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Development of a Highly β-Selective Ribosylation Reaction without Using Neighboring Group Participation: Total Synthesis of (+)-Caprazol, a Core Structure of Caprazamycins

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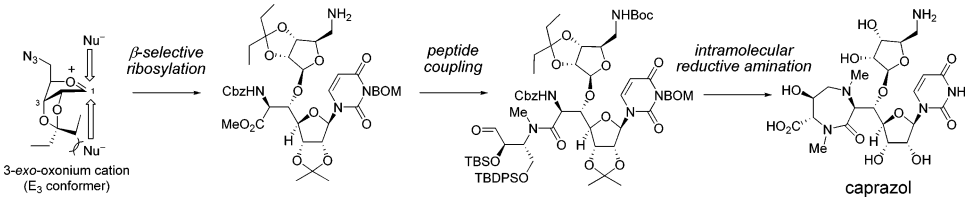

Full details of the total synthesis of (+)-caprazol are described. The key elements of our approach include the early stage introduction of the aminoribose in a highly β-selective manner, using the steric hindrance in the transition state and the construction of the diazepanone by a modified intramolecular reductive amination. The 5′-*C*-glycyluridine derivative **9**, which was prepared stereoselectively via Sharpless asymmetric aminohydroxylation, was ribosylated with 2,3-*O*-alkylidene ribofuranosyl donors. It was revealed that increasing the size of the alkyl substituents of the acetal unit resulted in improving the stereoselectivity of the anomeric position, and the desired ribosides **21b** (1″-β) and **22b** (1″-α) were obtained in 80% yield (**21b**/**22b** = 24.0/1) when the ribosyl fluoride **16** possessing a more sterically hindered 3-pentylidene group was used. The origin of the stereoselectivity of the ribosylation was also discussed. Construction of the diazepanone system was optimized with the model aldehyde **37**, and the desired diazepanone **38** was obtained in 88% yield via two-step reaction sequence including catalytic hydrogenation followed by hydride reduction. Application of this method to the aldehyde **44** successfully afforded the diazepanone derivatives **45** and **46**, functional group manipulation of which completed the total synthesis of (+)-caprazol.

Introduction

Caprazamycins (CPZs) (Figure 1, **1**) were isolated from a culture broth of the Actinomycete strain *Streptomyces sp*. MK730-62F2 in 2003[1] and represent the newest members of a class of naturally occurring 6′-*N*-alkyl-5′-β-*O*-aminoribosylglycyluridine antibiotics including liposidomycins[2] (LPMs, **2**), muraymycins[3] (MRYs, **3**), and FR-900493[4] (**4**), which have been shown to exhibit excellent antimicrobial activity against Gram-positive bacteria. In particular, the CPZs have shown excellent antimycobacterial 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 antituberculosis agents with a novel mode of action.

Caprazol (Figure 2, **5**) is a deacylated CPZs whose stereochemical structure (5′*S*,6′*S*,2‴*S*,3‴*S*) was recently revealed through X-ray crystal analysis[1b] and confirmed by total syn-

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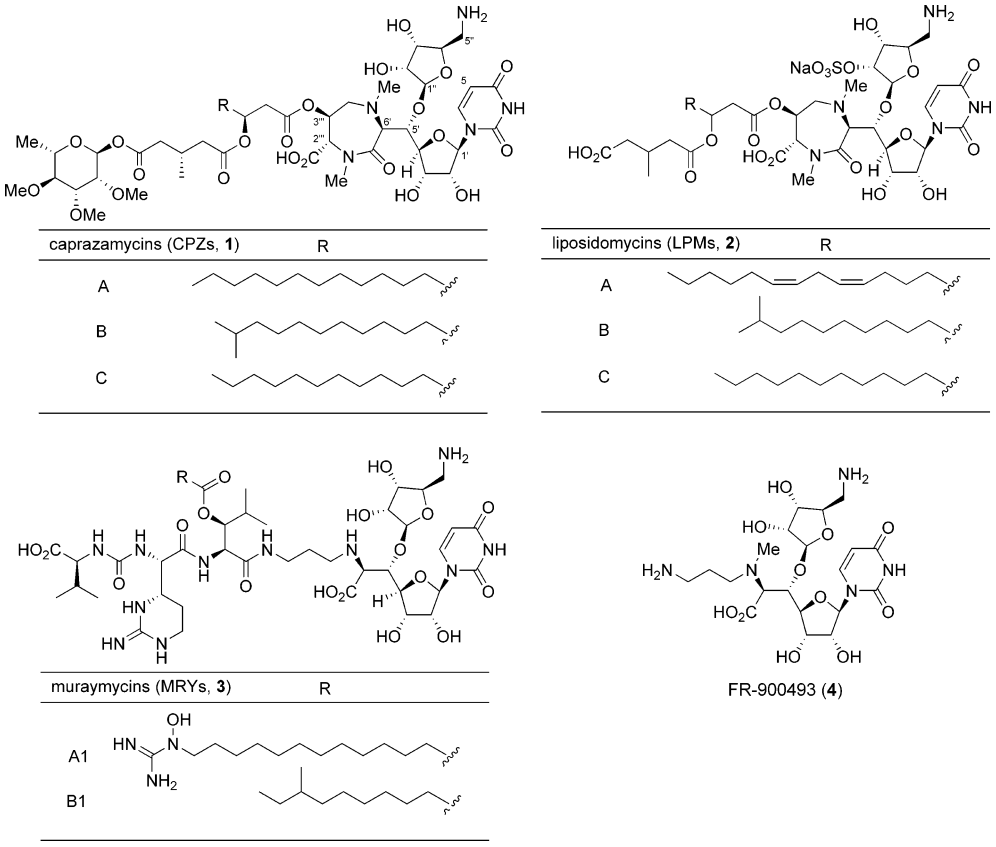

FIGURE 1. Structures of nucleoside antibiotics possessing the 6′-*N*-alkyl-5′-*O*-aminoribosyl-glycyluridine.

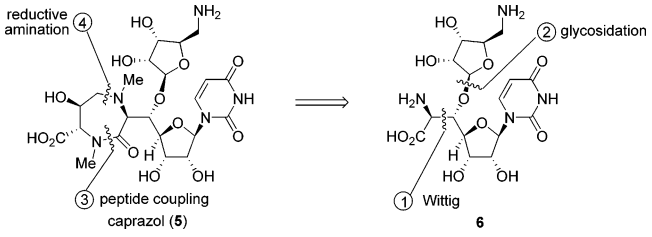

FIGURE 2. Synthetic strategy of caprazol (**5**).

thesis.[5] The CPZs and the LPMs consist of a uridine, an aminoribose, and a characteristic diazepanone, rendering them intriguing, challenging synthetic targets.[6−13] Most of the synthetic problems, based on the stereochemical assignment at the 5′-, 6′-, 2‴-, and 3‴-positions, have been addressed previously by the construction of the characteristic diazepanone system.

One of the major difficulties posed by the previous synthetic work is the introduction of the 5-aminoribose moiety after constructing the uridyldiazepanone moiety. The tertiary amine contained in the diazepanone structure inhibits the usual ribosylation promoted by Lewis acids,[14] and the 5′-hydroxyl group is presumed to be in a highly sterically hindered position.[15] In view of these observations, we selected to set up the 5′-*β*-*O*-aminoribosyl-glycyluridine structure **6** prior to the construction of the diazepanone ring (Figure 2). From a medicinal chemical point of view, this strategy would also be suitable for examining a general structure−activity relationship and for synthesizing novel analogues because the 5′-*β*-*O*-aminoribosyl-glycyluridine structure **6** is predicted to be a pharmacophore of this class of natural products. However, a key issue associated

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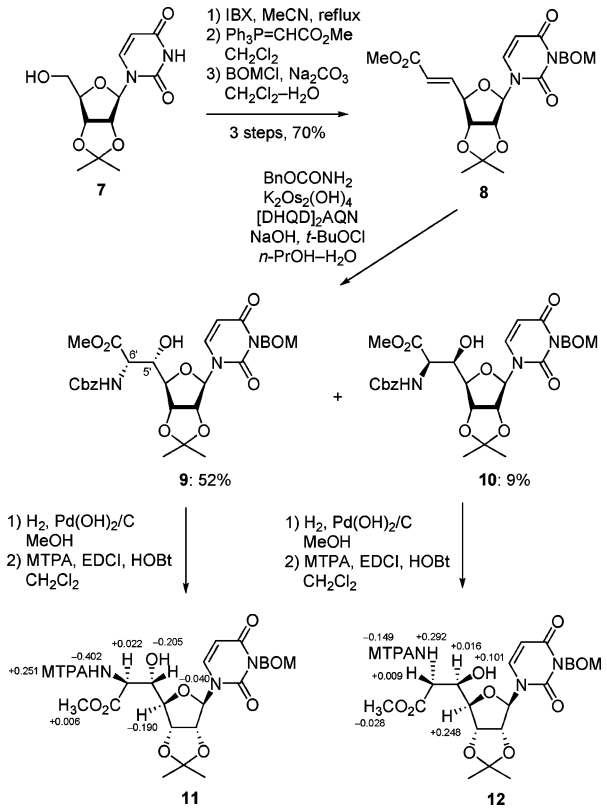
with the construction of the 5′-*β*-*O*-aminoribosyl-glycyluridine structure needs to be addressed. It was reported that the elimination of the fatty acyloxy group of the diazepanone moiety of the LPMs occurred under basic conditions because they contain *β*-heterosubstituted carboxyl moieties.[2b] Caprazol (**5**) as well as the CPZs would also be sensitive to similar basic conditions. A general method exists for the construction of *β*-glycosides, using a glycosyl donor protected with a 2-*O*-acyl group, via a neighboring group participation.[16] However, because a 2-*O*-acyl group is usually deprotected under basic conditions, this strategy would not be suitable for the synthesis of **5**. Compared to the neighboring group participation strategy, little attention has been focused on alternative methods to synthesize *β*-ribosides.[17,18] The anomeric effect has been used in pyranose chemistry to construct glycosyl bonds but due to the weak anomeric effect of furanoses, anomeric selectivities would be difficult to control.[19] Furthermore, furanosides are inherently flexible and can adopt both twist and envelope conformations, which can interconvert via pseudorotational itineraries.[20,2121] As a result, furanoses can glycosylate through several different transition states, potentially compromising anomeric selectivities.[22] Considering the inherent nature of furanoses, we planned to lock the conformation of the ribofuranose by introducing a cyclic acetal protecting group at the 2,3-hydroxyl groups, that could be deprotected under acidic conditions, thereby controlling the *β*-selectivity via the steric hindrance of the protecting group installed on the α-face of the ribofuranose. Recently we have completed the total synthesis of (+)-caprazol utilizing the above-mentioned concept.[5] Herein, we provide full details of *β*-selective ribosylation reaction utilizing a steric hindrance installed on the α-face of a ribosyl donor and the total synthesis of (+)-caprazol.

Control of the *β*-Selectivity in a Ribosylation Reaction Utilizing a Steric Hindrance Installed on the α-Face of a Ribosyl Donor. Our initial objective was to construct a *β*-ribofuranoside utilizing the steric hindrance installed on the α-face of a ribosyl donor to permit direct access to the predicted pharmacophore of the CPZs **6**. The 5′-*C*-glycyluridine derivative **9**, which is a ribosyl acceptor, was prepared as shown in Scheme 1. Oxidation of 2′,3′-*O*-isopropylideneuridine (**7**)[23] with IBX (3 equiv, MeCN, 80 °C)[24] followed by a two-carbon elongation with $Ph_3P{=}CHCO_2Me$ (1.2 equiv, CH_2Cl_2, −20 °C) and a BOM protection of the *N*-3-position of the uracil moiety by mild biphasic conditions (1.5 equiv of BOMCl, 4 equiv of Na_2CO_3, 0.05 equiv of Bu_4NI, $CH_2Cl_2-H_2O$, 66% overall) provided compound **8** (trans/cis = 37/1). The best reagent for the oxidation of **7**, furnishing the best quality of the corresponding aldehyde among other oxidation methods tested (i.e., Swern

SCHEME 1. Preparation of 5′-C-Glycyluridine 9



conditions, Pfitzner−Moffatt conditions, PDC, Dess−Martin periodinane), was IBX. Since the 4′-position of **8** became more acidic when the α,*β*-unsaturated ester functionality at the 5′-position was introduced, the use of the usual BOM protection conditions (i.e., Et_3N or $^iPr_2NEt$, CH_2Cl_2, 0 °C) resulted in near complete epimerization at the 4′-position. When a Sharpless aminohydroxylation[25] of **8** was carried out in the absence of chiral ligands, no diastereoselectivity was observed and compounds **9** and **10** (a ratio of **9**/**10** = 40/60) were obtained in low yield. The aminohydroxylation with $(DHQD)_2AQN$ as a chiral ligand[26−28] (15 mol % of $K_2[Os_2(OH)_4]$, 15 mol % of $(DHQD)_2AQN$, 3 equiv of benzyl carbamate, 2.6 equiv of NaOH, PrOH−H_2O, 15 °C, 52%) afforded **9** as the major diastereomer, with the ratio of **9**/**10** being 86/14. The regioselectivity of the aminohydroxylation reaction was relatively high compared with that reported in the literature[29] and only trace amounts of the corresponding *β*-amino-α-hydroxy derivatives were observed. The stereochemistry of the 5′-position of compounds **9** and **10** was determined to be the *S* and *R* configuration by using the modified Mosher method[30] with the amide derivatives **11** and **12**, respectively, which were prepared by deprotection of the Cbz protecting group of either **9** or **10** followed by acylation of the liberated amine with 2-methoxy-2-trifluoromethylphenylacetic acid. We also found that the

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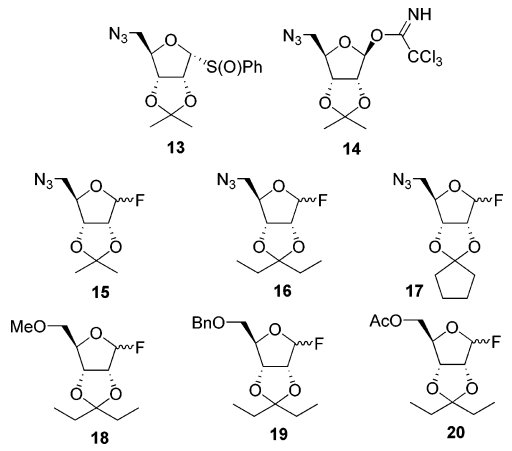

FIGURE 3. Structure of ribosyl donors used in this study.

aminohydroxylation of **8** was sensitive to the amount of chiral ligand and to the reaction temperature. When a reduced amount of $(DHQD)_2AQN$ was used or when the reaction was conducted at higher temperatures, the yields and diastereoselectivity of **9** were dramatically decreased.

We next examined the ribosylation of the 5′-hydroxyl group of **9** with a variety of ribosyl donors[31] listed in Figure 3, and the results are summarized in Table 1. First, we screened the leaving group of ribosyl donors protected with an isopropylidene group at the 2- and 3-positions. During the course of synthetic studies on nucleoside antibiotics by other groups[32,33] and by ours[15,34] it was revealed that the glycosylation or the introduction of a substituent at the sterically encumbered 5′-hydroxyl group of nucleoside derivatives proved quite difficult. Therefore, our initial attempts focused on finding glycosyl donors known to be highly reactive, for example, the sulfoxide **13** and the trichloroacetimidate **14**. When **13** was activated with Tf_2O in CH_2Cl_2 at −40 °C,[34] the corresponding ribosides **21a** and **22a** were obtained in 80% yield;[36] however, no β-selectivity was observed (entry 1). The ribosylation with **14** by using TfOH as an activator also resulted in no β-selectivity (entry 2).[37] On the other hand, when the ribosyl fluoride **15** was activated with $BF_3{\cdot}OEt_2$[38,39] at 0 °C, the ribosides **21a** and **22a** were obtained in 72% yield with moderate stereoselectivity at the anomeric position (**21a**/**22a** = 2.8/1, entry 3). Lower temperature did not affect the selectivity (entry 4). When other activators, including $AgOTf/Cp_2HfCl_2$,[40] $AgOTf/SnCl_2$,[41] or $AgClO_4/SnCl_2$, were used, the stereoselectivity did not improve (entries 5−8). Further exploration with the ribosyl fluoride **16** possessing a more sterically hindered 3-pentylidene group afforded the desired **21b** with excellent β-selectivity (**21b**/**22b** = 24.0/1) when activation was conducted with $BF_3{\cdot}OEt_2$ at 0 °C (entry 9). Crystallization of the mixture gave pure **21b**.

We further investigated the effect of the 5-*O*-substituent of ribofuranosyl donor **18**−**20**[31] and expanded the β-selective *O*-ribosylation reaction with other nucleophiles. The ribosylation was examined with ribosyl donors possessing a variety of substituents at the 5-position, using *N*-Cbz-L-threonine methyl ester as a nucleophile, to understand the effect of these substituents on the stereoselectivity of the *O*-ribosylation reaction, and the results are summarized in Table 2. When the 5-azidoribosyl fluoride **16** was activated with $BF_3{\cdot}OEt_2$ at −30 °C, the corresponding ribosides **23a** and **24a** were obtained in 95% yield with good stereoselectivity at the anomeric position (**23a**/**24a** = 97/3, entry 1). When a 5-*O*-alkyl-substituted ribosyl fluoride such as a methyl derivative **18** and a more sterically hindered benzyl derivative **19** were used, the corresponding ribosides were obtained in 99% and 94% yield with good stereoselectivity, respectively (entries 2 and 3). The observed high β-selectivity was not only the case for the azide group, and was revealed to be independent from the 5-*O*-alkyl substituent. On the other hand, the stereoselectivity was slightly decreased to 91/9 when a 5-*O*-acetylribosyl donor **20** was used (entry 4). Presumably, a neighboring group participation of the acetyl group to the oxocarbenium intermediate at the β-face and the rate of S_N2 displacement to the intermediate would be increased although the stereoselectivity was still a practical level.

Next, *O*-ribosylations with other nucleophiles, using the 5-azidoribosyl fluoride **16** as a donor, were examined as shown in Table 3. Reaction with *N*-Cbz-L-serine methyl ester, which has a primary alcohol, gave **25** in 58% with good selectivity (β/α = 95/5, entry 1). Ribosylation with the primary alcohol of methyl 2,3,5-tri-*O*-benzyl-α-D-glucoside, however, resulted in a reduced stereoselectivity (β/α = 82/18, entry 2). When other secondary alcohols such as choresterol and sterically more hindered menthol were used as nucleophiles, the stereoselectivity was moderate (β/α = 81/19−89/11, entries 3 and 4) compared to the excellent selectivity with *N*-Cbz-L-threonine methyl ester, which has also a secondary alcohol. In conjunction with the results observed in the reactions with the primary alcohols, alcohols at a side chain of the amino acid derivatives, which have an electron-withdrawing group and are unreactive, exhibit the better β-selectivity. These results suggested that the stereoselectivity largely depends on the reactivity of the alcohol, but not the steric hindrance.

During ribosylation, an oxocarbenium intermediate is formed by the activation of the fluoride. Oxocarbenium ions have a double-bond character between the endocyclic oxygen and anomeric carbon atoms. As a result, oxocarbenium ions of D-ribofuranosides can adopt either of two possible low-energy conformations, in which C-3 is either above or below the C-2−C-1−O−C-4 plane, the ^3E conformer or the E_3 conformer, respectively.[42] To obtain more insight into the factors responsible for the high β-selectivity with the 2,3-pentylidene protected ribosyl donors, we optimized these conformers for the two different 5-*O*-methylribofuranosyl oxocarbenium ions having the isopropylidene (Figure 4a) and the 3-pentylidene protected

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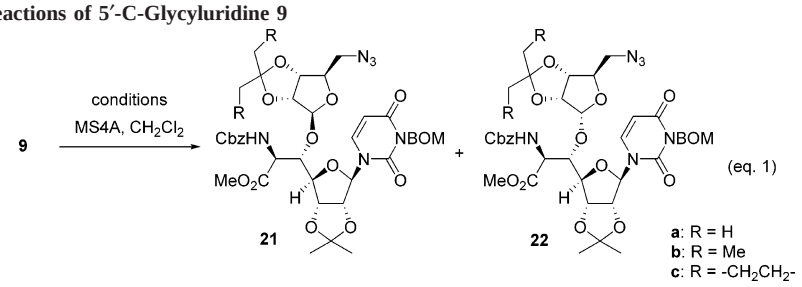
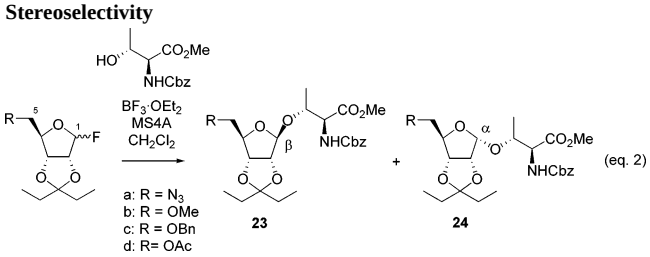
TABLE 1. Ribosylation Reactions of 5′-C-Glycyluridine 9



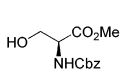
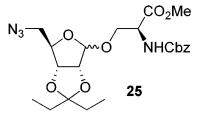
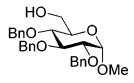
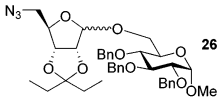
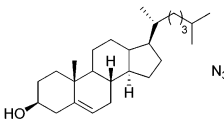
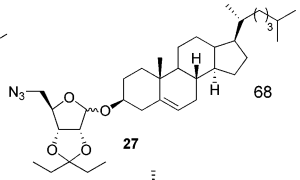
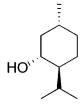
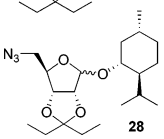
entry	donor	activator (equiv)	temp, °C	yield, %	ratio (**21/22**)
1	**13**	Tf_2O (2.0)	−40	80	1.2/1
2	**14**	TfOH (1.0)	−15	79	1.1/1
3	**15**	$BF_3{\cdot}OEt_2$ (1.5)	0	72	2.8/1
4	**15**	$BF_3{\cdot}OEt_2$ (1.2)	−30	78	2.7/1
5	**15**	TMSOTf (1.0)	0	trace	
6	**15**	AgOTf (1.5)/Cp_2HfCl_2 (1.5)	−40	quant.	1.2/1
7	**15**	AgOTf (1.5)/$SnCl_2$ (1.5)	0	60	2.0/1
8	**15**	$AgClO_4$ (1.5)/$SnCl_2$ (1.5)	0	40	2.6/1
9	**16**	$BF_3{\cdot}OEt_2$ (1.5)	0	80	24.0/1
10	**16**	AgOTf (1.5)/Cp_2HfCl_2 (1.5)	−40	quant.	8.1/1
11	**17**	$BF_3{\cdot}OEt_2$ (1.5)	0	75	2.4/1

TABLE 2. Effect of a Substituent at the 5-Position on the Stereoselectivity



entry	donor	R	yield, %	ratio (**23/24**)
1	**16**	N_3	95	97/3
2	**18**	OMe	99	96/4
3	**19**	OBn	94	96/4
4	**20**	OAc	96	91/9

TABLE 3. Nucleophilic Substitution Reaction of 3-Pentylidene-Protected Ribosyl Fluoride

entry	nucleophiles	products	yield (%)	ratio (β/α)
1		 **25**	58	95/5
2		 **26**	95	82/18
3		 **27**	68	89/11
4		 **28**	76	81/19

ribofuranosides (Figure 4b) by density functional theory (DFT) quantum mechanical calculations at the BL3LYP/6-31G** level.[43] From these results, we calculated the E_3 conformer to be lower in energy than the ^3E conformer, where the 3-oxy group was orientated in the pseudoaxial position, in both cases.[44,4545] Two potentially favorable modes of nucleophilic attack are possible for the oxocarbenium ions, and these modes are governed by both ground-state effects and transition-state effects, issues which have been extensively studied by Woerpel et al.[45] For the oxocarbenium ion in the E_3 conformer, nucleophilic attack from the α-face is favored by inside attack in the ground state to give the α-riboside. However, nucleophilic attack from the α-face of **29** or **30** would suffer significant steric interactions from one of the alkyl groups of the cyclic ketal moiety in its transition state. Thus, the approach of the nucleophile is diminished resulting in poor selectivity when the oxocarbenium ion **29** with the smaller methyl substituents of the isopropylidene group is used. Increasing the size of the alkyl substituents such as ethyl groups in the 3-pentylidene group would result in severe steric repulsion on the α-face of **30**, leading to outside attack with complete reversal of stereoselectivity. This mechanism was further supported by the following experiments. Ribosylation of **9** with the cyclopentylidene protected ribofuranosyl donor **17**, which has the same number of carbon atoms as the 3-pentylidene group, gave the corresponding ribosides with reduced selectivity (**21c**/**22c** = 2.4/1, entry 11 in Table 1). Thus, the cyclopentylidene group, held away from the course of the approaching nucleophile, did not exert severe steric repulsion

(43) (a) Becke, A. D. *Phys. Rev.* **1998**, *38*, 3098−3100. (b) Becke, A. D. *Phys. Rev.* **1998**, *37*, 785−789. (c) Becke, A. D. *J. Phys. Chem.* **1993**, *98*, 1372−1377.

(44) (a) Chang, G.; Guida, W. C.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 4379−4386. (b) Saunders, M.; Houk, K. N.; Wu, Y. D.; Still, W. C.; Lipton, M.; Chang, G.; Guida, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 1419−1427. (c) Halgren, T. A. *J. Comput. Chem.* **1999**, *20*, 720−729. (d) Halgren, T. A. *J. Comput. Chem.* **1999**, *20*, 730−748.

(45) Chamberland, S.; Ziller, J. W.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 5322−5323.

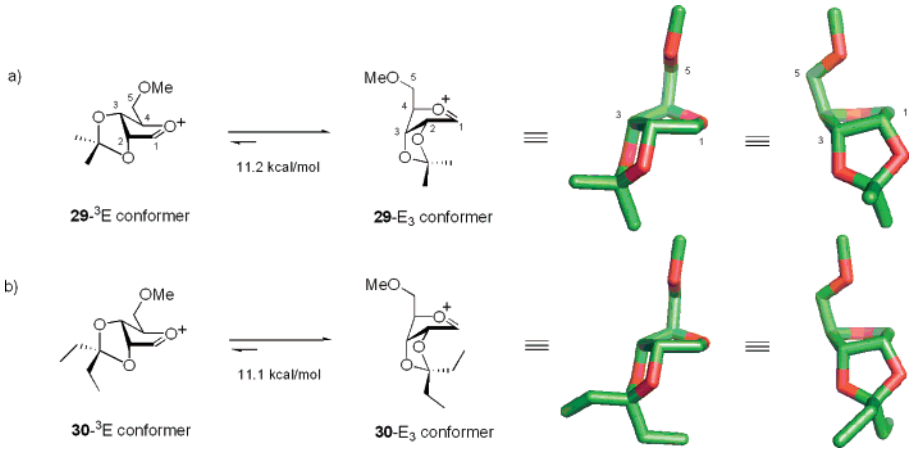
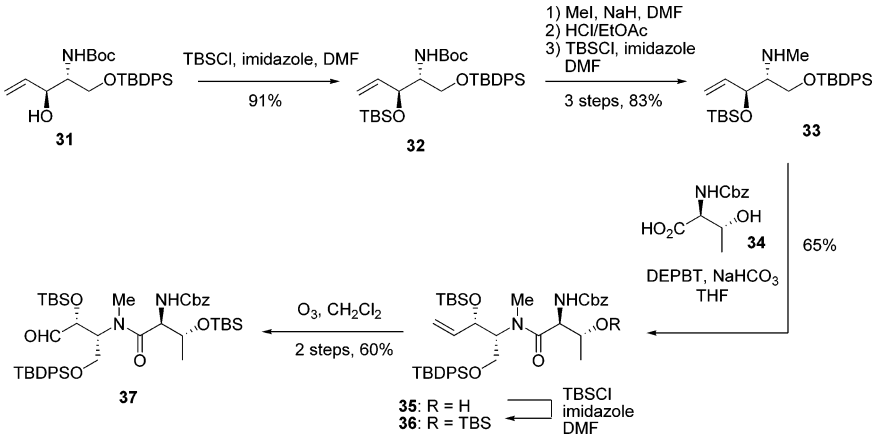


FIGURE 4. Optimized geometries (B3LYP/6-31G**) of the E_3 Conformers of the oxacarbenium ions of (a) 2,3-*O*-isopropylidene-5-*O*-methyl-D-ribofuranose and (b) 2,3-*O*-3-pentylidene-5-*O*-methyl-D-ribofuranose

SCHEME 2. Preparation of *N*-Methyl-2-amino-4-pentene-1,3-diol Derivative 37



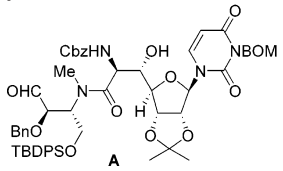
on the α-face thereby permitting inside attack, which results in a poor selectivity, similar to that with the isopropylidene-protected ribofuranosides. This would suggest that the steric effect in the transition state is largely responsible for the excellent *β*-selectivity seen with the ribosyl donor **16** in our study. Because of the inherent nature of the E_3 conformation, the terminal methyl substituent of the 3-pentylidene group on the α-face is oriented toward the anomeric carbon atom and not toward the C-4 carbon atom, an orientation that would also help to prevent the approach of the nucleophile from the α-face of **30**. This could be a possible explanation for the large disparity in the anomeric selectivity observed between the isopropylidene- and the 3-pentylidene-protected ribofuranosides. It should be noted that a decrease in *β*-selectivity was also observed under conditions where a trifluoromethanesulfonate ion was present ($AgOTf/Cp_2HfCl_2$, **21b**/**22b** = 8.1/1, entry 10). Presumably a *β*-*O*-trifluoromethanesulfonyl riboside intermediate[47] was formed, followed by S_N2 attack of the alcohol to give the undesired α-riboside **22b**.

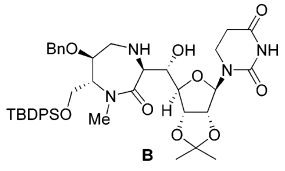
Total Synthesis of (+)-Caprazol. After selectively preparing the key aminoriboside **21b**, we directed our attention to the construction of the characteristic 7-membered diazepanone, the system on which most of the previous synthetic studies for the LPMs have been focused.[6−13] An intramolecular reductive amination strategy with an amino aldehyde derivative seemed to be an efficient way of constructing the diazepanone system, a strategy we decided to use to install the diazepanone moiety on **21b**. Optimization of the reductive amination was examined by using the model compound **37**, which was prepared as shown in Scheme 2.[48] The secondary alcohol of the 2-amino-4-pentene-1,3-diol derivative **31**,[49] prepared from D-serine in 7 steps, was protected with a TBS group to give **32** (1.2 equiv of TBSCl, 3.6 equiv of imidazole, DMF, 89%), which was successively *N*-methylated (2.5 equiv of MeI, 2 equiv of NaH, DMF) and deprotected (HCl/AcOEt). During the deprotection step of the isopropylidene group, the TBS group was partially deprotected. Therefore, the crude mixture was re-treated with TBSCl and

(46) Sonntag, L. S.; Schweizer, S.; Ochsenfeld, C.; Wennemers, H. *J. Am. Chem. Soc.* **2006**, *128*, 14697−14703.

(47) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217−11223.

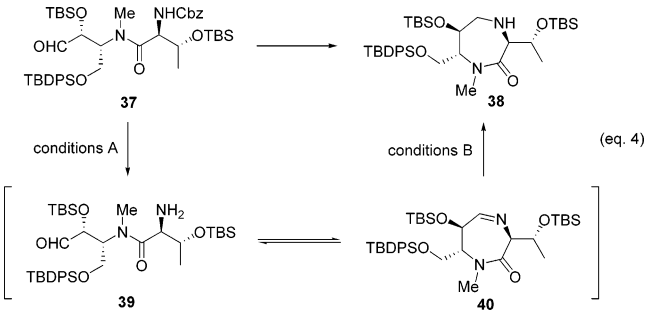
(48) Initial attempts to construct the diazepanone via deprotection of the Cbz group in a model compound such as **A** followed by reductive amination of the aldehyde, both promoted by catalytic hydrogenation with Pd/C, were unsuccessful because of difficulty in hydrogenating the corresponding cyclic imine. Additional forcing conditions under medium pressure gave a 5,6-dihydrouridine derivative **B** due to over-reduction





(49) (a) Garner, P.; Park, J. M. *J. Org. Chem.* **1988**, *53*, 2979−2984. (b) Garner, P.; Park, J. M. *J. Org. Chem.*, **1987**, *52*, 2361−2364. (c) Garner, P.; Park, J. M. *Org. Synth.* **1991**, *70*, 18−28.

TABLE 4. Formation of a Diazepanone by Intramolecular Reductive Amination



entry	conditions A	conditions B (equiv)	yield, %
1	H_2, Pd/C, MeOH		trace
2	H_2, Pd/C, MeOH	$NaBH_3CN$ (2.0), AcOH, EtOAc	25
3	H_2, Pd/C, EtOH	$NaBH_3CN$ (2.0), AcOH, EtOAc	46
4	H_2, Pd/C, EtOH	$NaBH(OAc)_3$ (3.0), AcOH, EtOAc	60
5	H_2, Pd/C, ^{i}PrOH	$NaBH(OAc)_3$ (4.0), AcOH, EtOAc	88

imidazole in DMF to afford the secondary amine derivative **33** (83% overall). The amine **33** was coupled with a commercially available *N*-Cbz-L-threonine **34** (1.5 equiv, 3 equiv of 3-(diethoxyphosphoryloxy)-1,2,3-benzotriazin-4(3*H*)-one (DEPBT),[50] 3 equiv of $NaHCO_3$, THF, 0 °C, 65%) to give the amide **35** without any racemization. As will be mentioned in the synthesis of **43**, other coupling conditions such as EDCI and HOBt gave unsatisfactory results. Protection of the secondary alcohol of **35** with a TBS group (2 equiv of TBSCl, 4 equiv of imidazole, DMF) followed by oxidative cleavage of the terminal olefin by ozonolysis provided the aldehyde **37** (O_3, CH_2Cl_2, −78 °C, 60% overall), a precursor to the cyclization. In a manner similar to previous studies, construction of the diazepanone via deprotection of the Cbz group in **37** followed by reductive amination of the amino aldehyde **39**, both promoted by catalytic hydrogenation of the Cbz and imino groups with Pd/C, was examined in MeOH as the solvent (Table 4, entry 1). However, only a trace amount of the desired diazepanone **38** was obtained. Careful analysis revealed several drawbacks in the reaction, the first one being that formation of a cyclic imine **40**, observed on TLC and isolable, was disfavored at equilibrium with the linear amino aldehyde **39**, indicating the presence of a possible conformational disadvantage in our system. The hemiacetal formation of **39** with MeOH, also observed on TLC (hexane:AcOEt = 5:1), might explain why the equilibrium favored the linear amino aldehyde **39**. The slow reaction rate of the imine reduction by hydrogenation presents another problem as does the removal of the TBS protecting group during the course of the reaction process promoted by catalytic hydrogenation in MeOH.[51] With these drawbacks in mind, we modified the conditions in our system to construct the diazepanone. Namely, each of the above troublesome steps in the intramolecular reductive amination process might be overcome by using hydride reagents after deprotection of the Cbz group on the amino group. Hydride reduction is much more reactive than hydrogenation of imines; moreover, dehydration of **39** would also be accelerated by the use of hydride reagents to give **40**. Decreasing the polarity of the solvent in the catalytic hydrogenation of the Cbz group was also examined to minimize the silyl group deprotection.[52] The use of a bulkier alcohol as solvent also was expected to minimize the formation of the hemiacetal. Hydrogenolysis of the Cbz group of **37** catalyzed by Pd/C in EtOH followed by hydride reduction with $NaBH_3CN$ (2 equiv, AcOH, AcOEt, 46% overall, entry 3) improved the yield of the desired **38**. A better yield was obtained with $NaBH(OAc)_3$ (3 equiv, AcOH, AcOEt, 60% overall, entry 4). However, cleavage of the silyl ether in **38** was still observed in the Cbz-deprotection step when EtOH was used as solvent. The use of the more hydrophobic ^{i}PrOH improved the yield of **38** up to 88% without extensive desilylation.

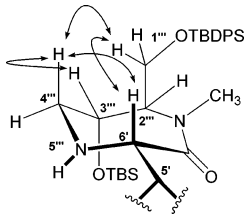


FIGURE 5. Key NOESY peaks for diazepanone **46**.

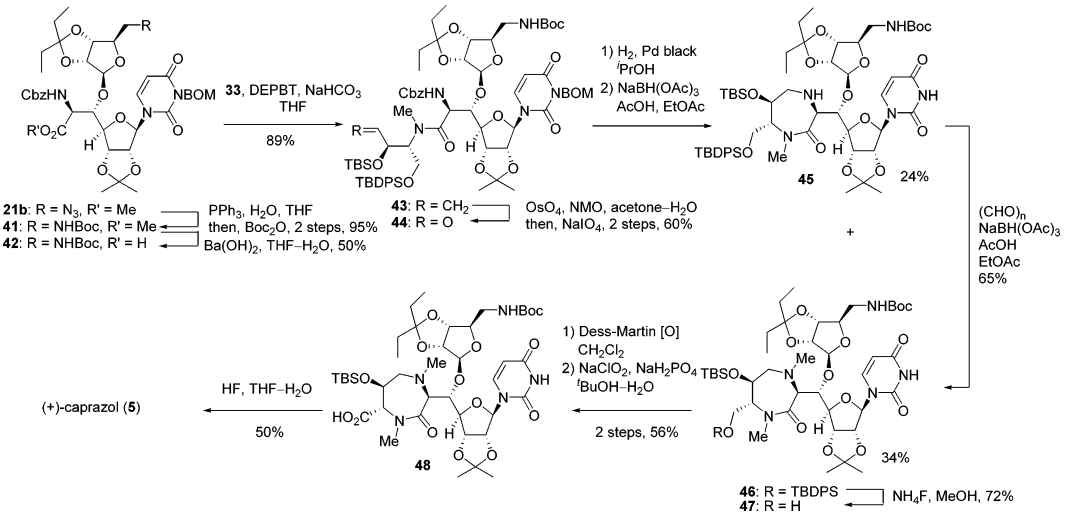
Having established the optimized method for construction of the diazepanone structure in our model system, the total synthesis of caprazol (**5**) was then undertaken (Scheme 3). The azide group in **21b** was reduced by Staudinger's conditions (3 equiv of PPh_3, 5 equiv of H_2O, benzene−THF, 50 °C) to the corresponding amine, which was sequentially protected with a Boc group to give **41** (2 equiv of Boc_2O, 2 equiv of $NaHCO_3$, 95% overall). Saponification of the methyl ester in **41** proved to be troublesome. Extensive efforts to obtain the acid **42** have been conducted for hydrolysis of **41** under other conditions (i.e., LiOH, THF−MeOH−H_2O; NaOH, CH_2Cl_2−H_2O; lipase, aqueous MeCN) and demethylation (PhSH, Cs_2CO_3, DMF), and resulted in decomposition of **41** to give a mixture of products containing an *N*-Boc-5-amino-2,3-*O*-(3-pentylidene)-ribose and a uracil. It was suggested that the acidic 6′-proton was prone to release the aminoribosyloxy group by β-elimination. In addition, the β-elimination would be thermodynamically favored because steric hindrance would be reduced by releasing the sterically encumbered aminoribose moiety installed at the $O^{5'}$-position. Therefore, the desired carboxylic acid **42** was obtained in only 50% yield when **41** was treated with $Ba(OH)_2$ in aqueous THF. Coupling of **42** with the secondary amine **33** with use of DEPBT (4 equiv, 1.5 equiv of **33**, 4 equiv of $NaHCO_3$, THF, 0 °C, 65%) gave the amide **43** without any racemization at the 6′-position. Unsatisfactory results were obtained when other coupling conditions (i.e., EDCI and HOBt, EDCI and HOAt) were used for the preparation of **43**. Under these conditions, starting materials remained unreacted in the reaction mixture, and only a trace amount of **43** was obtained. To convert the terminal olefin of **43** to an aldehyde, ozonolysis was first tried. However, oxidation of the double bond at the uracil moiety was favored. Alternatively, **43** was treated with OsO_4 (0.5 mol %, 2.5 equiv of *N*-methylmorpholine *N*-oxide, acetone−H_2O), and the resulting mixture of the diastereomeric diols was oxidatively cleaved to provide the aldehyde **44** (2.7 equiv of $NaIO_4$, acetone−phosphate buffer (pH 7), 60% overall) to afford the precursor for the cyclization. Then, the optimized reductive amination condition was applied to **44** (H_2, Pd black, ^{i}PrOH, followed by

(50) Jiang, H.; Li, X.; Fan, Y.; Ye, C.; Romoff, T.; Goodman, M. *Org. Lett.* **1999**, *1*, 91−93.

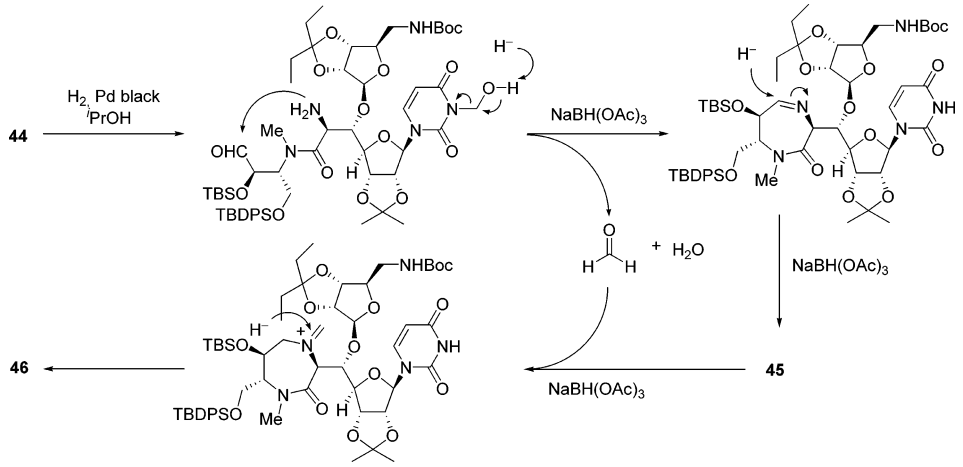
(51) Desilylation during Pd-catalyzed hydrogenation reactions was reported. See: Sajiki, H.; Ikawa, T.; Hattori, K.; Hirota, K. *Chem. Commun.* **2003**, 654−655.

(52) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1988**, *48*, 4155−4156.

SCHEME 3. Total Synthesis of (+)-Caprazol



SCHEME 4. Reaction Mechanism of Formation of 46



4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt), and the desired diazepanone **45** was obtained in 24% yield along with its *N*-methylated derivative **46**, which was the desired product of the next step of the synthesis, in 34% yield. The structure of **46** was confirmed by several NMR measurements including HMBC and HMQC. In the diazepanone moiety, the substituents at the 2‴ and 3‴ positions are placed in the pseudoaxial orientation as determined by NOESY experiments, where correlations were observed between H-6′, H-1‴, and H-4‴ (Figure 5). It was presumed that the methyl source in **46** was formaldehyde arising upon deprotection of the BOM protecting group at the *N*-3 position. Thus, the formaldehyde generated in situ reacted with the newly formed secondary amine of the diazepanone **45** to form the corresponding *exo*-iminium ion, which was further reduced with $NaBH(OAc)_3$ to afford **46** (Scheme 4). Compound **46** could also be prepared from **45** ($(CHO)_n$, 4 equiv of $NaBH(OAc)_3$, AcOH, AcOEt, 65%). At this stage, the remaining steps were functional group manipulations and deprotections. Treatment of **46** with NH_4F (20 equiv, MeOH, 60%) resulted in selective deprotection of the TBDPS protecting group at the primary hydroxyl to give **47**, which was transformed to the carboxylic acid **48** by a two-step sequence with Dess−Martin periodinane[52] (3.4 equiv, CH_2Cl_2) and $NaClO_2$ oxidation[53] (3.5 equiv, 1 equiv of $NaH_2PO_4 \cdot 2H_2O$, 4.5 equiv of 2-methyl-2-butene, $^tBuOH-H_2O$, 56% overall). Oxidation of the tertiary amine in the diazepanone was a side reaction that reduced the chemical yield of **48**. Finally, a global deprotection of **48** (40% aqueous HF, MeCN, 50%) provided (+)-(**5**), $[\alpha]^{25}_D$ +23.8 (*c* 0.24, DMSO) [lit.[1b] $[\alpha]^{19}_D$ +28 (*c* 0.5, DMSO)], the properties of which were identical in all respects with those reported for the natural material.[1b]

Conclusion. In summary, we have described the total synthesis of (+)-caprazol. The key elements of the approach include the early stage introduction of the aminoribose in a highly β-selective manner, using steric hindrance in the transition state and construction of the diazepanone by a modified intramolecular reductive amination. For the ribosylation, it was revealed that increasing the size of the alkyl substituents of the acetal unit resulted in severe steric repulsion on the α-face of the riboside and led to an unusual outside attack to provide β-ribosides with a complete reversal of stereoselectivity. This method can be considered as an alternative for the construction of β-ribosides without neighboring group participation. Construction of the diazepanone structure was optimized and the reductive amination with a hydride reagent proved to be effective.

(53) Andres, J. M.; Elena, N. D.; Pedrosa, R. *Tetrahedron* **2000**, *56*, 1523−1531.

Experimental Section

Methyl (*E*)-1-(3-Benzyloxymethyluracil-1-yl)-5,6-dideoxy-2,3-*O*-isopropylidene-β-D-*ribo*-5-ene-heptofuranuronate (8). A solution of 2′,3′-*O*-isopropylideneuridine (10.0 g, 41.0 mmol) and IBX (28.6 g, 103 mmol) in MeCN (400 mL) was heated at 80 °C for 1 h. The reaction mixture was cooled in an ice bath, then the white precipitates were filtered off. The filtrate was concentrated in vacuo. The residue in CH_2Cl_2 (400 mL) was cooled to −20 °C, to which a solution of $Ph_3P{=}CHCO_2Me$ (16.4 g, 49.2 mmol) in CH_2Cl_2 (100 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 in CH_2Cl_2 (300 mL) was treated with BOMCl (8.5 mL, 61.5 mmol), Bu_4NI (756 mg, 2.05 mmol), and Na_2CO_3 (17.4 g, 164 mmol) in H_2O (200 mL). The resulting biphasic layers were vigorously stirred at room temperature for 12 h. The organic phase 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 (15 × 20 cm, 25−45% AcOEt−hexane) to afford **8** (12.4 g, 66%) as a colorless syrup: $[\alpha]^{22}_D$ +52.0 (*c* 1.66, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32 (m, 5H, phenyl), 7.13 (d, 1H, H-6, $J_{6,5}$ = 8.1 Hz), 7.02 (dd, 1H, H-5′, $J_{5',6'}$ = 15.6 Hz, $J_{5',4'}$ = 5.6 Hz), 6.04 (dd, 1H, H-6′, $J_{6',5'}$ = 15.6 Hz, $J_{6',4'}$ = 1.5 Hz), 5.76 (d, 1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.57 (d, 1H, H-1′, $J_{1',2'}$ = 1.3 Hz), 5.48 (d, 1H, NCH_2-OBn, *J* = 9.8 Hz), 5.43 (d, 1H, NCH_2OBn, *J* = 9.8 Hz), 5.04 (dd, 1H, H-2′, $J_{2',1'}$ = 1.3 Hz, $J_{2',3'}$ = 6.4 Hz), 4.87 (dd, 1H, H-3′, $J_{3',2'}$ = 6.4 Hz, $J_{3',4'}$ = 1.1 Hz), 4.70 (s, 2H, NCH_2OCH_2Ph), 4.66 (ddd, 1H, H-4′, $J_{4',3'}$ = 1.1 Hz, $J_{4',5'}$ = 5.6 Hz, $J_{4',6'}$ = 1.5 Hz), 3.70 (s, 3H, COCH_3), 1.58 (s, 3H, acetonide), 1.36 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.1, 162.4, 150.6, 143.7, 141.1, 137.9, 128.3, 127.7, 127.6, 122.3, 114.7, 102.4, 96.0, 86.9, 84.6, 84.0, 72.3, 70.3, 51.7, 27.1, 25.3; FABMS-HR (NBA) calcd for $C_{23}H_{27}N_2O_8$ 459.1767, found 459.1756.

Methyl 6-Benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-6-deoxy-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronate (9) and Methyl 6-Benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-6-deoxy-2,3-*O*-isopropylidene-α-L-*glycero*-D-*allo*-heptofuranuronate (10). *tert*-Butyl hypochlorite (1.13 mL, 10.0 mmol) was added to a solution of benzyl carbamate (1.49 g, 9.87 mmol) in aqueous NaOH (0.6 M, 14 mL) and *n*-PrOH (16.5 mL) at 15 °C, and the mixture was stirred for 15 min, then allowed to reach room temperature. A solution of $[DHQD]_2AQN$ (422 mg, 0.49 mmol) in PrOH (8.3 mL), a solution of **8** (1.50 g, 3.28 mmol) in PrOH (8.3 mL), and a solution of $K_2OsO_2(OH)_4$ (180 mg, 0.498 mmol) were sequentially added to the mixture. The resulting mixture was stirred at room temperature for 2 h. After addition of saturated aqueous $Na_2S_2O_3$ (100 mL), 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 (6 × 15 cm, 40−45% AcOEt−hexane) to afford **9** (1.08 g, 52%) as a white foam and **10** (175 mg, 9%) as a white foam. Data for **9**; $[\alpha]^{22}_D$ +34.4 (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33−7.24 (m, 10H, phenyl), 7.15 (d, 1H, H-6, $J_{6,5}$ = 8.1 Hz), 5.72 (d, 1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.59 (br s, 1H, NH), 5.46−5.41 (m, 3H, NCH_2OBn, H-1′), 5.12 (d, 1H, CO_2CH_2Ph, *J* = 11.1 Hz), 5.06 (d, 1H, CO_2CH_2Ph, *J* = 11.1 Hz), 4.95 (m, 2H, H-2′, H-3′), 4.68 (m, 2H, NCH_2OCH_2Ph), 4.53 (m, 1H, H-6′), 4.26 (m, 2H, H-4′, H-5′), 3.72 (s, 3H, COCH_3), 3.72 (br s, 1H, OH), 1.54 (s, 3H, acetonide), 1.34 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.7, 162.2, 141.6, 151.2, 141.6, 137.7, 136.1, 128.5, 128.3, 128.2, 128.1, 127.8, 127.6, 114.8, 102.5, 97.0, 86.2, 82.8, 81.4, 72.4, 71.5, 70.4, 67.5, 56.5, 52.7, 27.2, 25.3, 12.0; FABMS-LR *m*/*z* 626 (MH^+); FABMS-HR (NBA) calcd for $C_{31}H_{36}N_3O_{11}$ 626.2356, found 626.2340. Data for **10**: $[\alpha]^{22}_D$ +24.9 (*c* 1.74, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.25 (m, 10H, phenyl), 7.12 (d, 1H, H-6, $J_{6,5}$ = 7.7 Hz), 5.74 (d, 1H, H-5, $J_{5,6}$ = 7.7 Hz), 5.58 (d, 1H, NH, $J_{NH,6'}$ = 8.6 Hz), 5.47 (d, 1H, NCH_2-OBn, *J* = 9.9 Hz), 5.40 (d, 1H, NCH_2OBn, *J* = 9.9 Hz), 5.35 (s, 1H, H-1′), 5.13 (m, 3H, H-3′, CO_2CH_2Ph), 5.08 (dd, 1H, H-2′, $J_{2',1'}$ = 1.6 Hz, $J_{2',3'}$ = 6.7 Hz), 4.66 (m, 2H, NCH_2OCH_2Ph), 4.58 (d, 1H, H-4′, $J_{4',5'}$ = 9.2 Hz), 4.42 (m, 1H, H-5′), 4.15 (m, 1H, H-6′), 3.71 (s, 3H, COCH_3), 3.26 (br s, 1H, OH), 1.53 (s, 3H, acetonide), 1.31 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 162.3, 157.0, 151.0, 142.2, 137.7, 136.2, 128.5, 128.3, 128.2, 128.0, 127.8, 127.6, 114.3, 102.3, 97.8, 87.8, 84.0, 81.2, 72.4, 71.5, 70.4, 67.2, 55.6, 52.7, 27.1, 25.1, 11.4; FABMS-HR (NBA) calcd for $C_{31}H_{36}N_3O_{11}$ 626.2350, found 626.2368.

Methyl 5-*O*-[5-Azido-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-ribofuranosyl]-6-benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-6-deoxy-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronate (21b) and Methyl 5-*O*-[5-Azido-5-deoxy-2,3-*O*-(3-pentylidene)-α-D-ribofuranosyl]-6-benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-6-deoxy-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronate (22b). A mixture of **9** (20.0 mg, 0.032 mmol), **16** (11.8 mg, 0.048 mmol), and MS4A (100 mg) in CH_2Cl_2 (1 mL) was stirred at −30 °C for 15 min. $BF_3{\cdot}OEt_2$ (1.2 μL, 0.01 mmol) was added five times at 1 h intervals. The reaction mixture was stirred for 5 h in total. Saturated aqueous $NaHCO_3$ (5 mL) 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 (6 × 15 cm, 33% AcOEt−hexane) to afford **21b** (20.9 mg, 77%) and **22b** (0.8 mg, 3%) each as a white foam. Data for **21b**: $[\alpha]^{22}_D$ +20.2 (*c* 1.36, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.28 (m, 11H, phenyl, H-6), 5.79 (d, 1H, NH, $J_{NH,6'}$ = 9.7 Hz), 5.71 (d, 1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.61 (s, 1H, H-1′), 5.48 (d, 1H, NCH_2OBn, *J* = 9.7 Hz), 5.43 (d, 1H, NCH_2-OBn, *J* = 9.7 Hz), 5.22 (d, 1H, CO_2CH_2Ph, *J* = 12.1 Hz), 5.12 (s, 1H, H-1″), 5.05 (d, 1H, CO_2CH_2Ph, *J* = 12.1 Hz), 4.81 (m, 2H, H-2′, H-3′), 4.70 (s, 2H, NCH_2OCH_2Ph), 4.65 (d, 1H, H-6′, $J_{6',NH}$ = 9.7 Hz), 4.56 (m, 2H, H-2″, H-3″), 4.46 (d, 1H, H-5′, $J_{5',4'}$ = 7.0 Hz), 4.22 (m, 2H, H-4′, H-4″), 3.74 (s, 3H, COCH_3), 3.38 (dd, 1H, H-5″a, $J_{5''a,5''b}$ = 12.7 Hz, $J_{5''a,4''}$ = 5.6 Hz), 3.32 (dd, 1H, H-5″b, $J_{5''b,5''a}$ = 12.7 Hz, $J_{5''b,4''}$ = 7.9 Hz), 1.59 (m, 2H, CH_2CH$_3$), 1.48 (m, 5H, CH_2CH$_3$, acetonide), 1.32 (s, 3H, acetonide), 0.83 (m, 6H, CH$_2$CH_3 × 2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5, 162.4, 156.3, 150.9, 140.7, 137.9, 136.3, 128.5, 128.3, 128.2, 127.7, 117.3, 114.9, 113.4, 102.2, 94.6, 86.8, 86.0, 85.4, 83.9, 81.9, 80.8, 78.8, 72.4, 70.4, 67.2, 54.6, 53.2, 52.8, 29.3, 28.9, 27.1, 25.4, 8.4, 7.4; FABMS-HR (NBA) calcd for $C_{41}H_{51}N_6O_{14}$ 851.3463, found 851.3447. Data for **22b**: $[\alpha]^{22}_D$ +14.9 (*c* 1.13, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.66 (d, 1H, H-6, $J_{6,5}$ = 7.9 Hz), 7.37−7.24 (m, 10H, phenyl), 5.97 (s, 1H, H-1′), 5.87 (d, 1H, NH, $J_{NH,6'}$ = 8.0 Hz), 5.73 (d, 1H, H-5, $J_{5,6}$ = 7.9 Hz), 5.48 (d, 1H, NCH_2OBn, *J* = 9.7 Hz), 5.44 (d, 1H,NCH_2OBn, *J* = 9.7 Hz), 5.17 (d, 1H, CO_2CH_2Ph, *J* = 12.3 Hz), 5.14 (br s, 1H, H-1″), 5.07 (d, 1H, CO_2CH_2Ph, *J* = 12.3 Hz), 4.87 (dd, 1H, H-3′, $J_{3',2'}$ = 6.2 Hz, $J_{3',4'}$ = 3.7 Hz), 4.70 (s, 2H, NCH_2OCH_2Ph), 4.63 (d, 1H, H-6′, $J_{6',NH}$ = 8.0 Hz), 4.59 (m, 2H, H-2′, H-2″), 4.53 (dd, 1H, H-3″, $J_{3'',2''}$ = 6.8 Hz, $J_{3'',4''}$ = 3.0 Hz), 4.44 (m, 1H, H-4′), 4.32 (m, 1H, H-5′), 4.22 (m, 1H, H-4″), 3.73 (s, 3H, COCH_3), 3.46 (m, 1H, H-5″a), 3.35 (m, 1H, H-5″b), 1.56 (s, 3H, acetonide), 1.49 (s, 3H, acetonide), 1.33 (s, 3H, acetonide), 1.32 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.7, 162.5, 156.0, 150.9, 139.9, 137.9, 136.2, 128.5, 128.3, 128.2, 128.0, 127.7, 127.6, 115.5, 114.7, 103.2, 102.4, 91.6, 84.8, 83.6, 80.9, 80.8, 80.6, 80.2, 78.0, 77.3, 72.3, 70.4, 67.2, 54.6, 52.8, 52.5, 29.7, 27.2, 26.2, 25.4, 25.3; FABMS-HR (NBA) calcd for $C_{39}H_{47}N_6O_{14}$ 823.3150, found 823.3167.

Methyl 5-*O*-[5-*tert*-Butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-ribofuranosyl]-6-deoxy-6-benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronate (41). A solution of **21b** (712 mg, 0.839 mmol) and Ph_3P (660 mg, 2.52 mmol) in benzene−THF (1:1, 8 mL) and H_2O (755 μL, 41.1 mmol) was heated at 50 °C for 12 h. The reaction mixture was allowed to warm to room temperature, to which $(Boc)_2O$ (389 μL, 1.68 mmol) and $NaHCO_3$ (141 mg, 1.68 mmol) were added. The resulting mixture was stirred at room temperature for 1 h and partitioned between AcOEt and H_2O. 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 (5 × 20 cm, 37−40% AcOEt−hexane) to afford **41** (736 mg, 95% in 2 steps) as a white foam: $[\alpha]^{23}_D$ +31.2 (*c* 0.63, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.27 (m, 10H, phenyl), 7.22 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.73 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.56 (d, 1H, NC*H*$_2$OBn, *J* = 9.8 Hz), 5.18 (m, 1H, NH), 5.12 (d, 1H, CO_2CH_2Ph, *J* = 12.3 Hz), 5.06 (s, 1H, H-1″), 5.02 (d, 1H, CO_2CH_2Ph, *J* = 12.3 Hz), 4.97 (d, 1H, H-2′, $J_{2',3'}$ = 6.3 Hz), 4.84 (dd, 1H, H-3′, $J_{3',2'}$ = 6.3 Hz, $J_{3',4'}$ = 4.4 Hz), 4.70 (s, 2H, NCH_2OCH_2Ph), 4.67 (m, 1H, H-6′), 4.52 (m, 2H, H-2″, H-3″), 4.42 (d, 1H, H-5′, $J_{5',4'}$ = 8.2 Hz), 4.21 (m, 2H, H-4′, H-4″), 3.77 (s, 3H, $COCH_3$), 3.20 (m, 1H, H-5″a), 3.07 (m, 1H, H-5″b), 1.57−1.44 (m, 4H, CH_2CH_3 × 2), 1.48 (s, 3H, acetonide), 1.41 (s, 9H, *tert*-butyl), 1.33 (s, 3H, acetonide), 0.79−0.73 (m, 6H, CH_2CH_3 × 2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.1, 162.4, 156.1, 156.0, 150.8, 141.4, 137.8, 136.1, 128.4, 128.3, 128.2, 127.7, 116.5, 114.7, 112.5, 102.2, 96.1, 87.0, 86.2, 84.1, 82.0, 81.1, 79.8, 79.3, 72.3, 70.3, 67.2, 54.9, 53.0, 43.3, 29.3, 28.8, 28.3, 27.0, 25.3, 8.3, 7.2; FABMS-HR (NBA) calcd for $C_{46}H_{61}N_4O_{16}$ 925.4083, found 925.4064.

***N*-[(1*R*,2*S*)-2-*tert*-Butyldimethylsiloxy-1-*tert*-butyldiphenylsiloxymethyl-3-butenyl]-*N*-methyl-6-benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronamide (43).** A mixture of barium hydroxide octahydrates (260 mg, 0.824 mmol) and **41** (558 mg, 0.60 mmol) in THF−H_2O (4:1, 10 mL) was stirred at room temperature for 10 h. The reaction mixture was poured onto 1 M aqueous HCl and extracted with $CHCl_3$. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a silica gel column (5 × 13 cm, 33% MeOH−$CHCl_3$) to afford crude **33** (319 mg, ca. 0.35 mmol, 50%) as a colorless foam. A solution of the crude **42** and **33** (254 mg, 0.527 mmol) in THF (3.5 mL) was treated sequentially with $NaHCO_3$ (118 mg, 1.40 mmol) and DEPBT (420 mg, 1.40 mmol) at 0 °C for 1 h, then the mixture was allowed to reach room temperature and stirred for an additional 28 h. The reaction mixture was partitioned between AcOEt and saturated aqueous $NaHCO_3$. The organic phase was washed with 1 M aqueous HCl and saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by a flash silica gel column (8 × 10 cm, 17−33% AcOEt−hexane) to afford **43** (315 mg, 65%) as a white foam: $[\alpha]^{23}_D$ −9.78 (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz, 3:1 mixture of the rotamers) δ 7.69−7.56 (m, 5.2H, phenyl), 7.45−7.23 (m, 22.1H, phenyl, H-6), 6.22 (m, 0.3H), 5.98 (m, 1.0H), 5.92−5.80 (m, 3.0H), 5.48−5.44 (m, 2.0H, CO_2CH_2Ph), 5.38 (d, 1.0H, CO_2CH_2Ph, *J* = 9.6 Hz), 5.28 (m, 0.6H), 5.18−5.09 (m, 3.6H), 5.05−4.98 (m, 3.9H), 4.82−4.76 (m, 1.9H), 4.71−4.68 (m, 4.0H), 4.51 (m, 1.8H), 4.23 (m, 1.0H), 4.32−4.22 (m, 4.0H), 4.16−4.09 (m, 2.6H), 4.09−3.90 (m, 2.7H), 3.62 (t, 0.3H, *J* = 10.2 Hz), 3.28 (m, 1.3H), 3.10 (m, 4.0H), 2.79 (s, 0.9H, include $CONCH_3$), 1.71−1.42 (m, 20.8H, *tert*-butyl, acetonide, CH_2CH_3), 1.30 (s, 3H, acetonide), 1.29 (s, 3H, acetonide), 1.03 (s, 9H, *tert*-butyl), 0.98 (s, 3H, *tert*-butyl), 0.82 (m, 7.8H, CH_2CH_3), 0.73 (s, 9H, *tert*-butyl), 0.72 (s, 3H, *tert*-butyl), −0.12 (m, 3.9H, $SiCH_3$), −0.15 (m, 3.9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 170.5, 162.4, 162.3, 156.2, 156.2, 151.0, 150.9, 139.9, 139.7, 138.7, 138.1, 137.9, 136.2, 135.7, 135.5, 135.4, 136.2, 133.1, 132.7, 132.6, 129.9, 129.8, 129.7, 129.6, 128.5, 128.4, 128.4, 128.3, 127.8, 127.7, 127.6, 117.5, 117.1, 116.7, 116.3, 115.2, 114.8, 112.0, 110.1, 102.6, 102.4, 92.7, 86.7, 86.2, 85.8, 84.8, 84.0, 83.5, 82.0, 81.8, 80.6, 79.2, 78.9, 78.3, 73.3, 73.0, 72.2, 70.5, 70.3, 67.1, 63.2, 60.8, 60.5, 50.9, 43.4, 43.2, 29.7, 29.5, 29.3, 29.0, 28.4, 27.2, 27.2, 26.9, 26.7, 25.7, 25.6, 25.5, 25.3, 19.0, 18.8, 17.8, 17.8, 8.3, 7.5, 7.4, −4.0, −4.2, −5.2, −5.3; FABMS-HR (NBA) calcd for $C_{73}H_{102}N_5O_{17}Si_2$ 1376.6807, found 1376.6800.

***N*-[(1*R*,2*S*)-2-*tert*-Butyldimethylsiloxy-1-*tert*-butyldiphenylsiloxymethyl-3-oxopropyl]-*N*-methyl-6-benzyloxycarbonylamino-1-(3-benzyloxymethyluracil-1-yl)-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-ribofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-β-D-*glycero*-L-*talo*-heptofuranuronamide (44).** A solution of **43** (310 mg, 0.23 mmol) and NMO (121 mg, 0.56 mmol) in acetone−H_2O (4:1, 2.5 mL) was treated with OsO_4 (5.0 mg/mL *t*-BuOH solution, 500 μL), and the resulting reaction mixture was stirred at room temperature for 24 h. After addition of saturated aqueous $Na_2S_2O_3$ (10 mL), 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 short silica gel column (3 × 5 cm, 33% AcOEt−hexane, then 2% MeOH, 50% AcOEt−hexane), and fractions containing the diol were combined and concentrated in vacuo. A solution of the diol in acetone−phosphate buffer (4:1, pH 7.5, 3 mL) was treated with $NaIO_4$ (123 mg, 0.61 mmol) at room temperature for 12 h. After addition of saturated aqueous $Na_2S_2O_3$ (10 mL), 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 (3 × 10 cm, 3% acetone−$CHCl_3$) to afford **44** (189 mg, 60%) as a white foam: $[\alpha]^{21}_D$ −19.8 (*c* 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz, 4:1 mixture of rotamers) δ 9.70 (s, 0.3H, H-1‴), 9.56 (s, 1.0H, H-1‴), 7.64−7.59 (m, 5.0H, phenyl), 7.42−7.20 (m, 21.3H), 6.07 (br s, 1.0H), 5.89 (br s, 0.3H, H-1′), 5.76 (m, 1.3H), 5.68−5.66 (m, 1.9H), 5.48 (d, 0.3H, NC*H*$_2$OBn, *J* = 9.7 Hz), 5.44 (d, 0.3H, NC*H*$_2$OBn, *J* = 9.7 Hz), 5.37 (d, 1.0H, NC*H*$_2$OBn, *J* = 9.6 Hz), 5.28 (d, 1.0H, NC*H*$_2$OBn, *J* = 9.6 Hz), 5.19 (m, 1.3H), 5.12 (m, 0.3H), 4.96−4.92 (m, 2.5H), 4.90−4.75 (m, 2.2H), 4.70−4.35 (m, 7.6H), 4.32−4.18 (m, 2.0H), 4.14−4.08 (m, 2.3H), 4.01−3.98 (m, 1.3H), 3.85 (m, 1.0H), 3.67 (m, 0.3H), 3.25−3.16 (m, 1.3H), 3.10 (m, 4.0H, $CONCH_3$), 2.86 (s, 0.7H, $CONCH_3$), 1.60−1.40 (m, 20H), 1.31 (m, 5.0H), 1.00 (s, 9H, *tert*-butyl), 0.98 (s, 3.0H), 0.93 (s, 3.0H), 0.87 (s, 9.0H, *tert*-butyl), 0.85−0.78 (m, 8H), 0.10 (s, 0.7H, $SiCH_3$), 0.07 (s, 0.7H, $SiCH_3$), 0.03 (s, 3.0H, $SiCH_3$), −0.05 (s, 3.0H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 199.9, 162.3, 156.2, 150.9, 140.7, 137.8, 136.2, 135.5, 135.4, 132.7, 132.5, 129.8, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 127.6, 116.7, 114.6, 112.7, 102.4, 86.8, 85.9, 84.3, 82.0, 80.8, 79.7, 79.1, 72.2, 70.4, 70.1, 67.2, 60.0, 51.5, 43.2, 29.3, 28.8, 28.4, 27.2, 27.1, 26.6, 26.5, 25.8, 25.7, 25.3, 19.0, 18.0, 17.9, 8.4, 7.3, 7.2, −4.2, −4.6, −5.3, −5.4; FABMS-HR (NBA) calcd for $C_{72}H_{100}N_5O_{18}Si_2$ 1378.6602, found 1378.6580.

Diazepanone (45) and *N*-Methyldiazepanone (46). A mixture of **44** (78.3 mg, 0.054 mmol) and Pd black (150 mg) in *i*-PrOH (10 mL) was vigorously stirred under H_2 atmosphere at room temperature for 12 h. The catalyst was filtered off through a Celite pad, and the filtrate was concentrated in vacuo. The residue in AcOEt (4 mL) was treated with AcOH (40 μL) and $NaBH(OAc)_3$ (45.4 mg, 0.22 mmol), and the reaction mixture was stirred at room temperature for 12 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 neutral silica gel column (1.5 × 13 cm, 33−50% AcOEt−hexane) to afford **45** (eluted with 40% AcOEt−hexane, 20.0 mg, 34% in 2 steps) and **46** (eluted with 50% AcOEt−hexane, 14.4 mg, 24% in 2 steps) each as a white solid. Data for **45**; $[\alpha]^{21}_D$ +19.8 (*c* 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.71 (br s, 1H, H-3), 7.67−7.38 (m, 10H, phenyl), 7.21 (d, 1H, H-6, $J_{6,5}$ = 8.3 Hz), 6.22 (m, 1H,

N*H*Boc), 5.65 (d, 1H, H-5, $J_{5,6}$ = 8.3 Hz), 5.45 (s, 1H, H-1′), 5.33 (s, 1H, H-1″), 4.84 (d, 1H, H-2′, $J_{2',3'}$ = 6.1 Hz), 4.63 (d, 1H, H-2″, $J_{2'',3''}$ = 5.9 Hz), 4.54 (dd, 1H, H-3′, $J_{3',2'}$ = 6.1 Hz, $J_{3',4'}$ = 6.1 Hz), 4.49 (d, 1H, H-5′, $J_{5',4'}$ = 7.7 Hz), 4.44 (d, 1H, H-3″, $J_{3'',2''}$ = 5.9 Hz), 4.25 (dd, 1H, H-4″, $J_{4'',5''a}$ = 8.9 Hz, $J_{4'',5''b}$ = 5.2 Hz), 4.23 (dd, 1H, H-4′, $J_{4',3}$ = 6.1, $J_{4',5'}$ = 7.7 Hz), 3.95 (m, 1H, H-6‴), 3.80 (m, 2H, H-8‴a, H-8‴b), 3.49 (m, 1H, H-7‴, H-5″a), 3.15 (s, 1H, H-3‴), 3.09 (s, 3H, CONCH_3), 2.98 (dd, 1H, H-5‴a, $J_{5'''a,5'''b}$ = 14.7, $J_{5'''a,6'''}$ = 3.2 Hz), 2.77 (d, 1H, H-5‴b, $J_{5'''b,'''a}$ = 14.7 Hz), 2.72 (m, 1H, H-5″b), 1.59 (m, 2H, CH_2CH_3), 1.45 (m, 2H, CH_2-CH_3), 1.40 (s, 9H, *tert*-butyl), 1.26 (s, 3H, acetonide), 1.23 (s, 3H, acetonide), 1.05 (s, 9H, *tert*-butyl), 0.86 (s, 9H, *tert*-butyl), 0.81 (m, 6H, CH_2CH_3 × 2), 0.09 (s, 3H, $SiCH_3$), 0.05 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.3, 162.3, 156.1, 149.3, 142.4, 135.5, 135.4, 132.8, 132.7, 130.1, 130.1, 128.0, 128.0, 116.3, 114.8, 110.5, 102.3, 93.8, 87.0, 86.6, 86.4, 84.2, 82.1, 80.1, 80.3, 78.4, 68.5, 66.8, 62.6, 59.9, 50.7, 43.7, 40.3, 29.8, 29.0, 28.5, 27.3, 26.7, 25.7, 25.6, 19.1, 17.8, 8.3, 7.3, −4.8, −4.9; FABMS-LR *m*/*z* 1108 (MH^+) FABMS-HR (NBA) calcd for $C_{56}H_{86}N_5O_{14}Si_2$ 1108.5711, found 1108.5700. Data for **46**: $[\alpha]^{21}_D$ −17.6 (*c* 0.67, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.06 (br s, 1H, H-3), 7.66−7.30 (m, 11H, phenyl, H-6), 6.67 (m, 1H, N*H*Boc), 5.59 (m, 2H, H-5, H-1′), 5.26 (s, 1H, H-1″), 4.68 (m, 2H, H-2′, H-3′), 4.56 (m, 2H, H-2″, H-3″), 4.33 (d, 1H, H-5′, $J_{5',6'}$ = 7.3 Hz), 4.24−4.14 (m, 2H, H-4′, H-4″), 4.01 (m, 1H, H-6‴), 3.92 (dd, 1H, H-8‴a, $J_{8'''a,8'''b}$ = 10.4, $J_{8'''a,7'''}$ = 7.5 Hz), 3.86 (dd, 1H, H-8‴b, $J_{8'''b,8'''a}$ = 10.4 Hz, $J_{8'''b,7'''}$ = 6.9 Hz), 3.52−3.48 (m, 2H, H-7‴, H-3‴), 3.20 (m, 1H, H-5″a), 3.12 (m, 1H, H-5″b), 3.07 (d, 1H, H-5‴a, $J_{5'''a,5'''b}$ = 14.6 Hz), 2.98 (s, 3H, CONCH_3), 2.87 (d, 1H, H-5‴b, $J_{5'''b,5'''a}$ = 14.6 Hz), 2.41 (s, 3H, NCH_3), 1.62 (m, 2H, CH_2CH$_3$), 1.52 (m, 2H, CH_2-CH_3), 1.48 (s, 3H, acetonide), 1.35 (s, 9H, *tert*-butyl), 1.26 (s, 3H, acetonide), 0.99 (s, 9H, *tert*-butyl), 0.88 (s, 9H, *tert*-butyl), 0.86−0.79 (m, 6H, CH_2CH_3 × 2), 0.07 (s, 3H, $SiCH_3$), 0.06 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.3, 162.4, 156.4, 149.3, 139.9, 135.3, 135.3, 132.8, 132.6, 130.2, 127.9, 116.8, 114.8, 112.1, 102.4, 89.8, 87.4, 86.7, 85.9, 84.3, 82.7, 79.6, 78.9, 75.8, 69.3, 63.8, 63.2, 59.7, 43.2, 39.0, 37.7, 29.7, 29.4, 28.0, 28.6, 27.3, 26.7, 25.7, 25.6, 19.0, 17.8, 8.4, 7.5, −4.9, −5.0; FABMS-HR (NBA) calcd for $C_{57}H_{88}N_5O_{14}Si_2$ 1122.5866, found 1122.5820.

Alcohol (47). A solution of **46** (10.0 mg, 7.8 mmol) in MeOH (1 mL) was treated with NH_4F (50 mg) at room temperature for 48 h. The mixture was diluted with AcOEt, and the insoluble materials were filtered off. The filtrate was concentrated in vacuo, and the residue was purified by preparative TLC (33% AcOEt−hexane) to afford **47** (5.7 mg, 72%) as a white solid: $[\alpha]^{21}_D$ −17.6 (*c* 0.67, $CHCl_3$); ^{1}H NMR (CD_3CN, 500 MHz, 10:1 mixtures of the conformers) δ 9.00 (br s, 1.0 H, N*H*-3), 7.56 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 6.82 (br s, 1H, N*H*Boc), 5.81 (s, 1H, H-1′), 5.64 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.27 (s, 1H, H-1″), 4.80 (m, 2H, H-2′, H-3′), 4.59 (m, 2H, H-2″, H-3″), 4.34 (m, 1H, H-5′), 4.26 (m, 2H, H-4′, H-4″), 4.00 (m, 1H, H-6″), 3.69 (m, 3H, H-3‴, H-8‴a, H-8‴b), 3.42 (m ,1H, H-7‴), 3.18 (m, 3H, H-5″a, H-5″b, H-5‴a), 3.04 (s, 3H, CONCH_3), 3.02 (br s, 1H, OH), 2.83 (m, 1H, H-5‴b), 2.41 (s, 3H, NCH_3), 1.63 (m, 2H, CH_2CH$_3$), 1.52 (m, 5H, CH_2-CH_3, acetonide), 1.39 (s, 9H, *tert*-butyl), 1.31 (s, 3H, acetonide), 0.89 (s, 9H, *tert*-butyl), 0.83 (m, 6H, CH_2CH_3 × 2), 0.09 (s, 6H, $SiCH_3$ × 2); ^{13}C NMR (CD_3CN, 125 MHz) δ 163.7, 157.2, 151.1, 142.0, 142.0, 117.1, 115.2, 113.0, 103.1, 90.9, 87.8, 87.5, 87.0, 84.9, 83.2, 80.8, 79.2, 77.8, 70.9, 70.3, 63.8, 62.1, 60.5, 43.9, 38.3, 30.1, 29.6, 28.7, 27.5, 26.1, 25.6, 18.4, 14.3, 11.3, 8.7, 7.7, −4.7, −4.9; FABMS-HR (NBA) calcd for $C_{41}H_{70}N_5O_{14}Si$ 884.4689, found 884.4678.

Carboxylic Acid (48). A solution of **47** (6.5 mg, 7.8 mmol) in CH_2Cl_2 (0.5 mL) was treated with Dess−Martin periodinane (11.4 mg, 26.5 mmol) at 0 °C for 40 min. Saturated aqueous $NaHCO_3$−saturated aqueous $Na_2S_2O_3$ (2:1, 2 mL), and AcOEt (2 mL) were added to the mixture, and the resulting biphasic layers were vigorously stirred at room temperature for 10 min. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was dissolved in *t*-BuOH−H_2O (3:1, 0.5 mL) and treated sequentially with 2-methyl-2-butene (3.7 μL, 35.1 mmol), NaH_2PO_4·$2H_2O$ (1.2 mg, 7.8 mmol), and $NaClO_2$ (3.1 mg, 27.3 mmol). The resulting reaction mixture was stirred at room temperature for 10 min. After addition of phosphate buffer (pH 7.5, 2 mL), the mixture was extracted with $CHCl_3$. The organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by preparative TLC (17% MeOH−$CHCl_3$) to afford **48** (3.9 mg, 56% in 2 steps) as a white solid: $[\alpha]^{21}_D$ −27.5 (*c* 0.39, $CHCl_3$); ^{1}H NMR (CD_3CN, 500 MHz) δ 9.50−9.23 (br s, 1H, CO_2H), 7.65 (d, 1H, H-6, $J_{6,5}$ = 6.5 Hz), 6.52 (br s, 1H, N*H*Boc), 5.80 (s, 1H, H-1′), 5.65 (d, 1H, H-5, $J_{5,6}$ = 6.5 Hz), 5.25 (s, 1H, H-1″), 4.78 (m, 2H), 4.55 (m, 2H), 4.40 (m, 1H), 4.36 (m, 1H), 4.29 (m, 1H), 4.16 (m, 1H), 3.57 (m, 1H), 3.28−3.26 (m, 2H), 3.11 (m, 1H), 3.06 (s, 3H, CONCH_3), 2.94 (m, 2H), 2.44 (s, 3H, NCH_3), 1.60 (m, 2H, CH_2CH$_3$), 1.52 (m, 5H, CH_2CH$_3$, acetonide), 1.36 (s, 9H, *tert*-butyl), 0.89 (s, 9H, *tert*-butyl), 0.83 (m, 6H, CH_2CH_3 × 2), 0.11 (s, 6H, $SiCH_3$ × 2); ^{13}C NMR (CD_3-OD, 100 MHz) δ 173.6, 166.1, 158.4, 151.8, 144.0, 143.9, 117.5, 115.8, 112.7, 102.6, 92.2, 88.3, 87.9, 86.7, 85.3, 83.7, 81.9, 81.6, 80.4, 71.4, 71.2, 64.2, 61.2, 44.3, 39.6, 38.9, 30.8, 30.5, 30.0, 29.0, 27.7, 27.6, 26.4, 25.8, 18.8, 8.8, 7.9, −4.8, −4.9; FABMS-HR (NBA) calcd for $C_{41}H_{68}N_5O_{15}Si$ 898.4481, found 898.4475.

Synthetic (+)-Caprazol (5). A solution of **48** (7.4 mg, 8.25 μmol) in MeCN (1.0 mL) was treated with 40% aqueous HF (100 μL), and the resulting mixture was stirred at room temperature for 18 h. After the mixture was neutralized with saturated aqueous $NaHCO_3$ and concentrated in vacuo, the residue was purified by C18 reverse-phase HPLC (20 × 250 mm, 100% H_2O) to afford synthetic (+)-caprazol (**5**, 2.4 mg, 50%) as a white solid: $[\alpha]^{25}_D$ +23.8 (*c* 0.24, DMSO); ^{1}H NMR (D_2O, 500 MHz) δ 7.77 (d, 1H, H-6, $J_{6,5}$ = 8.1 Hz), 5.81 (d, 1H, H-5, $J_{6,5}$ = 8.1 Hz), 5.59 (s, 1H, H-1′), 5.16 (s, 1H, H-1″), 4.43 (m, 1H, H-3‴), 4.38 (d, 1H, H-5′, $J_{5',6'''}$ = 9.5 Hz), 4.30 (d, 1H, H-2′, $J_{2',3'}$ = 5.1 Hz), 4.24 (m, 1H, H-3″), 4.21−4.18 (m, 2H, H-4″, H-2‴), 4.13−4.11 (m, 2H, H-4′, H-2″), 4.07 (dd, 1H, H-3′, $J_{3',2'}$ = 5.2 Hz, $J_{3',4'}$ = 7.8 Hz), 3.84 (d, 1H, H-6‴, $J_{6''',5'}$ = 9.5 Hz), 3.32 (dd, 1H, H-5″a, $J_{5''a,5''b}$ = 14.0 Hz, $J_{5''a,4''}$ = 3.3 Hz), 3.19 (dd, 1H, H-5″b, $J_{5''b,5''a}$ = 14.0 Hz, $J_{5''b,4''}$ = 4.4 Hz), 3.12 (d, 1H, H-4‴a, $J_{4'''a,4'''b}$ = 14.7 Hz), 3.06 (s, 3H, $CONCH_3$), 3.00 (d, 1H, H-4‴b, $J_{4'''b,4'''a}$ = 14.7 Hz), 2.42 (s, 3H, NCH_3); ^{13}C NMR (D_2O, 100 MHz) δ 174.1, 172.7, 167.0, 151.8, 143.0, 111.2, 101.7, 91.9, 82.5, 79.0, 77.7, 75.5, 74.2, 70.6, 70.1, 69.4, 63.6, 59.2, 40.2, 39.4, 37.0; ESIMS-HR (NBA) calcd for $C_{22}H_{32}N_5O_{13}$ 574.1997, found 574.2012.

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Supporting Information Available: Experimental procedures, ^{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.

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