possessing new mechanisms of action remains critical.[3] Caprazamycins (CPZs) (Figure 1, **1**) were isolated from a culture broth of the Actinomycete strain *Streptomyces sp*. MK730-62F2 in 2003[4] and represent the newest members of a class of naturally occurring 6′-*N*-alkyl-5′-*β*-*O*-aminoribosyl-glycyluridine antibiotics including liposidomycins[5] (LPMs, **2**) and FR-900493[6] (**3**), which have been shown to exhibit excellent antimicrobial activity against Gram-positive bacteria. In par-

* Address correspondence to this author. A.M.: phone (+81) 11-706-3228; fax (+81) 11-706-4980. S.I.: phone (+81) 11-706-3763; fax (+81) 11-706-4980.

(1) Barry, C.; Cole, S.; Fourie, B.; Geiter, L.; Gosey, L.; Grosset, J.; Kanyok, T.; Laughon, B.; Mitchison, D.; Numnn, P.; O'Brienn, R.; Robinson, T. *Scientific Blueprint for Tuberculosis Drug Development*, 2001; see: http://www.tballiance.org/.

(2) (a) Russell, D. G. *Nature* **2001**, *2*, 1−9. (b) Espinal, M. A. *Tuberculosis* **2003**, *83*, 44−51. (c) Perri, G. D.; Bonora, S. *J. Antimicrob. Chemther*. **2004**, *54*, 593−602.

(3) (a) Nayyar, A.; Jain, R. *Curr. Med. Chem*. **2005**, *12*, 1873−1886. (b) Duncan, K.; Barry, C. E., III *Curr. Opin. Microbiol.* **2004**, *7*, 460−465.

(4) (a) Igarashi, M.; Nakagawa, N.; Doi, N.; Hattori, S.; Naganawa, H.; Hamada, M. *J. Antibiot.* **2003**, *56*, 580−583. (b) Igarashi, M.; Takahashi, Y.; Shitara, T.; Nakamura, H.; Naganawa, H.; Miyake, T.; Akamatsu, Y. *J. Antibiot.* **2005**, *58*, 327−337. (c) Takeuchi, T.; Igarashi, M.; Naganawa, H.; Hamada, M. JP 2003012687, 2001. (d) Miyake, M.; Igarashi, M.; Shidara, T.; Takahashi, Y. WO 2004067544, 2004.

(5) (a) Isono, K.; Uramoto, M.; Kusakabe, H.; Kimura, K.; Izaki, K.; Nelson, C. C.; McCloskey, J. A. *J. Antibiot.* **1985**, *38*, 1617−1621. (b) Ubukata, M.; Kimura, K.; Isono, K.; Nelson, C. C.; Gregson, J. M.; McCloskey, J. A. *J. Org. Chem.* **1992**, *57*, 6392−6403. (c) Ubukata, M.; Isono, K. *J. Am. Chem. Soc*. **1988**, *110*, 4416−4417. (d) Kimura, K.; Ikeda, Y.; Kagami, S.; Yoshihama, M.; Suzuki, K.; Osada, H.; Isono, K. *J. Antibiot.* **1998**, *51*, 1099−1104. (e) Muroi, M.; Kimura, K.; Osada, H.; Inukai, M.; Takatsuki, A. *J. Antibiot.* **1997**, *50*, 103−104. (f) Kimura, K.; Ikeda, Y.; Kagami, S.; Yoshihama, M.; Ubukata, M.; Esumi, Y.; Osada, H.; Isono, K. *J. Antibiot.* **1998**, *51*, 647−654. (g) Kimura, K.; Kagami, S.; Ikeda, Y.; Takahashi, H.; Yoshihama, M.; Kusakabe, H.; Osada, H.; Isono, K. *J. Antibiot.* **1998**, *51*, 640−646. (h) Kimura, K.; Miyata, N.; Kawanishi, G.; Kamio, Y.; Izaki, K.; Isono, K. *Agric. Biol. Chem*. **1989**, *53*, 1811−1815.

10.1021/jo702264e CCC: $40.75 © 2008 American Chemical Society
Published on Web 12/20/2007

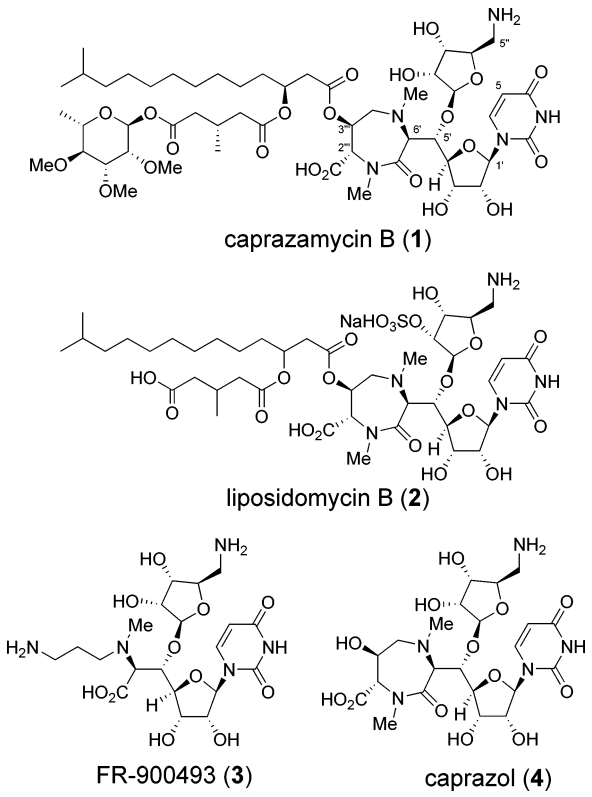


FIGURE 1. Structures of nucleoside antibiotics possessing the 6′-*N*-alkyl-5′-*O*-aminoribosyl-glycyluridine.

ticular, the CPZs have shown excellent anti-mycobacterial activity in vitro against drug-susceptible (MIC = 3.13 μg/mL) and multi-drug-resistant *Mycobacterium tuberculosis* strains (MIC = 3.13 μg/mL), and exhibit no significant toxicity in mice. With such excellent biological properties, CPZs are expected to become promising leads for the development of anti-tuberculosis agents with a novel mode of action. A biological target of the 6′-*N*-alkyl-5′-β-*O*-aminoribosyl-glycyluridine class of antibiotics is believed to be the phospho-MurNAc-pentapeptide translocase (MraY, translocase I, Figure 2), and it is known that this class of antibiotics strongly inhibits MraY (*E. coli* translocase, IC_{50} = 0.05 μg/mL for LPMs).[5h] Because of their complex structural and biological similarities, it has been suggested that the CPZs may possess the same mode of action as the LPMs. Peptide glycan biosynthesis consists of three stages, including the formation of uridine diphosphate *N*-acetylmuraminylpentapeptide (UDP-MurNAc-pentapeptide) in cytoplasm, the membrane-anchored synthesis of lipid I and lipid II, a precursor to the peptide glycan, and polymerization of the resulting lipid II by transpeptidation and transglycosidation. The second and the third stages are involved in a lipid cycle, and the MraY catalyzes the first step of the lipid-linked cycle of the reactions, where UDP-MurNAc-pentapeptide is attacked by the undecaprenol monophosphate in the bacterial cell membrane providing lipid I (Figure 2). Lipid I anchored to the cell membrane is further glycosylated by *N*-acetylglucosamine to afford lipid II. Since MraY is an essential enzyme among bacteria, it is potentially a target for the development of anti-TB agents as well as general antibacterial agents.[7] To keep pace with the serious public health problem due to multiantibiotic resistant bacterial pathogens arising from the extensive use of antibiotics,[8] new antibiotics to treat multidrug-resistant *Mycobacterium tuberculosis*, methyciline-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE) and vancomycin-resistant *Staphylococcus aureus* (VRSA) are urgently needed. Therefore, the CPZs including the LPMs, a target of which is MraY, are promising leads for novel antibacterial agents, too. We designed a palmitoyl caprazol **7** (Figure 3), which possesses a simple fatty acyl side chain at the 3‴-position of the diazepanone moiety, as an initial study for the structure−activity relationship of the 6′-*N*-alkyl-5′-β-*O*-aminoribosyl-glycyluridine class of antibiotics. Here we described the synthesis of simplified CPZ analogues and their antibacterial activity. The key elements of our approach include the improved synthesis of the key 5′-β-*O*-aminoribosyl-glycyluridine derivative, installation of the palmitoyl side chain to the cyclization precursor, and construction of the diazepanone by an intramolecular reductive amination. The second generation synthesis of (+)-caprazol was also established.

Results and Discussion

Synthesis of Palmitoylcaprazol. We have recently completed the total synthesis of (+)-caprazol (**4**), which is a deacylated CPZs.[9] To understand the impact on the fatty acyl side chain, we embarked on the synthesis of palmitolyl caprazol **7**, in which the fatty acyl side chain of the CPZs has been replaced with a simple palmitoyl residue. Initially, we attempted to derive the palmitoly caprazol from **5**, which is a key intermediate of the synthesis of **4**, as shown in Scheme 1. Namely, protecting group manipulation of **5**[9] followed by acylation with palmitic acid and deprotection of the temporal *tert*-butyldiphenylsilyl (TBDPS) group gave **6**. Oxidation of the primary alcohol of **6** was conducted with several conditions such as Dess−Martin periodinane and $NaIO_4$. However, the desired carboxylic acid was not obtained at all because the intermediate aldehyde derivative was susceptible to β-elimination of the palmitoyloxy group.

An alternative to this approach, employing the more accessible amino acid derivative **14** derived from **9** (Scheme 2) to minimize transformations at a later stage of the synthesis, was developed as shown in Figure 3. In addition to this modification, the synthesis was conducted without the benzyloxymethyl (BOM) protection at the *N*-3-position of the uracil moiety because the presence of the BOM group complicated the construction of the diazepanone moiety, as described in the total synthesis of caprazol,[9] and removal of the BOM group was sometimes problematic.[10] Preparation of the amino acid derivative **14** is outlined in Scheme 2. Deprotection of the Boc group of **9**[9] (80% aqueous TFA) followed by protection of the resulting amino group (2 equiv of 2,2,2-trichloroethoxycarbonyl chloride

(6) (a) Ochi, K.; Ezaki, M.; Morita, I.; Komori, T.; Kohsaka, M. ER 0333177, 1989, A2. (b) Yoshida, Y.; Yamanaka, H.; Sakane, K. JP H05-78385, 1993.

(7) (a) Dini, C. *Curr. Top. Med. Chem.* **2005**, *5*, 1221−1236. (b) Kimura, K.; Bugg, T. D. H. *Nat. Prod. Rep.* **2003**, *20*, 252−273. (c) Ichikawa, S.; Matsuda, A. *Expert Opin. Ther. Pat.* **2007**, *17*, 487−498.

(8) (a) Sapico, F. L.; Montgomerie, J. Z.; Canawati, H. N. *Am. J. Med.* **1981**, *281*, 101−109. (b) Hayden, M. K.; Koenig, G. I. *Antimicrob. Agents Chemother.* **1994**, *38*, 1225−1229. (c) Wootton, M.; Howe, R. A.; Walsh, T. R.; Bannett, P. M.; MacGowan, A. P. *J. Antimicrob. Chemother.* **2002**, *50*, 760−761. (d) Hiramatsu, K. *Infect. Dis.* **2001**, *1*, 147−155.

(9) (a) Hirano, S.; Ichikawa, S.; Matsuda, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1854−1856. (b) Hirano, S.; Ichikawa, S.; Matsuda, A. *J. Org. Chem.*, published Nov 21, http://dx.doi.org/10.1021/jo701699h.

(10) Hirano, S.; Ichikawa, S.; Matsuda, A. *Tetrahedron* **2007**, *63*, 2798−2804.

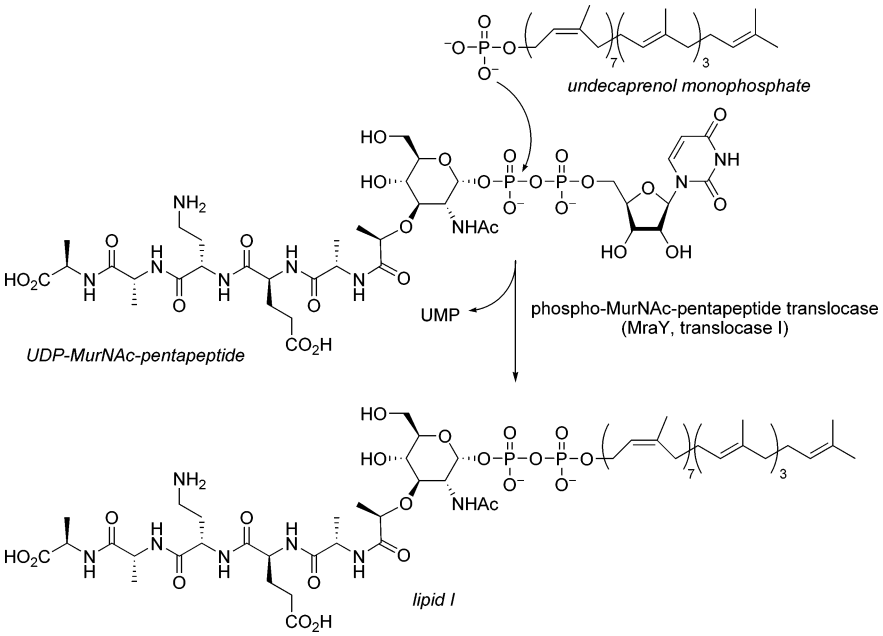


FIGURE 2. Formation of lipid I catalyzed by MraY (translocase I).

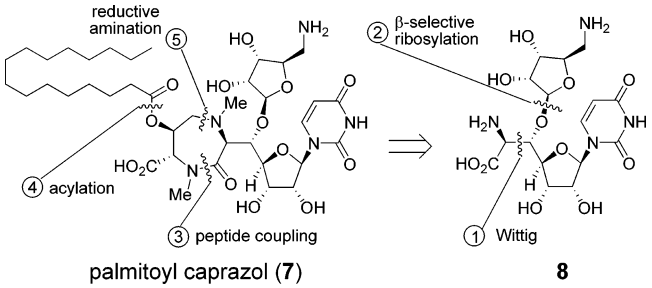


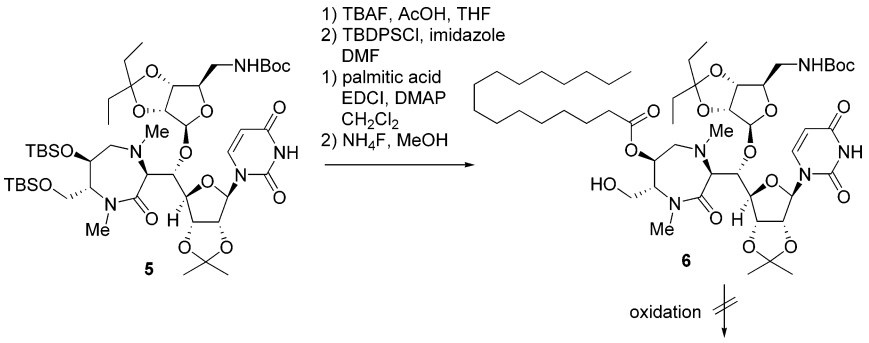
FIGURE 3. Synthetic strategy of palmitoyl caprazol.

(TrocCl), CH_2Cl_2, 90% overall) gave **10**, protecting group manipulation of which was further carried out to afford **11** (30 equiv of NH_4F, MeOH; 1.5 equiv of 4,4′-dimethoxytrityl chloride (DMTrCl), pyridine; 3 equiv of TBDPSCl, 6 equiv of imidazole, DMF, 68% overall). Compound **11** was successively *N*-methylated (2.5 equiv of MeI, 2 equiv of NaH, DMF) and deprotected (aqueous AcOH, 74% overall) to afford the secondary amine derivative **12**. The primary alcohol of **12** was oxidized (0.5 equiv of 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO), 2.4 equiv of $PhI(OAc)_2$, aqueous MeCN), and the resulting carboxylic acid was protected as a ^{t}Bu ester to afford **13** (10 equiv of ^{t}BuOC(NH)CCl_3, 0.3 equiv of $BF_3{\cdot}OEt_2$, CH_2Cl_2, 89% overall). Finally, the Troc group of **13** was removed by Zn (10 equiv, 30 equiv of NH_4Cl, MeOH, 91%) to give **14**.

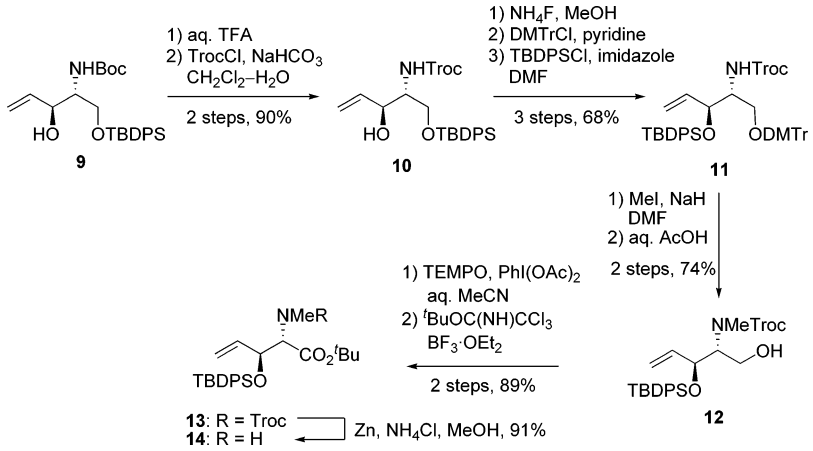
With the secondary amine **14** in hand, the synthesis of the palmitoyl caprazol **7** was undertaken as shown in Scheme 3. Oxidation of **15**[11] with 2-iodoxybenzoic acid (IBX)[12] (3 equiv, MeCN, 80 °C) followed by a two-carbon elongation with $Ph_3P{=}CHCO_2Me$ (1.2 equiv, CH_2Cl_2, −20 °C, 91% overall) provided **16** (trans/cis = 37/1). The aminohydroxylation[13−16] of **16** resulted in superb improvement of the yield, regioselectivity, and stereoselectivity compared to our original synthesis to afford **17** (15 mol % of $K_2[Os_2(OH)_4]$, 15 mol % of hydroquinidine (anthraquinone-1,4-diyl) diether ($(DHQD)_2AQN$), 3 equiv of benzyl carbamate, 2.6 equiv of NaOH, ^{i}PrOH−H_2O, 15 °C, 96% yield, 98% de). β-Selective ribosylation of **17** with the 3-pentylidene-protected ribosyl donor **18**[9] gave the desired **19** with excellent β-selectivity (1.2 equiv of $BF_3{\cdot}OEt_2$, CH_2Cl_2, −30 °C, 81%, β/α = 24.0/1). Thus, it was revealed that protection of the *N*-3-position of the uracil moiety was unnecessary in the ribosylation step. Further crystallization of the mixture gave the pure **19** (β/α = >99/1). The azide group in **19** was reduced to the corresponding amine (3 equiv of PPh_3, 5 equiv of H_2O, benzene−THF, 50 °C), which was protected with a Boc group to give **20** (2 equiv of Boc_2O, 2 equiv of $NaHCO_3$, 90% overall). The yield of the hydrolysis of the methyl ester **20** giving **21** (1 equiv of $Ba(OH)_2$, aqueous THF, 73%) was also improved, as was the case with the Sharpless aminohydroxylation. Coupling of **21** with the secondary amine **14** using 3-(diethoxyphosphoryloxy)-1,2,3-benzotriazin-4(3*H*)-one (DEPBT)[17] (4 equiv, 1.5 equiv of **14**, 4 equiv of $NaHCO_3$, THF, 0 °C, 66%) gave the amide **22**, the TBDPS deprotection of which afforded **23** (5 equiv of TBAF, AcOH, THF, 78%). Acylation of the resulting secondary alcohol of **23** with palmitic acid (3 equiv, 3 equiv of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDCI), 0.3 equiv of DMAP, CH_2Cl_2) and conversion of the terminal olefin of **24** to the aldehyde with the two-step sequence provided the precursor **25** for the cyclization (0.5 mol % of OsO_4, 2.5 equiv of NMO, acetone−H_2O; 2.7 equiv of $NaIO_4$, acetone−phosphate buffer (pH 7),

(11) Asakura, J.; Matsubara, Y.; Yoshihara, M. *J. Carbohydr. Chem.* **1996**, *15*, 231−239.
(12) More, J. D.; Finny, N. S. *Org. Lett.* **2002**, *4*, 3001−3003.
(13) Rudolph, J.; Sennhenn, P. C.; Vlaar, C. P.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2810−2817.
(14) O'Brlen, P.; Osborne, S. A.; Parkaer, D. D. *Tetrahedron Lett.* **1998**, *39*, 4099−4102.
(15) Tao, B.; Schlingloft, G.; Sharpless, K. B. *Tetrahedron Lett.* **1998**, *39*. 2507−2510.
(16) Morgan, A. J.; Masse, C. E.; Panek, J. S. *Org. Lett.* **1999**, *1*, 1949−1952.
(17) Jiang, H.; Li, X.; Fan, Y.; Ye, C.; Romoff, T.; Goodman, M. *Org. Lett.* **1999**, *1*, 91−93.
(18) Brandish, P. E.; Burnham, M. K.; Lonsdale, J. T.; Southgate, R. S.; Ibukai, M.; Bugg, T. D. H. *J. Biol. Chem.* **1996**, *271*, 7609−7614.

SCHEME 1. Initial Attempts to Prepare 3‴-*O*-palmitoyl Caprazol Derivative



SCHEME 2. Preparation of *N*-Methyl-2-amino-3-hydroxyl-4-pentonoate

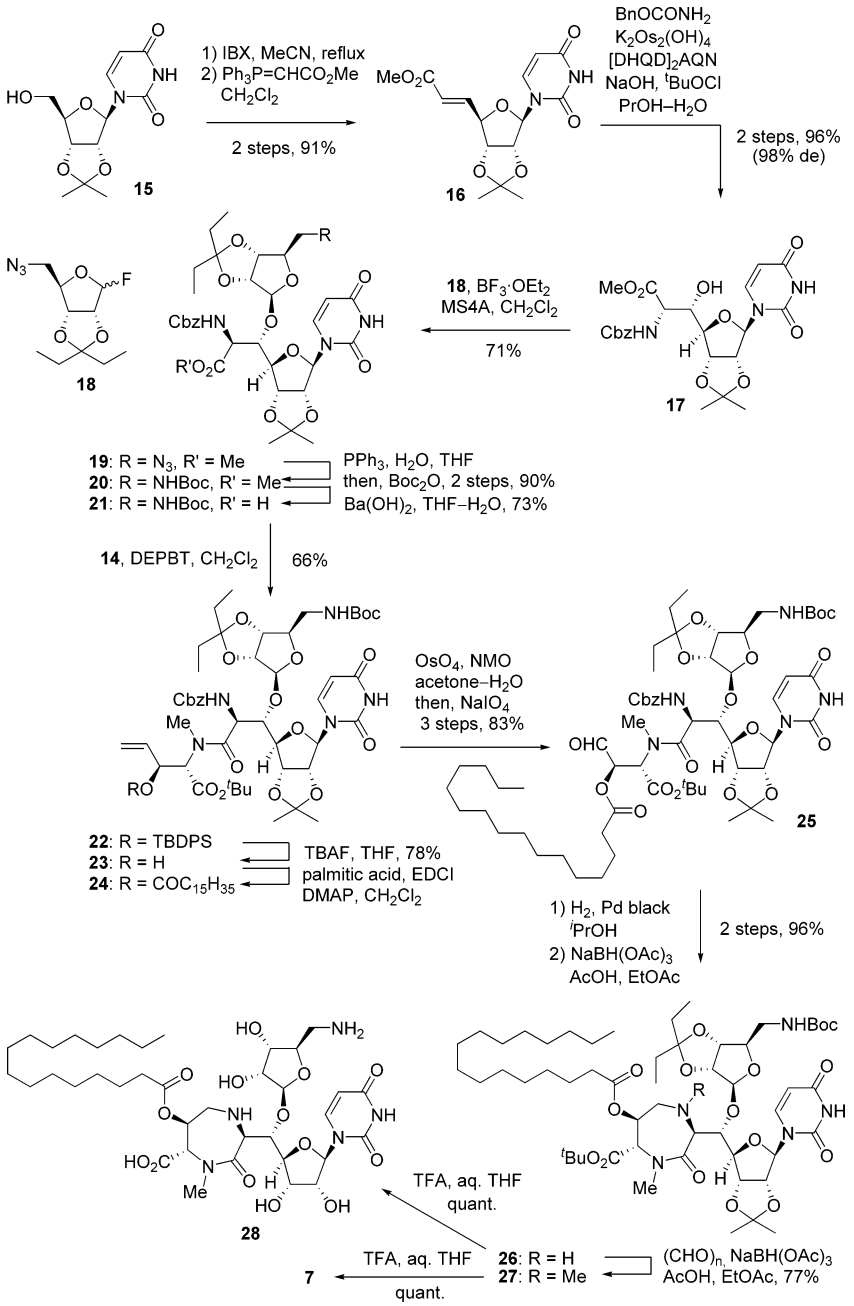


83% overall). Then, the intramolecular reductive amination was applied to **25**, and the desired diazepanone **26** was obtained in excellent yield (H_2, Pd black, ^{i}PrOH, then 4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt, 96% overall). Spectrometric analysis by NMR unambiguously confirmed the structure of **26**. Therefore, no epimerization had occurred despite the two-step diazepanone construction at the α-palmitoyloxy formyl moiety, which should be sensitive to epimerization. Methylation of **26** gave **27** (5 equiv of $(CH_2O)_n$, 4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt, 77%). Finally, a global deprotection of **27** (80% aqueous TFA, quant.) provided the palmitoyl caprazol **7**. The diazepanone derivative **26** was also deprotected to give $N^{6'}$-desmethyl palmitoyl caprazol **28** (80% aqueous TFA, quant.). This modified synthetic strategy enabled us to prepare **7** in 10.2% over 16 steps, starting from uridine, in a highly concise manner.

Second Generation Synthesis of (+)-Caprazol. Improvement of the number of steps and total chemical yield of the preparation of (+)-caprazol were also accomplished with this modified synthesis as shown in Scheme 4. Thus, protection of the allylic alcohol of the amide derivative **23** with a triethylsilyl (TES) group (TESCl, imidazole, DMF) and conversion of the terminal olefin of **29** to an aldehyde with the two-step sequence provided **30** (0.5 mol % of OsO_4, 2.5 equiv of NMO, acetone−H_2O; 2.7 equiv of $NaIO_4$, acetone−phosphate buffer (pH 7), 69% overall) to afford a precursor for the cyclization reaction. The intramolecular reductive amination of **30** gave the diazepanone **31** (H_2, Pd black, ^{i}PrOH, then 4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt, 78% overall). After *N*-methylation at the diazepanone moiety (5 equiv of $(CH_2O)_n$, 4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt, 91%), a global deprotection of **32** (80% aqueous TFA, quant.) provided (+)-(**7**). This second generation synthetic strategy enabled us to prepare **7** in 10.5% over 16 steps starting from uridine. Several analogues of the CPZs, where the fatty acyl side was modified, had already been semisynthesized from (+)-caprazol, which was obtained by hydrolysis of the naturally occurring CPZs. Therefore, our second generation synthesis of (+)-caprazol would provide a full chemical process toward the preparation of the CPZs analogues.

Evaluation of the Antibacterial Activity. Antibacterial activity of the synthetic compounds was evaluated against a range of bacterial strains including *Mycobacterium sp*, and the minimum inhibitory concentrations (MIC, μg/mL) are summarized in Table 1. Palmitoyl caprazol **7**, which possesses a simple fatty acyl side chain, exhibited antibacterial activity against *Mycobacterium smegmatis* ATCC607 (MIC = 6.25 μg/mL) with a potency similar to that of the CPZs. Consistent with these observations and with previous studies,[4e] simplification of the fatty acyl side chain in the CPZs to the palmitoyl group, lacking substituents and stereocenters, was tolerated for antibacterial activity. Removal of the methyl group at the N^6-position had a relatively high impact on anti-*Mycobacterium* activity, and **28** resulted in a modest 4-fold reduction in potency. Clinically used β-lactams and vancomycin inhibit peptidoglycan biosynthesis; their mode of action is inhibition of the polymerization of the lipid II at the bacterial surface. The CPZs may have a similar mode of action as the LPMs, which also inhibit peptidoglycan biosynthesis, but they would inhibit MraY in a different manner from those of the β-lactams and vancomycin. Since the reaction catalyzed by MraY is located upstream of the lipid II polymerization and is the essential step for the growth of most bacteria, it is expected that MraY inhibitors would exhibit antibacterial activity against drug-resistant strains. As

SCHEME 3. Synthesis of Palmitoyl Caprazol 7 and Its Des-*N*-methyl Analogue 28



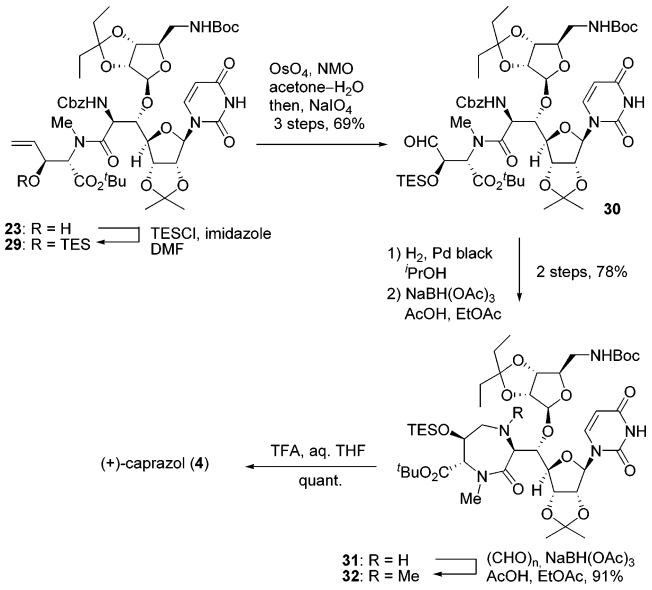
expected, **7** and **28** exhibited antibacterial activity against drug-resistant bacteria including MRSA and VRE strains (MIC = 3.13−12.5 μg/mL). Different from the case with *Mycobacterium smegmatis*, the desmethyl analogue **28** exhibited a similar potency to **7** in antibacterial activity against MRSA and VRE strains. Mycobacteria have an extra cell wall structure that is extraordinarily thick and tight, located outside the peptidoglycan layer. This cell wall structure contains the characteristic long chain fatty acid, mycolic acid.[19] The difference in antibacterial activity between **7** and **28** observed in *Mycobacterium sp.* might be correlated to the subtle difference in lipophilicity introduced by the methyl group at the diazepanone moiety. Of significance is the antibacterial activity against drug-resistant bacteria including MRSA and VRE strains. Therefore, the CPZs including the LPMs and the MRYs, a target of which is MraY, are promising leads for the novel antibacterial agents against drug-resistant bacteria. More precise optimization (simplification) of the lipophilic side chain is, however, necessary to improve the

TABLE 1. Antibacterial Activity of CPZ Analogues

	MIC (μg/mL)		
strain	**4**	**7**	**28**
M. smegmatis ATCC607	>100	6.25	25
S. aureus FDA 209P	>100	1.56	1.56
S. aureus MS9610 (MDR)	>100	3.13	3.13
S. aureus MRSA No. 5 (MRSA)	>100	6.25	6.25
S. aureus MRSA No. 17 (MRSA)	>100	6.25	6.25
S. aureus MS16526 (MRSA)	>100	6.25	6.25
S. aureus TY04282 (MRSA)	>100	6.25	12.5
E. faecalis NCTC 12201 (VRE)	>100	12.5	12.5

(19) (a) Crick, D. C.; Mahapatra, S.; Brennan, P. J. *Glycobiology* **2001**, *11*, 107R−118R. (b) Hong, X.; Hopfinger, A. J. *Biomacromolecular* **2004**, *5*, 1052−1065.

SCHEME 4. The Second Generation Synthesis of (+)-Caprazol (4)



permeability in bacterial cells.[20] It is also extremely important to simplify the hydrophilic core structures to reduce the size of the molecules and to stabilize the chemically labile structure. Although this aspect of the research will likely be the most difficult to accomplish, a full chemical synthetic approach with novel agents, based on nucleoside antibiotic research and rational drug design, should result in the discovery of novel antibacterial drugs.

Conclusion. In summary, we have described the synthesis of caprazamycin analogues and their structure−activity relationship. The key elements of our approach include the improved synthesis of the key 5′-*β*-*O*-aminoribosyl-glycyluridine derivative, installation of the palmitoyl side chain to the cyclization precursor, and the construction of the diazepanone by an intramolecular reductive amination. Palmitoyl caprazol **7**, which possesses a simple fatty acyl side chain, exhibited antibacterial activity against *Mycobacterium smegmatis* ATCC607 (MIC = 6.25 μg/mL) with a potency similar to that of the CPZs. Analogues **7** and **28** also exhibited antibacterial activity against drug-resistant bacteria including MRSA and VRE strains (MIC = 3.13−12.5 μg/mL). This strategy would be suitable for examining a general structure−activity relationship and for synthesizing novel analogues because the 5′-*β*-*O*-aminoribosyl-glycyluridine structure is predicted to be a pharmacophore of this class of natural products.

Experimental Section

(2*R*,3*S*)-1-*O*-*tert*-Butyldiphenylsilyl-2-(2,2,2-trichloroethoxycarbonylamino)-4-pentene-1,3-diol (10). Compound **9** (100 mg, 0.22 mmol) was treated with 80% aqueous TFA (5 mL) at room temperature for 2 h. The mixture was concentrated in vacuo. The residue in CH_2Cl_2−H_2O (1:1, 10 mL) was treated with TrocCl (91 mg, 0.44 mmol) at room temperature for 12 h. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a flash silica gel column (3 × 10 cm, 20% AcOEt−hexane) to afford **10** (105 mg, 90% in 2 steps) as a colorless syrup: $[\alpha]^{21}_D$ −13.6 (*c* 2.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.65−7.61 (m, 4H, phenyl), 7.47−7.37 (m, 6H, phenyl), 5.91 (m, 1H, H-4), 5.67 (d, 1H, TrocNH, $J_{NH,2}$ = 8.0 Hz), 5.43 (d, 1H, H-5a, $J_{5a,4}$ = 17.1 Hz), 5.28 (d, 1H, H-5b, $J_{5b,4}$ = 10.3 Hz), 4.71 (m, 2H, CH_2CCl_3), 4.36 (m, 1H, H-3), 3.96 (dd, 1H, H-1a, $J_{1a,1b}$ = 10.8 Hz, $J_{1a,2}$ = 3.4 Hz), 3.79 (dd, 1H, H-1b, $J_{1b,1a}$ = 10.8 Hz, $J_{1b,2}$ = 3.4 Hz), 3.76 (m, 1H, H-2), 1.07 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 154.4, 137.1, 136.5, 135.5, 135.4, 135.4, 132.3, 132.2, 130.3, 130.2, 130.1, 128.0, 128.0, 127.9, 127.9, 116.7, 95.5, 74.6, 74.1, 63.7, 55.2, 26.8, 26.8, 19.1; FABMS-HR (NBA) calcd for $C_{24}H_{31}Cl_3NO_4Si$ 530.1088, found 530.1097.

(2*R*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyl-1-*O*-(4,4′-dimethoxytrityl)-2-(2,2,2-trichloroethoxycarbonylamino)-4-pentene-1,3-diol (11). Compound **10** (1.24 g, 2.35 mmol) in MeOH (25 mL) was treated with NH_4F (2.5 g) at 45 °C for 2 h. The reaction mixture was diluted with AcOEt and the insoluble materials were filtered off though a Celite pad. The filtrate was concentrated in vacuo. The residue in pyridine (20 mL) was treated with DMTrCl (1.19 g, 3.53 mmol) at room temperature for 24 h. The reaction mixture was concentrated in vacuo, and the residue was partitioned between AcOEt and H_2O. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue in DMF (20 mL) was treated with imidazole (1.4 g, 21 mmol) and TBDPSCl (1.8 mL, 7.1 mmol) at room temperature for 24 h. The reaction mixture was partitioned between AcOEt and H_2O, and the organic phase was washed with H_2O (twice) and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by a neutral silica gel column (10 × 15 cm, 15% AcOEt−hexane) to give **11** (1.33 g, 68% in 3 steps) as a colorless glass: $[\alpha]^{21}_D$ +4.7 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.63−7.58 (m, 4H, phenyl), 7.42−7.17 (m, 15H, phenyl), 6.77 (m, 4H, phenyl), 5.62 (m, 1H, H-4), 5.10 (d, 1H, H-5a, $J_{5a,4}$ = 17.0 Hz), 5.02 (d, 1H, H-5b, $J_{5b,4}$ = 10.3 Hz), 4.77 (d, 1H, TrocNH, $J_{NH,2}$ = 8.2 Hz), 4.73 (d, 1H, CH_2CCl_3, J = 13.5 Hz), 4.61 (d, 1H, CH_2CCl_3, J = 13.5 Hz), 4.48 (m, 1H, H-3), 4.01 (m, 1H, H-2), 3.77 (s, 6H, OMe × 2), 3.20 (m, 1H, H-1a), 3.08 (m, 1H, H-1b), 0.99 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.6, 158.4, 154.5, 154.3, 147.3, 144.7, 139.4, 136.6, 136.1, 136.0, 135.9, 135.9, 135.8, 135.8, 135.7, 133.4, 132.8, 130.2, 130.0, 129.9, 129.9, 129.8, 129.7, 129.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.1, 126.7, 118.0, 117.7, 113.1, 113.0, 95.6, 86.1, 86.4, 76.1, 74.5, 79.4, 74.1, 62.1, 56.7, 55.9, 55.2, 55.2, 27.0, 27.0, 26.9, 19.3, 19.3, 19.2; FABMS-HR (NBA) calcd for $C_{45}H_{49}Cl_3NO_6Si$ 832.2395, found 832.2390.

(2*R*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyl-2-(*N*-methyl-2,2,2-trichloroethoxycarbonylamino)-4-pentene-1,3-diol (12). A solution of **11** (185 mg, 0.22 mmol) in DMF (3 mL) was treated with MeI (222 μL, 0.44 mmol) and NaH (14 mg, 60% purity, 0.33 mmol) at 0 °C for 8 h. The reaction mixture was partitioned between AcOEt and H_2O, and the organic phase was washed with H_2O (twice) and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (3 mL) and treated with 90% aqueous AcOH (10 mL) at room temperature for 1 h. The reaction mixture was carefully concentrated in vacuo (being kept under 10 °C). The residue was purified by a flash silica gel column (3 × 20 cm, 33% AcOEt−hexane) to give **12** (87.9 mg, 74% in 2 steps) as a colorless glass: ^{1}H NMR ($CDCl_3$, 500 MHz, 10:1 mixture of the rotamers, assignment for the major isomer) δ 7.69−7.63 (m, 4H, phenyl), 7.44−7.36 (m, 6H, phenyl), 5.75 (ddd, 1H, H-4, $J_{4,5a}$ = 17.2 Hz, $J_{4,5a}$ = 10.1 Hz, $J_{4,5b}$ = 8.3 Hz), 4.86 (d, 1H, H-5b, $J_{5b,4}$ = 10.1 Hz), 4.76 (m, 1H, CH_2CCl_3), 4.74 (d, 1H, H-5a, $J_{5a,5b}$ = 17.2 Hz), 4.62 (m, 1H, CH_2CCl_3), 4.34 (dd, 1H, H-3, $J_{3,4}$ = 8.3 Hz, $J_{3,2}$ = 8.2 Hz), 4.11 (m, 1H, H-2), 4.01 (m, 1H, H-1a), 3.81 (m, 1H, H-1b), 2.83 (s, 3H, NMe), 1.06 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.5, 154.6, 137.5, 137.4, 136.1, 136.1, 135.9, 135.9, 133.5, 133.4, 133.2, 133.1, 129.9, 129.9, 129.8, 129.7, 127.7, 127.4, 118.2, 117.9, 95.7, 95.4, 75.3, 75.2, 75.1, 74.6, 63.6, 60.9, 31.9, 27.0, 19.3; FABMS-HR (NBA) calcd for $C_{25}H_{33}Cl_3NO_4Si$ 544.1245, found 544.1238.

(20) Green, D. W. *Expert Opin. Ther. Targets* **2002**, *6*, 1−19.

***tert*-Butyl (2*S*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyloxy-2-(*N*-methyl-2,2,2-trichloroethoxycarbonylamino)-4-pentenate (13).** A solution of **12** (46.5 mg, 0.086 mmol) in 60% aqueous MeCN (1 mL) was treated with $PhI(OAc)_2$ (69 mg, 0.21 mmol) and TEMPO (7.0 mg, 0.045 mmol) at room temperature for 24 h. The reaction mixture was concentrated in vacuo, and the residue was purified by a silica gel column (1 × 3 cm, 25% MeOH/CHCl) to give the crude acid as a colorless oil. The crude acid in CH_2Cl_2 (1 mL) was treated with *t*-BuC(NH)CCl_3 (186 mg, 0.86 mmol) and BF_3·OEt_2 (3.2 μL, 0.026 mmol) at 0 °C for 1 h. The mixture was partitioned between AcOEt and saturated aqueous $NaHCO_3$. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a silica gel column (3 × 10 cm, 16% AcOEt−hexane) to afford **13** (47 mg, 89% in 2 steps) as a colorless foam: ^{1}H NMR ($CDCl_3$, 500 MHz, 1:1.5 mixture of the rotamers) δ 7.71−7.67 (m, 4H, phenyl), 7.43−7.34 (m, 6H, phenyl), 5.75 (m, 1H, H-4), 4.86−4.60 (m, 6H, H-2, H-3, H-5a, H-5b, CH_2CCl_3), 2.91 (s, 1.8H, NMe), 2.86 (s, 1.2H, NMe), 1.46 (s, 3.6H, *tert*-butyl), 1.44 (s, 5.4H, *tert*-butyl), 1.03 (s, 3.6H, *tert*-butyl), 1.02 (s, 5.4H, *tert*-butyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.8, 169.8, 154.8, 154.9, 136.1, 135.8, 118.2, 117.9, 95.5, 95.2, 83.3, 83.2, 75.2, 71.6, 71.4, 65.1, 64.4, 34.2, 28.0, 28.0; FABMS-HR (NBA) calcd for $C_{29}H_{39}Cl_3NO_5Si$ 614.1663, found 614.1664.

***tert*-Butyl (2*S*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyloxy-2-methylamino-4-pentenate (14).** A mixture of **13** (184 mg, 0.3 mmol), NH_4Cl (477 mg, 9 mmol), and Zn powder (230 mg, 85% purity, 3 mmol) in MeOH (5 mL) was stirred at room temperature for 12 h. Insoluble materials were filtered off through a Celite pad, and the filtrate was concentrated in vacuo. The residue was purified by a neutral silica gel column (3 × 5 cm, 50% AcOEt−hexane) to give **14** (120 mg, 91%) as a colorless syrup: $[\alpha]^{22}_D$ +3.9 (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.72 (dd, 2H, phenyl, J = 1.5, 7.9 Hz), 7.67 (dd, 2H, phenyl, J = 1.5, 7.9 Hz), 7.43−7.34 (m, 6H, phenyl), 5.81 (ddd, 1H, H-4, $J_{4,5a}$ = 17.2 Hz, $J_{4,5b}$ = 10.3 Hz, $J_{4,3}$ = 6.9 Hz), 5.00 (dd, 1H, H-5b, $J_{5b,4}$ = 10.3 Hz, $J_{5b,5a}$ = 1.0 Hz), 4.96 (dd, 1H, H-5a, $J_{5a,4}$ = 10.3 Hz, $J_{5a,5b}$ = 1.0 Hz), 4.45 (m, 1H, H-3), 3.06 (d, 1H, H-2, $J_{2,3}$ = 3.6 Hz), 2.34 (s, 3H, NMe), 1.63 (br s, 1H, NH), 1.40 (s, 9H, *tert*-butyl), 1.07 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 136.6, 136.0, 135.9, 133.7, 133.5, 129.7, 129.6, 127.6, 127.4, 127.3, 126.9, 126.5, 126.1, 116.8, 81.1, 76.3, 69.3, 35.1, 28.2, 28.1, 27.0, 19.4; FABMS-HR (NBA) calcd for $C_{26}H_{38}NO_3Si$ 440.2621, found 440.2629.

Methyl (*E*)-5,6-Dideoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*ribo*-5-eneheptofranuronate (16). A solution of **15** (4.0 g, 14.2 mmol) and IBX (9.9 g, 35.5 mmol) in MeCN (140 mL) was heated at 80 °C for 1 h. The reaction mixture was cooled in an ice bath, and the resulting white precipitates were filtered off through a Celite pad. The filtrate was concentrated in vacuo. The residue in CH_2Cl_2 (140 mL) was cooled to −20 °C, to which a solution of $Ph_3P{=}CHCO_2Me$ (5.7 g, 17.0 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The reaction mixture was stirred at −20 °C for 1 h. The mixture was diluted with AcOEt, then washed with H_2O and saturated aqueous NaCl. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a silica gel column (10 × 20 cm, 25−45% AcOEt−hexane) to afford **16** (4.3 g, 91% in 2 steps) as a colorless syrup: $[\alpha]^{23}_D$ +45.4 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.60 (br s, 1H, NH-3), 7.19 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.01 (dd, 1H, H-5′, $J_{5',6'}$ = 15.8 Hz, $J_{5',4'}$ = 5.9 Hz), 6.04 (dd, 1H, H-6′, $J_{6',5'}$ = 15.8 Hz, $J_{6',4'}$ = 1.7 Hz), 5.75 (dd, 1H, H-6, $J_{6,5}$ = 8.0 Hz, $J_{6,OH}$ = 2.2 Hz), 5.62 (d, 1H, H-1′, $J_{1',2'}$ = 1.6 Hz), 5.08 (dd, 1H, H-2′, $J_{2',1'}$ = 1.6 Hz, $J_{2',3'}$ = 6.4 Hz), 4.84 (dd, 1H, H-3′, $J_{3',2'}$ = $J_{3',4'}$ = 6.4 Hz), 4.66 (m, 1H, H-4′), 3.75 (s, 3H, OMe), 1.59 (s, 3H, acetonide), 1.36 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.1, 162.6, 145.6, 143.6, 142.5, 122.3, 114.9, 102.9, 95.2, 86.8, 84.5, 84.0, 51.8, 27.1, 25.3; FABMS-HR (NBA) calcd for $C_{15}H_{19}N_2O_7$ 339.1192, found 339.1199.

Methyl 6-Benzyloxycarbonylamino-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronate (17). *tert*-Butyl hypochlorite (2.9 mL, 25.4 mmol) was added to a solution of benzyl carbamate (2.6 g, 17.3 mmol) in aqueous NaOH (0.6 M, 28.5 mL) and *n*-PrOH (57 mL) at 0 °C, and the mixture was stirred for 10 min, then allowed to reach room temperature. $[DHQD]_2AQN$ (738 mg, 0.86 mmol), **16** (1.94 g, 5.74 mmol), and $K_2OsO_2(OH)_4$ (317 mg, 0.86 mmol) were sequentially added to the mixture. The resulting whole mixture was stirred at room temperature for 2 h. After addition of saturated aqueous $Na_2S_2O_3$, the reaction mixture was extracted with AcOEt. The combined organic phases were washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a silica gel column (15 × 20 cm, 40−45% AcOEt−hexane) to afford **17** (2.78 g, 96%, >98% de) as a white foam: $[\alpha]^{23}_D$ +20.7 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.45 (br s, 1H, NH-3), 7.35−7.31 (m, 5H, phenyl), 7.18 (d, 1H, H-6, $J_{6,5}$ = 7.8 Hz), 5.70 (dd, 1H, H-5, $J_{5,6}$ = 7.8 Hz, $J_{5,OH}$ = 1.9 Hz), 5.62 (d, 1H, NH-6′, $J_{NH,6'}$ = 8.2 Hz), 5.45 (s, 1H, H-1′), 5.13 (d, 1H, benzyl, J = 11.9 Hz), 5.08 (d, 1H, benzyl, J = 11.9 Hz), 5.01 (dd, 1H, H-2′, $J_{2',3'}$ = 6.5 Hz, $J_{2',3'}$ = 3.1 Hz), 4.94 (dd, 1H, H-3′, $J_{3',2'}$ = 6.5 Hz, $J_{3',4'}$ = 3.3 Hz), 4.54 (m, 1H, H-6′), 4.27 (m, 2H, H-4′, H-5′), 3.76 (m, 4H, OMe, OH), 1.54 (s, 3H, acetonide), 1.26 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 163.1, 156.23, 150.4, 143.2, 136.2, 128.5, 128.2, 114.8, 102.8, 96.2, 86.1, 82.7, 81.4, 71.4, 67.1, 56.6, 52.8, 27.2, 25.3; FABMS-HR (NBA) calcd for $C_{23}H_{28}N_3O_{10}$ 506.1774, found 506.1778.

Methyl 5-*O*-[5-Azido-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-benzyloxycarbonylamino-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronate (19). A mixture of **17** (50.5 mg, 0.1 mmol), **18** (37 mg, 0.15 mmol), and MS4A (150 mg) in CH_2Cl_2 (1 mL) was stirred at −30 °C for 15 min. BF_3·OEt_2 (20 μL, 0.15 mmol) was added five times at each hour, and the reaction mixture was stirred for a total of 12 h. Saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with AcOEt. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a silica gel column (1.5 × 15 cm, 33−50% AcOEt−hexane) to afford **19** (52 mg, 71%, >97% de) as a white foam: $[\alpha]^{25}_D$ +6.3 (*c* 0.73, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.40 (br s, 1H, NH-3), 7.40−7.30 (m, 6H, phenyl, H-6), 5.86 (d, 1H, NH-6′, $J_{NH,6'}$ = 9.8 Hz), 5.70 (d, 1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.67 (s, 1H, H-1′), 5.22 (d, 1H, benzyl, J = 12.3 Hz), 5.15 (s, 1H, H-1″), 5.05 (d, 1H, benzyl, J = 12.3 Hz), 4.81 (m, 2H, H-2′, H-3′), 4.67 (d, 1H, H-6′, $J_{6',NH}$ = 9.8 Hz), 4.58 (m, 2H, H-2′, H-3′), 4.47 (d, 1H, H-5′, $J_{5',4'}$ = 7.3 Hz), 4.24 (dd, 1H, H-4″, $J_{4'',5''a}$ = 5.8 Hz, $J_{4'',5''b}$ = 6.3 Hz), 3.77 (s, 3H, OMe), 3.39 (dd, 1H, H-5″a, $J_{5''a,5''b}$ = 12.8 Hz, $J_{5''a,4''}$ = 4.8 Hz), 3.36 (dd, 1H, H-5″b, $J_{5''b,5''a}$ = 12.8 Hz, $J_{5''b,4''}$ = 6.3 Hz), 1.62 (m, 2H, CH_2CH$_3$), 1.53 (m, 2H, CH_2CH$_3$), 1.50 (s, 3H, acetonide), 1.30 (s, 3H, acetonide), 0.84 (m, 6H, 2 × CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5, 163.2, 156.2, 150.0, 142.1, 136.2, 128.4, 128.2, 128.1, 117.3, 114.9, 111.2, 102.5, 93.4, 86.2, 86.0, 85.3, 83.7, 81.8, 80.5, 78.5, 67.2, 54.4, 53.1, 52.8, 29.3, 28.9, 27.0, 25.3, 8.3, 7.3; FABMS-HR (NBA) calcd for $C_{33}H_{43}N_6O_{13}$ 731.2888, found 731.2892.

Methyl 6-Benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronate (20). A mixture of **19** (793 mg, 1.09 mmol), Ph_3P (854 mg, 3.26 mmol), and H_2O (900 μL) in THF−benzene (1:1, 10 mL) was stirred at 45 °C for 12 h. After the reaction mixture was cooled to room temperature, $(Boc)_2O$ (918 μL, 3.96 mmol) was added, and the resulting mixture was stirred for an additional 5 h. The reaction mixture was partitioned between AcOEt and H_2O, and the organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by a silica gel column (3.0 × 15 cm, 50% AcOEt−hexane) to give **20** (782 mg, 90% in 2 steps) as a white foam: $[\alpha]^{23}_D$ +25.2 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.73 (br s, 1H, NH-

3), 7.36−7.31 (m, 5H, phenyl), 7.27 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.70 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.55 (s, 1H, H-1′), 5.51 (d, 1H, NH-6′, $J_{NH,6'}$ = 8.5 Hz), 5.39 (br s, 1H, NH-5″), 5.19 (d, 1H, benzyl, J = 12.2 Hz), 5.14 (s, 1H, H-1″), 5.07 (d, 1H, benzyl, J = 12.2 Hz), 5.00 (d, 1H, H-2′, $J_{2',3'}$ = 4.7 Hz), 4.84 (m, 1H, H-3′), 4.67 (d, 1H, H-6′, $J_{6',NH}$ = 8.5 Hz), 4.54 (m, 2H, H-2″, H-3″), 4.43 (d, 1H, H-5′, $J_{5',4'}$ = 7.5 Hz), 4.23 (m, 2H, H-4′, H-4″), 3.79 (s, 3H, OMe), 3.25 (m, 1H, H-5″a), 3.03 (m, 1H, H-5″b), 1.72 (s, 3H, acetonide), 1.57 (m, 2H, CH_2CH$_3$), 1.55 (m, 2H, CH_2CH$_3$), 1.48 (s, 9H, *tert*-butyl), 1.32 (s, 3H, acetonide), 0.80 (m, 6H, 2 × CH$_2$CH_3); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 171.1, 162.8, 156.2, 156.0, 150.0, 142.9, 136.1, 128.5, 128.2, 116.6, 114.8, 112.0, 102.7, 95.4, 87.1, 86.2, 84.0, 82.1, 81.2, 79.6, 79.0, 67.3, 54.8, 53.0, 43.3, 29.4, 28.8, 28.4, 27.0, 25.3, 8.3, 7.3; FABMS-HR (NBA) calcd for $C_{38}H_{53}N_4O_{15}$ 805.3527, found 805.3517.

6-Benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronoic acid (21). A solution of **20** (32 mg, 0.04 mmol) in THF−H_2O (4:1, 1 mL) was treated with Ba(OH)$_2$·8H$_2$O (13 mg, 0.04 mmol) at −30 °C for 12 h. The solution was partitioned between AcOEt and 0.3 N aqueous HCl, and the organic phase was washed with saturated aqueous NaCl, dried (Na$_2$SO$_4$), and concentrated in vacuo. The residue was purified by a silica gel column (1.5 × 5 cm, 17% MeOH−CHCl$_3$) to give **21** (23 mg, 73%) as a white foam: $[\alpha]^{21}_D$ +21.6 (*c* 1.00, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.64 (br d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.38−7.27 (m, 5H, phenyl), 5.74 (br s, 1H, H-1′), 5.65 (br d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.22 (s, 1H, H-1″), 5.16 (d, 1H, benzyl, J = 12.5 Hz), 5.11 (m, 1H, H-2′), 5.02 (d, 1H, benzyl, J = 12.5 Hz), 4.98 (m, 1H, H-3′), 4.90 (m, 1H, H-2″), 4.65 (m, 1H, H-6′), 4.56 (d, 1H, H-3″, $J_{3'',2''}$ = 5.8 Hz), 4.50 (m, 1H, H-5′), 4.18−4.11 (m, 2H, H-4′, H-4″), 3.13 (m, 2H, H-5″a, H-5″b), 1.60 (m, 4H, 2 × CH_2CH$_3$), 1.49 (s, 3H, acetonide), 1.48 (s, 9H, *tert*-butyl), 1.31 (s, 3H, acetonide), 0.79 (m, 6H, 2 × CH$_2$CH_3); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 177.5, 166.2, 158.5, 152.0, 138.3, 130.3, 129.7, 129.2, 128.7, 117.4, 115.6, 88.4, 87.9, 83.8, 83.4, 80.5, 57.4, 44.5, 30.5, 29.0, 28.6, 28.2, 27.8, 27.3, 25.8, 8.6, 7.9, 7.6; FABMS-HR (NBA) calcd for $C_{37}H_{49}N_4O_{15}$ 789.3194, found 789.3194.

***N*-[(1*S*,2*S*)-2-*tert*-Butyldiphenylsiloxy-1-*tert*-butoxycarbonyl-3-butenyl]-*N*-methyl-6-benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronamide (22).** A mixture **21** (55 mg, 0.13 mmol) and **14** (129 mg, 0.16 mmol) in THF (2 mL) was treated with DEPBT (194 mg, 0.65 mmol) at room temperature for 18 h. The reaction mixture was partitioned between AcOEt and 0.5 N aqueous HCl, and the organic phase was washed with saturated aqueous NaHCO$_3$ and saturated aqueous NaCl, dried (Na$_2$SO$_4$), and concentrated in vacuo. The residue was purified by a silica gel column (3 × 22 cm, 40% AcOEt−hexane) to give **22** (108 mg, 66%) as a white foam: ^{1}H NMR (CDCl$_3$, 500 MHz, 7:1 mixture of the rotamers) δ 8.67 (br s, 1H, NH-3), 7.69−7.65 (m, 4H, phenyl), 7.48 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.41−7.31 (m, 11H, phenyl), 5.43 (br s, 1H, NHBoc), 5.80 (s, 1H, H-1′), 5.77−5.74 (m, 3H, H-11′, H-5, NHCbz), 5.19 (d, 1H, H-2′, $J_{2',3'}$ = 6.6 Hz), 5.14 (d, 1H, benzyl, J = 12.3 Hz), 5.06 (s, 1H, H-1″), 4.98 (d, 1H, benzyl, J = 12.3 Hz), 4.90 (m, 1H, H-3′), 4.78 (m, 3H, H-12′a, H-6′, H-10′), 4.67 (d, 1H, H-12′b, $J_{12'b,11'}$ = 17.2 Hz), 4.59 (d, 1H, H-2″, $J_{2'',3''}$ = 7.7 Hz), 4.56 (d, 1H, H-3″, $J_{3'',2''}$ = 7.7 Hz), 4.23 (m, 1H, H-4′), 4.19 (dd, 1H, H-4″, $J_{4'',5''a}$ = 5.4 Hz, $J_{4'',5''b}$ = 4.8 Hz), 4.05 (m, 1H, H-9′), 3.25 (m, 1H, H-5′a), 3.04 (m, 1H, H-5″b), 3.03 (s, 3H, NMe), 1.61 (m, 2H, CH$_2$CH$_3$), 1.54 (s, 3H, acetonide), 1.48 (m, 2H, CH_2CH$_3$), 1.44 (s, 9H, *tert*-butyl), 1.42 (s, 9H, *tert*-butyl), 1.27 (s, 3H, acetonide), 1.00 (s, 9H, *tert*-butyl), 0.81 (t, 6H, 2 × CH$_2$CH_3, J = 7.4 Hz); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 170.5, 167.6, 162.6, 156.4, 156.0, 152.0, 149.9, 146.2, 142.8, 141.7, 136.6, 136.2, 136.1, 136.1, 133.7, 133.0, 129.7, 129.5, 128.5, 128.3, 128.3, 128.2, 128.1, 127.5, 127.3, 118.2, 116.9, 116.4, 114.9, 113.6, 112.5, 112.3, 103.4, 103.0, 98.9, 92.9, 87.5, 87.5, 86.6, 86.0, 85.4, 84.3, 83.9, 83.0, 82.1, 81.9, 80.5, 80.3, 79.56, 79.1, 78.7, 74.5, 67.1, 61.7, 53.8, 51.0, 43.2, 39.6, 36.2, 32.9, 29.7, 29.5, 28.8, 28.4, 28.4, 28.0, 27.9, 27.9, 27.1, 27.0, 27.0, 26.7, 25.3, 25.1, 22.7, 19.2, 14.1, 8.4, 7.8, 7.3; FABMS-HR (NBA) calcd for $C_{63}H_{86}N_5O_{17}Si$ 1212.5788, found 1212.5790.

***N*-[(1*S*,2*S*)-1-*tert*-Butoxycarbonyl-2-hydroxy-3-butenyl]-*N*-methyl-6-benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronamide (23).** A solution of **22** (435 mg, 0.34 mmol) in THF (2 mL) was treated with AcOH (98 μL) and TBAF solution (1 M solution in THF, 1.7 mL) at room temperature for 1 week. The mixture was partitioned between AcOEt and saturated aqueous NaHCO$_3$, and the organic phase was washed with saturated aqueous NaCl, dried (Na$_2$SO$_4$), and concentrated in vacuo. The residue was purified by a neutral flash silica gel column (3.0 × 10 cm, 60% AcOEt−hexane) to give **23** (279 mg, 78%) as a colorless foam: ^{1}H NMR (CDCl$_3$, 500 MHz, 8:1 mixture of the rotamers) δ 9.32 (br s, 1H, NH-3), 7.45 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.89−5.74 (m, 5H, H-1′, H-5′, H-11′, NHBoc, NHCbz), 5.38 (d, 1H, H-12′a, $J_{12'a,11'}$ = 17.2 Hz), 5.18 (d, 1H, H-12′b, $J_{12'b,11'}$ = 12.6 Hz), 5.17 (d, 1H, benzyl, J = 13.0 Hz), 4.99 (s, 1H, H-1″), 5.04 (d, 1H, benzyl, J = 13.0 Hz), 4.89 (m, 1H, H-2′), 4.86 (m, 1H, H-3′), 4.81 (m, 2H, H-2″, H-3″), 4.63 (m, 1H, H-10′), 4.56 (m, 1H, H-6′), 4.51 (m, 2H, H-5′, H-9′), 4.22 (m, 1H, H-4″), 4.11 (m, 1H, H-4′), 3.78 (d, 1H, OH, $J_{OH,10}$ = 3.4 Hz), 3.26 (m, 1H, H-5″a), 3.15 (s, 3H, NMe), 3.03 (m, 1H, H-5″b), 1.59 (m, 2H, CH_2CH$_3$), 1.52 (s, 3H, acetonide), 1.50 (m, 2H, CH_2CH$_3$), 1.45 (s, 9H, *tert*-butyl), 1.43 (s, 9H, *tert*-butyl), 1.39 (s, 3H, acetonide), 0.82 (m, 6H, 2 × CH$_2$CH_3); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 170.6, 169.5, 163.1, 156.2, 156.1, 150.1, 141.8, 136.1, 128.5, 128.4, 128.3, 118.0, 116.8, 114.9, 112.3, 103.0, 93.0, 86.5, 85.9, 85.6, 83.9, 83.2, 81.9, 80.5, 79.4, 79.2, 71.4, 67.1, 64.0, 50.8, 43.1, 35.6, 29.5, 28.7, 28.4, 27.8, 27.7, 27.7, 25.3, 8.4, 7.2; FABMS-HR (NBA) calcd for $C_{47}H_{68}N_5O_{17}$ 974.4610, found 974.4602.

***N*-[(1*S*,2*S*)-1-*tert*-Butoxycarbonyl-3-oxo-2-palmitoyloxypropyl]-*N*-methyl-6-benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-*β*-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-*β*-D-*glycero*-L-*talo*-heptofuranuronamide (25).** A solution of **23** (50 mg, 0.051 mmol) in CH_2Cl_2 (1 mL) was treated with DMAP (2 mg, 0.015 mmol), palmitic acid (39 mg, 0.15 mmol), and EDCI (29 mg, 0.15 mmol) at room temperature for 24 h. After the reaction was quenched by addition of MeOH, the mixture was partitioned between AcOEt and saturated aqueous NaHCO$_3$, and the organic phase was washed with 0.3 N aqueous HCl and saturated aqueous NaCl, dried (Na$_2$SO$_4$), and concentrated in vacuo to give crude **24**. The residue in 80% aqueous dioxane was treated with NMO (33 mg, 0.15 mmol) and $K_2OsO_2(OH)_4$ (6 mg, 0.15 mmol) at room temperature for 7 h. $NaIO_4$ (88 mg, 0.41 mmol) was added to the mixture, and the resulting mixture was stirred for an additional 18 h. The mixture was diluted with AcOEt, and the organic phase was washed with saturated aqueous NaHCO$_3$ and saturated aqueous NaCl, dried (Na$_2$SO$_4$), and concentrated in vacuo. The residue was purified by a silica gel column (2 × 5 cm, 50% AcOEt−hexane) to give **25** (50 mg, 83% in 3 steps) as a colorless foam. Data for major rotamer: ^{1}H NMR (CDCl$_3$, 500 MHz, 7:1 mixture of the rotamers) δ 9.50 (s, 1H, H-11′), 8.36 (br s, 1H, NH-3), 7.46 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.35−7.32 (m, 5H, phenyl), 5.82−5.61 (m, 3H, NHBoc, NHCbz, H-10′), 5.82 (s, 1H, H-1′), 5.78 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.42 (m, 1H, H-2′), 5.19 (d, 1H, benzyl, J = 12.1 Hz), 5.08 (s, 1H, H-1″), 5.02 (d, 1H, benzyl, J = 12.1 Hz), 4.96 (m, 1H, H-3′), 4.83 (m, 1H, H-6′), 4.79 (m, 1H, H-5′), 4.57 (d, 1H, H-2″, $J_{2'',3''}$ = 5.2 Hz), 4.50 (d, 1H, H-3″, $J_{3'',2''}$ = 5.2 Hz), 4.22−4.10 (m, 3H, H-4′, H-4″, H-9′), 3.23 (m, 1H, H-5″a), 3.21 (s, 3H, NMe), 2.95 (m, 1H, H-5″b), 2.43 (m, 2H, COCH$_2$), 1.68−1.48 (m, 9H, 2 × CH_2CH$_3$, acetonide, COCH$_2$CH_2) 1.45 (s, 9H, *tert*-butyl), 1.43 (s, 9H, *tert*-butyl), 1.34 (s, 3H, acetonide), 1.26 (m, 24H, palmitoyl),

0.88 (t, 3H, palmitoyl terminal-Me, $J = 6.4$ Hz), 0.82 (m, 6H, 2 × CH_2CH_3); FABMS-LR *m/z* 1214 (MH^+); FABMS-HR (NBA) calcd for $C_{62}H_{96}N_5O_{19}$ 1214.6694, found 1214.6694.

Diazepanone (26). A mixture of **25** (13.4 mg, 0.011 mmol) and Pd black (15 mg) in *i*-PrOH (2 mL) was vigorously stirred under H_2 atmosphere for 2 h. The insoluble materials were filtered off through a Celite pad, and the filtrate was concentrated in vacuo. The residue in CH_2Cl_2 (2 mL) was treated with AcOH (10 μL) and $NaBH(OAc)_3$ (10 mg, 0.044 mmol) at room temperature for 24 h. The mixture was partitioned between AcOEt and saturated aqueous $NaHCO_3$, and the organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by a silica gel column (1 × 5 cm, 33−50% AcOEt−hexane) to give **26** (11 mg, 96%) as a colorless foam: $[\alpha]_D^{23}$ +9.4 (*c* 0.89, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.18 (s, 1H, NH-3), 7.33 (d, 1H, H-6, $J_{6,5} = 8.1$ Hz), 6.91 (br s, 1H, NHBoc), 5.70 (d, 1H, H-5, $J_{5,6} = 8.1$ Hz), 5.68 (s, 1H, H-1′), 5.41 (s, 1H, H-1″), 5.22 (m, 1H, H-3‴), 4.89 (dd, 1H, H-2′, $J_{2',3'} = 6.5$ Hz, $J_{2',1'} = 1.6$ Hz), 4.63 (m, 2H, H-3′, H-2″), 4.53 (d, 1H, H-5′, $J_{5',6'} = 9.6$ Hz), 4.49 (d, 1H, H-3″, $J_{3'',2''} = 5.9$ Hz), 4.42 (d, 1H, H-2‴, $J_{2''',3'''} = 5.2$ Hz), 4.38 (m, 1H, H-4′), 4.26 (dd, 1H, H-4″, $J_{4'',5''a} = 4.2$ Hz, $J_{4'',5''b} = 7.5$ Hz), 3.35 (m, 1H, H-5″a), 3.30 (m, 1H, H-6′), 3.30 (d, 1H, H-4‴a, $J_{4'''a,4'''b} = 12.7$ Hz), 3.02 (s, 3H, NMe), 2.98 (d, 1H, H-4‴b, $J_{4'''b,4'''a} = 12.7$ Hz), 2.97 (m, 1H, H-5″b), 2.33 (m, 2H, $COCH_2$), 1.61 (m, 6H, 2 × CH_2CH_3, $COCH_2CH_2$), 1.52 (s, 3H, acetonide), 1.49 (s, 9H, *tert*-butyl), 1.42 (s, 9H, *tert*-butyl), 1.29 (s, 3H, acetonide), 1.25 (m, 24H, palmitoyl), 0.88 (m, 3H, palmitoyl terminal-Me), 0.82 (m, 6H, 2 × CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.5, 173.1, 166.9, 162.5, 156.1, 149.6, 141.9, 116.5, 114.8, 110.9, 102.5, 93.1, 87.2, 86.8, 86.5, 84.5, 83.8, 82.2, 81.1, 78.9, 69.4, 64.9, 60.4, 49.5, 43.5, 39.5, 34.2, 31.9, 29.7, 29.6, 29.6, 29.5, 29.3, 29.3, 29.1, 28.5, 28.0, 27.3, 25.5, 24.9, 22.7, 14.1, 8.3, 7.4; FABMS-HR (NBA) calcd for $C_{54}H_{90}N_5O_{16}$ 1064.6383, found 1064.6375.

Diazepanone (27). A solution of **26** (10 mg, 9.4 μmol) in AcOEt (1 mL) was treated with paraformaldehyde (1.5 mg, 47 μmol), AcOH (20 μL), and $NaBH(OAc)_3$ (8 mg, 38 μmol) at room temperature for 72 h. The mixture was partitioned between AcOEt and saturated aqueous $NaHCO_3$, and the organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by a silica gel column (1 × 5 cm, 50% AcOEt−hexane) to give **27** (7.8 mg, 77%) as a colorless foam: $[\alpha]_D^{22}$ −20.2 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11 (s, 1H, NH-3), 7.72 (d, 1H, H-6, $J_{6,5} = 8.0$ Hz), 6.36 (br s, 1H, NHBoc), 5.98 (s, 1H, H-1′), 5.67 (d, 1H, H-5, $J_{5,6} = 8.0$ Hz), 5.35 (m, 1H, H-3‴), 5.25 (s, 1H, H-1″), 4.84 (d, 1H, H-3′, $J_{3',2'} = 4.5$ Hz), 4.67 (d, 1H, H-2″, $J_{2'',3''} = 4.5$ Hz), 4.59 (d, 1H, H-2″, $J_{2'',3''} = 6.0$ Hz), 3.53 (d, 1H, H-6′, $J_{6',5'} = 9.0$ Hz), 3.43 (m, 1H, H-5″a), 3.36 (d, 1H, H-4‴a, $J_{4'''a,4'''b} = 15.0$ Hz), 3.19 (d, 1H, H-4‴b, $J_{4'''b,4'''a} = 15.0$ Hz), 3.15 (m, 1H, H-5″b), 3.09 (s, 3H, CONMe), 2.43 (s, 3H, NMe), 2.32 (t, 2H, $COCH_2$, $J = 7.5$ Hz), 1.65 (dd, 2H, CH_2CH_3, $J = 7.4$, 14.8 Hz), 1.61 (s, 3H, acetonide), 1.53 (dd, 2H, CH_2CH_3, $J = 7.4$, 14.8 Hz), 1.45 (s, 9H, *tert*-butyl), 1.42 (m, 2H, $COCH_2CH_2$), 1.40 (s, 9H, *tert*-butyl), 1.36 (s, 3H, acetonide), 1.28 (m, 24H, palmitoyl), 0.89−0.82 (m, 9H, 2 × CH_2CH_3, palmitoyl terminal-Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.7, 171.4, 166.6, 162.3, 156.2, 149.6, 140.5, 116.7, 115.1, 111.4, 102.5, 99.1, 89.7, 86.9, 86.8, 85.1, 83.9, 83.6, 82.5, 80.3, 79.3, 75.8, 71.0, 64.9, 63.0, 43.2, 38.7, 34.5, 31.9, 29.7, 29.6, 29.7, 29.4, 29.3, 29.2, 29.2, 28.9, 28.5, 27.7, 27.3, 25.3, 24.9, 22.7, 14.1, 8.4, 7.4; FABMS-HR (NBA) calcd for $C_{55}H_{92}N_5O_{16}$ 1078.6539, found 1078.6536.

Des-*N*-methyl Palmitoyl Caprazol (28). Compound **26** (10 mg, 9.4 μmol) was treated with 80% aqueous TFA (1 mL) at room temperature for 1 h. The mixture was concentrated in vacuo, and the residue was lyophilized to afford **28** (a TFA salt, 8.6 mg, quant.) as a white solid: mp 195 °C dec; $[\alpha]_D^{23}$ +18.1 (*c* 0.4, DMSO); ^{1}H NMR (CD_3OD, 500 MHz) δ 7.65 (d, 1H, H-6, $J_{6,5} = 8.1$ Hz), 5.70 (d, 1H, H-5, $J_{5,6} = 8.1$ Hz), 5.67 (d, 1H, H-1′, $J_{1',2'} = 2.1$ Hz), 5.61 (m, 1H, H-3‴), 5.45 (s, 1H, H-1″), 4.80 (d, 1H, H-2‴, $J_{2''',3'''} = 5.1$ Hz), 4.22 (dd, 1H, H-2′, $J_{2',1'} = 2.1$ Hz, $J_{2',3'} = 6.7$ Hz), 4.21 (m, 1H, H-3′), 4.11−4.02 (m, 5H, H-4′, H-4″, H-6′, H-2″, H-3″), 3.51 (m, 2H, H-4‴a, H-4‴b), 3.27 (m, 2H, H-5″a, H-5″b), 3.09 (s, 3H, CONMe), 2.41 (t, 2H, $COCH_2$, $J = 7.5$ Hz), 1.64 (m, 2H, $COCH_2CH_2$), 1.28 (m, 24H, palmitoyl), 0.89 (m, 3H, palmitoyl terminal-Me); ^{13}C NMR (CD_3OD, 125 MHz) δ 173.8, 170.3, 165.9, 151.9, 143.2, 108.8, 102.8, 94.2, 84.9, 80.3, 76.3, 75.9, 74.4, 73.5, 73.2, 71.3, 68.7, 65.4, 62.2, 60.4, 50.2, 43.0, 39.5, 35.0, 34.8, 33.1, 30.8, 30.7, 30.6, 30.5, 30.5, 30.2, 26.1, 25.8, 23.8, 14.5; FABMS-HR (NBA) calcd for $C_{37}H_{60}N_5O_{14}$ 798.4142, found 798.4142.

Palmitoyl Caprazol (7). Compound **27** (7.8 mg, 7.3 μmol) was treated with 80% aqueous TFA (1 mL) at room temperature for 1 h. The mixture was concentrated in vacuo, and the residue was lyophilized to afford **7** (a TFA salt form, 6.7 mg, quant.) as a white solid: mp 210 °C dec; $[\alpha]_D^{23}$ +17.0 (*c* 0.5, DMSO); ^{1}H NMR (CD_3OD, 500 MHz) δ 7.74 (d, 1H, H-6, $J_{6,5} = 8.0$ Hz), 5.70 (d, 1H, H-5, $J_{5,6} = 8.0$ Hz), 5.63 (s, 1H, H-1′), 5.43 (m, 1H, H-3‴), 5.19 (s, 1H, H-1″), 4.65 (d, 1H, H-2‴, $J_{2''',3'''} = 4.6$ Hz), 4.37 (d, 1H, H-5′, $J_{5',6'} = 8.8$ Hz), 4.24 (d, 1H, H-3″, $J_{3'',2''} = 8.0$ Hz), 4.15 (m, 2H, H-3′, H-4′), 4.11−4.07 (m, 3H, H-2′, H-2″, H-4″), 3.78 (d, 1H, H-6′, $J_{6',5'} = 8.8$ Hz), 3.44 (d, 1H, H-4‴a, $J_{4'''a,4'''b} = 16.3$ Hz), 3.26 (m, 1H, H-5″a), 3.19 (m, 1H, H-5″b), 3.14 (d, 1H, H-4‴b, $J_{4'''b,4'''a} = 16.3$ Hz), 3.13 (s, 3H, CONMe), 3.48 (s, 3H, NMe), 2.38 (m, 2H, $COCH_2$), 1.60 (m, 2H, $COCH_2CH_2$), 1.30 (m, 24H, palmitoyl), 0.89 (m, 3H, palmitoyl terminal-Me); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 171.9, 170.3, 163.4, 150.3, 140.1, 110.1, 101.0, 100.2, 89.3, 82.7, 78.2, 76.0, 74.4, 74.2, 70.0, 69.7, 68.8, 67.4, 38.1, 35.9, 33.8, 31.2, 29.8, 29.0, 28.9, 28.8, 28.8, 28.6, 28.5, 28.4, 24.3, 23.2, 22.3, 22.0, 13.9; FABMS-HR (NBA) calcd for $C_{38}H_{62}N_5O_{14}$ 812.4299, found 812.4301.

Acknowledgment. This work was supported by grants-in-aid for scientific research from the Ministry of Education. We thank Dr. Masayuki Igarashi (Bioresources Unit, Bioactive Molecular Research Group, Microbial Chemistry Research Center) for evaluating the antibacterial activities of the synthesized analogues. We thank Ms. S. Oka (Center for Instrumental Analysis, Hokkaido University) for measurement of the mass spectra.

Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO702264E