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Total Synthesis of (−)-Muraymycin D2 and Its Epimer

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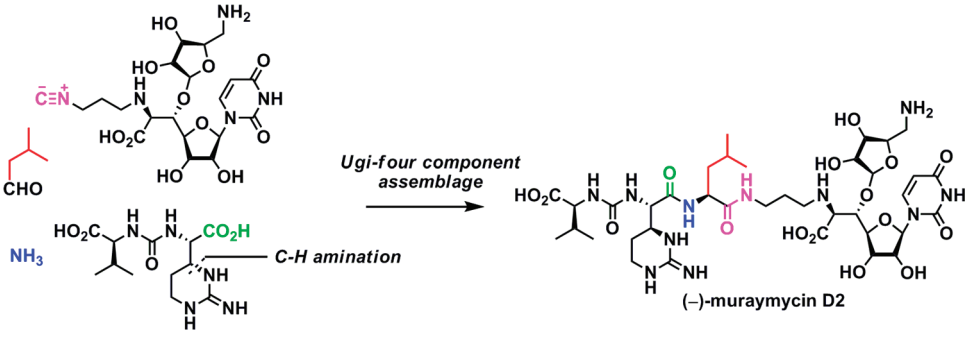

Full details of the first total synthesis of (−)-muraymycin (MRY) D2 and its epimer, the antibacterial nucleoside natural product, are described. Key strategic elements of the approach include the preparation of the urea dipeptide moiety found in the muraymycins containing an L-*epi*-capreomycidine via a nitrene C−H insertion of the sulfamate **10** and the fully protected muraymycin skeleton at a late stage by an Ugi four-component reaction. Thus, the nitrene C−H insertion of the sulfamate **10** with 10 mol % of $Rh_2(esp)_2$ catalyst gave the cyclic sulfamates **11a** and **11b** in 47% yield (**11a**:**11b** = 1:2.0). Construction of the cyclic guanidine skeleton was effected through the $HgBr_2$-promoted cyclization of **42** followed by desulfonylation upon acetolysis of the oxathiazinane ring to give **43** in good yield. The amine obtained by selective removal of the Cbz group of the alcohol **44** was reacted with MeSC(=O)-L-Val-O-*t*-Bu (**38**) to provide **45**, which was oxidized to the carboxylic acid **46**. Reaction of **46**, isonitrile **51**, isovaleraldehyde, and 2,4-dimethoxybenzylamine furnished the desired Ugi products, the final deprotection of which successfully afforded (−)-MRY D2 and *epi*-MRY D2 (**53**) after HPLC separation of the diastereomers. This approach would afford ready access to a range of analogues simply by altering each component.

Introduction

Multidrug resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Staphylococcus aureus* (VRSA), pose an ongoing public health concern. Keeping pace with their mutations continues to be a priority and challenge for the medical community.[1] In choosing novel antibacterial agents to address this problem, several factors come into consideration: the target must be essential for growth, the agent different from existing drugs, and the initial "hit" scaffold amenable to structural changes that allow for potency optimization and efficacy to generate "lead" compounds.[2−4] Antibacterial drugs tend to have higher molecular weight and increased polarity, and they are known to occupy a unique physicochemical property

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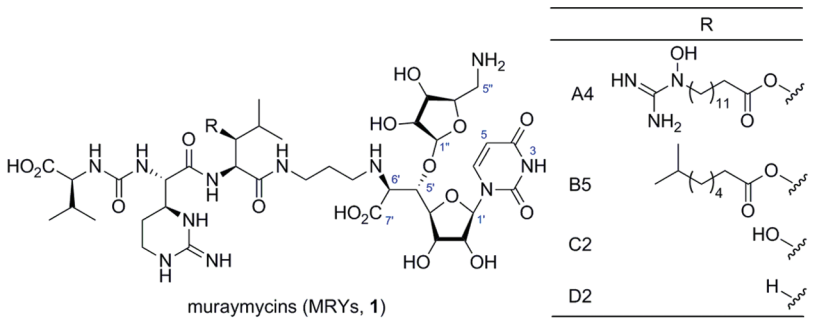

FIGURE 1. Structures of muraymycins.

space and are remarkably different from drugs of other therapeutic areas.[5−9] The antibacterial drugs currently in use originated largely from natural products, in part because they are likely to cover the physicochemical property space required for antibacterial compounds better than synthetic compounds. Therefore, natural products are still a rich source for the discovery of novel antibacterial agents.[10]

Muraymycins (MRYs) (Figure 1, **1**), isolated from a culture broth of *Streptomyces sp.*,[11] are members of a class of naturally occurring 6′-*N*-alkyl-5′-*β*-*O*-aminoribosyl-*C*-glycyluridine antibiotics.[12] The MRYs possessing a lipophilic side chain have been shown to exhibit excellent antimicrobial activity against Gram-positive bacteria. In particular, the efficacy of the MRYs in *S. aureus* infected mice represents a promising lead for the development of new antibacterial agents. The MRYs are strong inhibitors of the phospho-MurNAc-pentapeptide translocase (MraY), which is responsible for the formation of the lipid I in the peptidoglycan biosynthesis. Since MraY is an essential enzyme among bacteria, it is potentially a novel target for the development of general antibacterial agents.[13] Common features of the molecules include a 5′-*O*-aminoribosyl-5′-*C*-glycyluridine moiety and an amino acid−urea−amino acid motif involving an L-*epi*-capreomycidine (L-*epi*-Cpm), which is a cyclic guanidine amino acid. MRYs possess a relatively higher molecular weight and polarity, and these structural features are in good agreement with the property space characteristic of antibacterial agents. The promising biological properties in conjunction with their interesting chemical structure render the MRYs intriguing and challenging synthetic targets.[14] However, their total synthesis has not yet been accomplished. Since chemical modifications of the natural product are limited, a synthetic supply would be necessary for pursuing a structure−activity relationship in order to develop novel antibacterial agents, and the synthetic route is preferred because of its accessibility to a range of analogues. Herein, we provide full details of the total synthesis of MRY D2 and its epimer,[15] thereby establishing a general synthetic route toward a range of MRY analogues.

Results and Discussion

The Ugi four-component reaction (U4CR) has long been considered a useful method for the preparation of *N*-acyl-α-aminocarboxyamides from an aldehyde, amine, isonitrile, and carboxylic acid.[16] Because of the inherent high convergent potential of the multicomponent assembly, the U4CR has been applied not only to medicinal chemistry for the preparation of libraries but also to the total synthesis of complex molecules.[17] The MRYs consist of three fragments, namely, the aminoribosyluridine, lipophilic side chain, and urea dipeptide. Mindful of the contribution of these fragments to antibacterial activity and of their efficacy in obtaining a set of analogues, we retrosynthetically divided the target MRY D2 into the urea dipeptide **3**, ammonia, isovaleraldehyde, and the isonitrile derivative of the aminoribosyluridine **2** for U4CR (Scheme 1). The final goal of our study is to reveal the structure−activity relationship of MRYs. Basically, the U4CR is nonstereoselective at the newly formed stereogenic center to give a mixture of products, and the number of steps is almost the same as a conventional peptide coupling strategy. In terms of the total synthesis of MRYs itself, it is true that it is less advantageous to use the U4CR in the final assemblage of the nucleoside and urea dipeptide moieties. From the medicinal chemical point of view, however, this strategy is appropriate to examine the structure−activity relationship. Thus, the U4CR gives us a diastereomer, which is a useful

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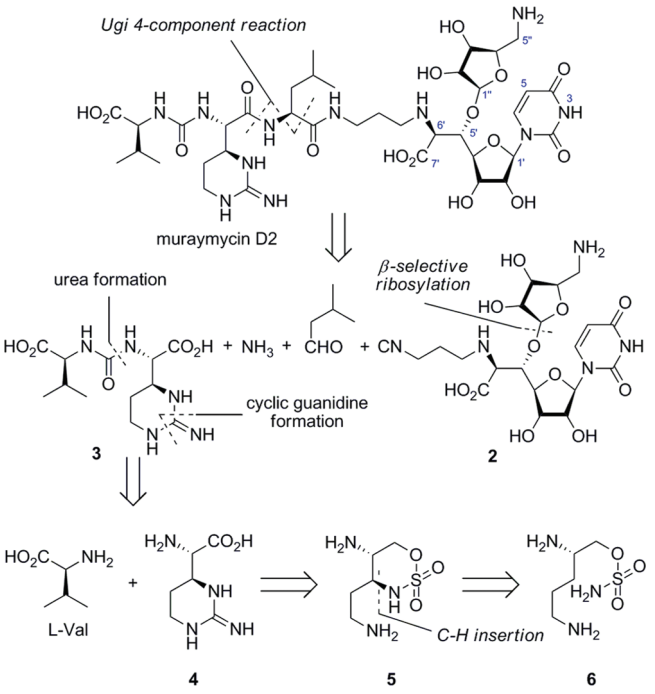
SCHEME 1



compound in order to examine the structure−activity relationship. In conjunction with the nature of the multicomponent assemblage, this strategy allows us to diversify accessible analogues. For these reasons, the U4CR was chosen for the total synthesis of MRYs in this study. Among the four components, the urea dipeptide moiety contains a rare L-*epi*-Cpm (**4**). Most of the previous syntheses of the Cpm class of amino acids were racemic.[18] Although an elegant asymmetric synthesis of L-Cpm has been reported by the Williams group,[19] only a few asymmetric and stereoselective syntheses of its epimer, L-*epi*-Cpm, have been reported.[20] Thus, an efficient asymmetric preparation of L-*epi*-Cpm was required for the total synthesis. The structure of the L-*epi*-Cpm can be regarded as an arginine analogue, where the terminal nitrogen atom of the guanidine is inserted into the C−H bond at the β-position constructing a cyclic guanidine moiety. Therefore, the C−H insertion of a nitrogen atom is a straightforward strategy to functionalize the β-position. Nitrene C−H insertion has recently attracted much attention in organic synthesis.[21] Consequently, we embarked on the synthesis of an L-*epi*-Cpm unit by using the C−H insertion of the sulfamate **10** as summarized in Scheme 2. This strategy can be quite challenging since the C−H bond at the 3-position is less activated toward nitrene insertion. Methylation of the commercially available δ-*N*-Boc-α-*N*-Cbz-L-ornithine (**7**) followed by reduction of the resulting ester **8** gave the alcohol **9**, which

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TABLE 1. Nitrene C−H Insertion of 10

entry	catalyst	solvent	yield of **11** (%)	ratio (**11a**/**11b**)
1	$Rh_2(OAc)_4$	CH_2Cl_2	21	1:1.6
2	$Rh_2(esp)_2$	CH_2Cl_2	47	1:2.0
3	$Rh_2(esp)_2$	$(CH_2Cl)_2$	27	1:2.0
4	$Rh_2(esp)_2$	benzene	35	1:1.9
5	$Rh_2(esp)_2$	CF_3Ph	45	1:1.5
6	$Rh_2(esp)_2$	MeCN	45	1:2.0

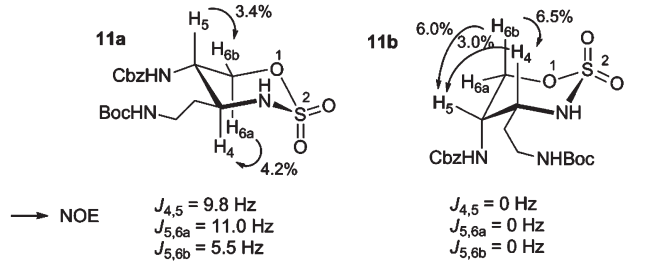
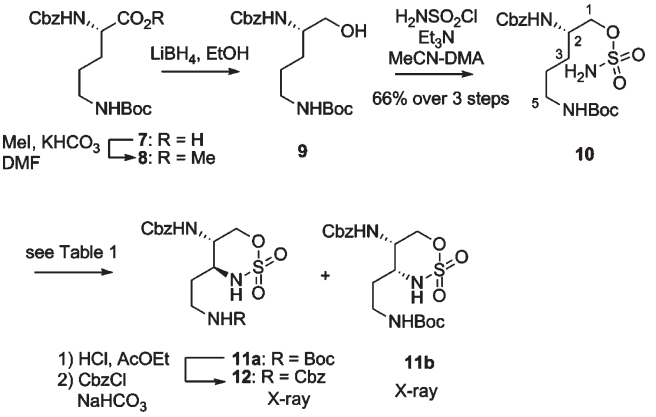


FIGURE 2. Selected NMR data for **11a** and **11b**.

SCHEME 2



was subsequently converted to the corresponding sulfamate **10** without chromatography in 66% yield over three steps. With the sulfamate **10** in hand, we then examined the C−H insertion, the first key reaction of the synthesis of the MRYs; the results are summarized in Table 1. The precursor **10** was treated with 10 mol % of $Rh_2(OAc)_4$ in the presence of $PhI(OAc)_2$ and MgO in refluxing CH_2Cl_2 for 1.5 h, and the desired oxathiazinane derivatives **11a** and **11b** were obtained in 21% yield, respectively (entry 1, **11a**/**11b** = 1:1.6). Structures **11a** and **11b** were confirmed by several NMR measurements, including HMBC and HMQC. For instance, the preferred conformation of the oxathiazinane ring moiety of **11a** was initially postulated from the fact that relatively large coupling constants were observed for H-4 and H-5 ($J_{4,5}$ = 9.8 Hz) and H-5 and H-6a ($J_{5,6a}$ = 11.0 Hz) in acetone-d_6 (Figure 2), indicating that both the *N*-Boc-aminoethyl group at the 4-position and the benzyloxycarbonylamino group at the 5-position are in the equatorial orientation. This was confirmed by NOE experiments, where correlations were observed between H-4 and H-6a (4.2%), and H-5 and H-6b (3.4%). As for **11b**, H-5 was observed as a singlet which implies that the coupling constants for H-4 and H-5, H-5 and H-6a, and H-5 and H-6b were 0 Hz in CD_3OD. NOEs were also observed for

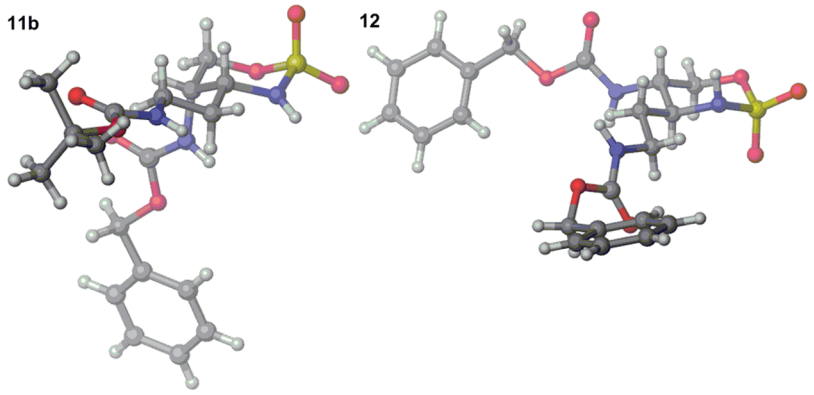


FIGURE 3. X-ray crystal structures of **11b** and **12**.

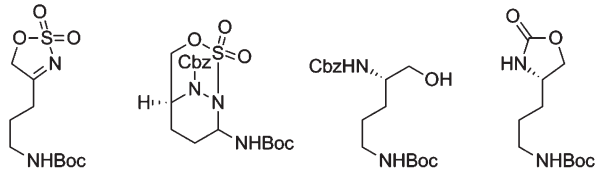


FIGURE 4. Structure of byproduct in the reaction of **10**.

H-4 (6.5%) "and H-5 (6.0%)" upon irradiation of H-6b and for H-5 (3.0%) upon irradiation of H-4. These results would indicate that the *N*-Boc-aminoethyl group at the 4-position and the benzyloxycarbonylamino group at the 5-position are in the equatorial and axial orientation, respectively. In addition to the structural analysis by NMR experiments, the newly introduced stereogenic center at the 4-position of **11a** was unambiguously determined to be the *S*-configuration by X-ray crystal structure analysis of **12**, which was obtained from **11a** by deprotection of the Boc group followed by protection of the liberated amine with a Cbz group (Figure 3). The X-ray crystal structural analysis of **12** further revealed that the oxathiazinane ring of **12** adopted a chairlike conformation in the solid state. The structure of **11b** was also determined by its X-ray crystal structure analysis, revealing that the oxathiazinane ring of **11b** had a similar conformation to that of **11a**. Structural determination of **11a** and **11b** indicated that the major diastereomer was the undesired **11b** in entry 1. With 10 mol % of bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] ($Rh_2(esp)_2$) catalyst,[22] the yields of the oxathiazinanes **11a** and **11b** were improved to 47% yield with **10** being recovered in 11% yield (entry 2). However the catalyst had little influence on the diastereoselectivity (**11a**/**11b** = 1:2.0). We also examined the effect of solvents in the reaction of **10**; however, no appreciable improvement in diastereoselectivity was observed (entries 3−6). It should be noted that the chemical yields of **11a** and **11b** were moderate and some byproduct were isolated during the course of the reaction in entry 2, the structures of which are described in Figure 4. Presumably, **13** (17% yield) and **14** (5% yield) were produced via 1,5- or 1,8-insertion of the nitrene, respectively.[23] Partial removal of the sulfamate group of **10** occurred to give **9** (4% yield) and **15** (9% yield). In order to circumvent the observed regio- and diastereochemical outcome, the following experiments were conducted. Generally, carbenes react with an electron-rich C−H bond and the reaction rate is governed by the electron density of the inserted C−H bond,[24] and nitrenes behave in a similar manner. It was expected that reducing the electron density at the carbon atom at the 5-position of the sulfamate might prevent the undesired 1,8-insertion. In order to improve the regioselectivity of the nitrene C−H insertion, the protecting group of the amine at the 5-position was changed to a more electron-withdrawing phthaloyl (Phth) group and the C−H insertion was examined (Scheme 3). Treatment of **16** with 10 mol % of $Rh_2(esp)_2$, $PhI(OAc)_2$, and MgO in refluxing CH_2Cl_2 gave the 1,6-insertion products **17a** (17% yield) and **17b** (30% yield), the 1,5-insertion product **18** (17% yield), and other decomposition products such as **19** (5% yield) and **20** (7% yield). As expected, formation of the 1,8-insertion product was not observed at all. Because of the electron-withdrawing nature of the Phth group, the reaction rate became slower, and the reaction took 7 h to complete. The diastereoselectivity (**17a**/**17b** = 1:1.8) was similar to that in the C−H insertion of **10**. Du Bois et al. reported the stereoselective nitrene insertion of 3-(2-*N*-phthalimido-3-sulfamoyloxypropyl)indole derivative in which the amino group was protected with a Phth group.[25] Two possible transition states were proposed in the reaction, and the reaction predominantly proceeded via the transition state 1 (**TS1**) with less steric repulsion than **TS2** (Figure 5).[25] Contrary to this study, the undesired diastereomers **11b** and **17b** were obtained as the major products in our case. We hypothesized that the reversed stereoselectivity observed in the nitrene C−H insertion of **10** or **16** could be attributed to the existence of a free hydrogen atom attached to the nitrogen atom at the 2-position, presumably affording an intramolecular hydrogen bond to the oxygen atom of the sulfamate group. This being the case, **TS4** would be expected to be more stable than **TS3** due to the formation of the intramolecular hydrogen bond with the substituent at the 2-position in a pseudoaxial orientation as shown in Figure 5. As a result, the reaction via **TS4** would be favored to give the undesired oxathiazinane derivatives such as **11b** and **17b** with the 4*R*-configuration. Therefore, we decided to study the effect of the protecting group at the

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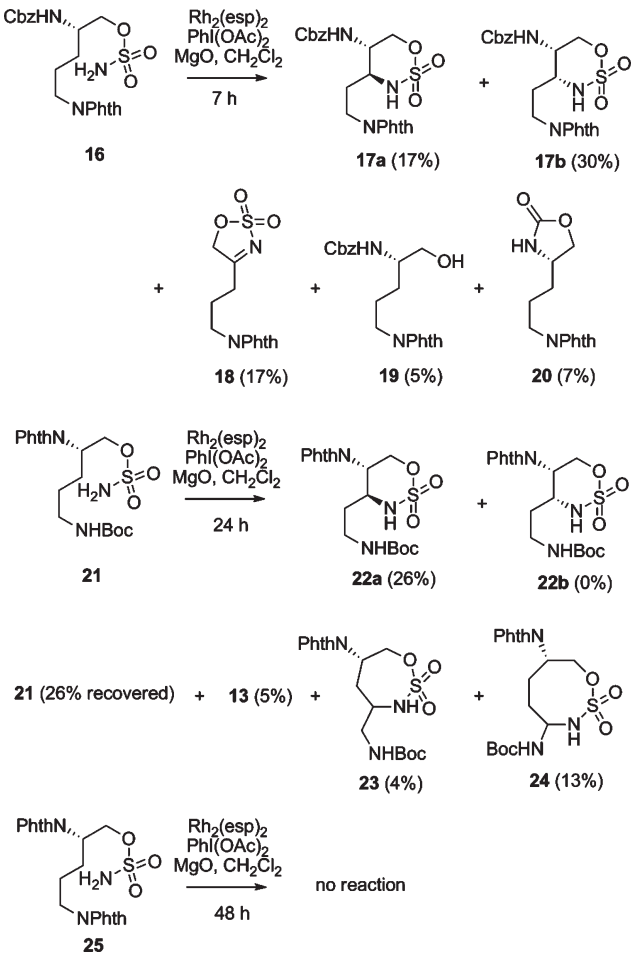
SCHEME 3



2-amino group. The 2-Phth derivative **21** was prepared to examine the impact of the hydrogen atom on the diastereoselectivity (Scheme 3). The nitrene C−H insertion of **21** proceeded under the same conditions as those for the reactions of **10** and **16**, and the desired oxathiazinane derivative **22a** with the S-configuration at the 4-position was obtained selectively in 26% yield (35% based on 26% recovered starting material) in addition to some byproducts including **13** (5% yield), **23** (4% yield), and **24** (13% yield). The corresponding diastereomer **22b** was not obtained at all, and good diastereoselectivity was achieved. These results suggest that the free hydrogen atom at the 2-amino group influences the diastereoselectivity, although it should be further elucidated in detail. The electron-withdrawing nature of the Phth group also reduced the reactivity of the C−H insertion, and the reaction rate was much slower than that of **10** which was protected with the Cbz group (24 h vs 1.5 h). We further conducted the C−H insertion of a substrate **25**, where both the amino groups were protected with Phth groups in order to control both the regio- and diastereoselectivity. However, the electron density of the substrate in the nitrene C−H insertion was so sensitive that no reaction occurred to provide the oxathiazinane derivative even over 48 h. Further efforts will be made to improve the yield and stereochemical outcome of the nitrene C−H insertion reaction and verify that **TS4** is indeed favored over **TS3** in Figure 5 because it is not ideal.

In terms of medicinal chemistry, the impact of the L-*epi*-Cpm residue of MRYs on the MraY inhibitory and antibacterial activities is of interest. Muraymycin analogues containing an L-Cpm residue, a diastereomer of the L-*epi*-Cpm, are key in determining the structure−activity relationship (SAR). For a future SAR study of the MRYs that would be analogous to our previous studies of the caprazamycins,[26] we decided to establish a synthetic route to the urea dipeptide containing either L-*epi*-Cpm or L-Cpm. The major isomer **11b** was first used to test the synthetic route to the urea dipeptide **41**. Initially, we planned to construct the bicyclic *S*-methylisothiourea derivative **28** as the key intermediate, which could be transformed to the bicyclic guanidine derivative **29** upon substitution of the methylthio group with nitrogen nucleophiles as shown in Scheme 4. Therefore, the amine **26**, obtained by removal of the Boc protecting group of **11b**, would be converted to the *S*-methylisothiourea **28** ($SO_2(OMe)_2$, K_2CO_3) via the cyclic thiourea **27** (*N*,*N*′-thiocarbonyldiimidazole) (Scheme 4). Substitution of the methylthio group of **28** under a variety of conditions with nitrogen nucleophiles (e.g., ammonia, *O*-benzylhydroxylamine) in the presence of $AgNO_3$ was then examined. However none of these efforts was successful to give **29**, partly because of a competitive ring-opening of the oxathiazinane moiety by attack of the nitrogen nucleophiles on the carbon atom attached to the sulfamate group. Next, direct formation of the cyclic guanidine was attempted by cyclization of the methylisothiourea **30** protected with 2,2,2-trichloroethoxysulfonyl (Tces) group as shown in Scheme 5. Thus, the amine **26** was treated with MeSC(=NTces)Cl[27] to afford **30** in 84% yield over two steps. Construction of the cyclic guanidine skeleton was realized through $HgBr_2$-promoted cyclization in the presence of Et_3N in MeCN, and the desired **31** was obtained in 74% yield. Desulfonylation of **31** upon solvolysis of the oxathiazinane ring was first conducted in refluxing aq MeCN to give the desired alcohol **33** in 58% yield. No improvement of the chemical yield of **33** was achieved under basic conditions, the aim of which was to neutralize the sulfonic acid generated during the reaction. The corresponding acetate **32** was obtained in 81% yield when **31** was treated with Bu_4NOAc in AcOH and MeCN. Removal of the acetyl group of **32** (K_2CO_3, MeOH) followed by protection of the resulting primary hydroxyl group with a TBDPS group gave **34** quantitatively. The next task involved the removal of the Cbz group selectively in the presence of the Tces group by catalytic hydrogenolysis. In fact, a conventional procedure for the catalytic hydrogenation of **34** (H_2, Pd/C, MeOH) resulted in removal of both the Cbz and Tces groups to give the undesired amine **36** instead of the desired amine **35**, which was obtained only in a trace amount. The selective reduction was accomplished by the procedure previously reported using trichloroacetic acid (TCA) as an additive.[28] Therefore, hydrogenolysis of **34** in the presence of 10 equiv of TCA in MeOH selectively afforded the amine **35** in 76% yield. With the key amine **35** in hand, we then pursued the synthesis of the urea dipeptide **41** as shown in Scheme 6. L-Val-O-*t*Bu **37** was treated with *N*,*N*′-carbonyldiimidazole to give a carbonylimidazolate intermediate, which was reacted

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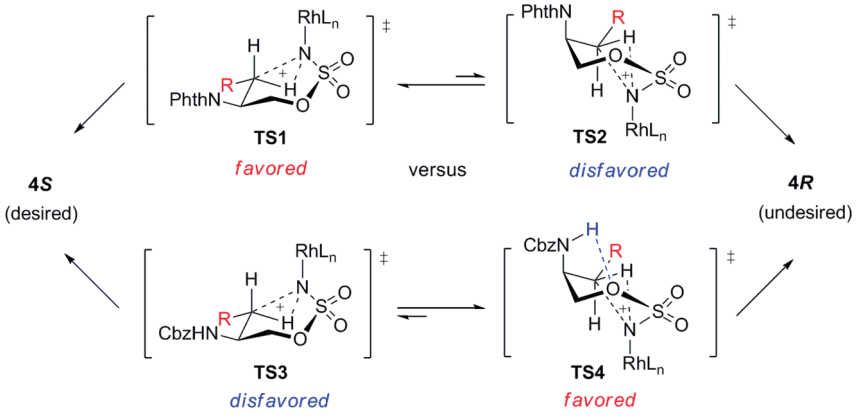
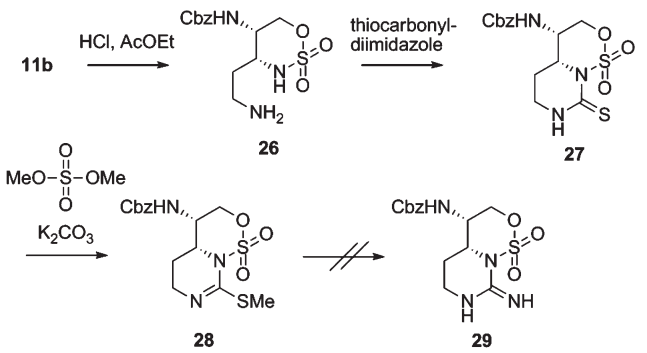
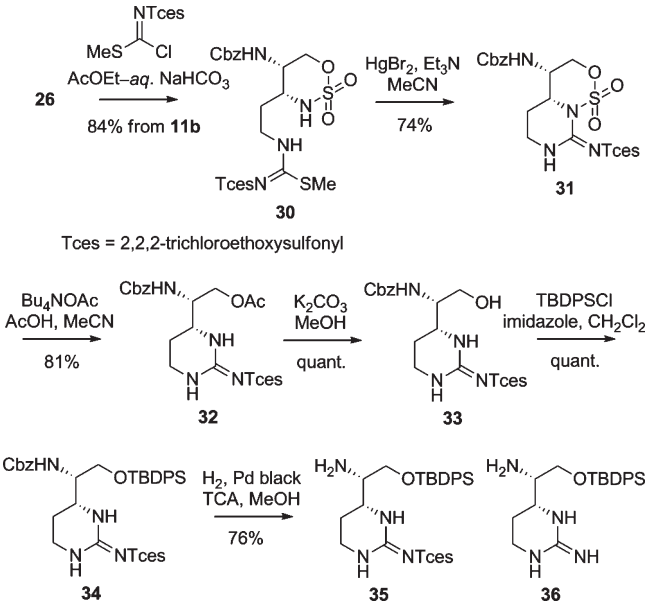


FIGURE 5. Proposed transition states.

SCHEME 4



SCHEME 5



with the amine **35**. However, only a trace amount of the urea derivative **39** was isolated from the reaction mixture (Table 2, entry 1). Presumably, the primary amine **35** was sterically encumbered by the presence of the cyclic guanidine moiety. In order to increase the reactivity, DMAP was used as an additive. Although the yield of **39** was increased to 30%, significant epimerization occurred at the α-position to the Val

SCHEME 6

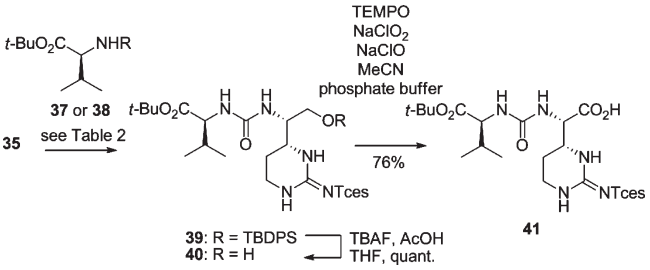


TABLE 2. Optimization of Urea Formation

entry	R	reagents and conditions	yield of **39** (%)
1	H, **37**	*N*,*N*′-carbonyldiimidazole, CH_2Cl_2	trace
2	H	*N*,*N*′-carbonyldiimidazole, DMAP, CH_2Cl_2	30[a]
3	H	triphosgene, Et_3N, CH_2Cl_2	62
4	COSMe, **38**	$HgBr_2$, *N*-methylmorpholine	82

[a]Epimerization at the α-position to the ester group of L-Val moiety was observed.

carbonyl group, resulting in a failure to obtain pure **39** (entry 2). On the other hand, once we had obtained the isocyanate as a more reactive intermediate derived from the reaction of **37** with triphosgene, the desired **39** was produced in 62% yield (entry 3). Ultimately the urea **39** was prepared in 82% yield without any epimerization by the reaction with MeSC(=O)-L-Val-O-*t*-Bu (**38**) in the presence of $HgBr_2$ and *N*-methylmorpholine in AcOEt (entry 4). After the TBDPS group deprotection, the resulting primary alcohol in **40** was oxidized in a one-pot procedure[29] to provide the carboxylic acid **41**. Since we had established the synthetic route to the urea carboxylic acid **41**, we next applied the route to synthesize the urea dipeptide containing L-*epi*-Cpm as shown in Scheme 7; namely the *S*-methylisothiourea derivative **42** was first prepared from **11a**. Construction of the cyclic guanidine skeleton was effected through cyclization of **42** promoted by $HgBr_2$, and the following desulfonylation upon acetolysis of the oxathiazinane ring gave **43** in 82% yield over two steps. After removal of the acetyl group of **43**, the amine obtained by selective removal of the Cbz group of **44** was reacted with **38** to provide **45** in 64% yield over

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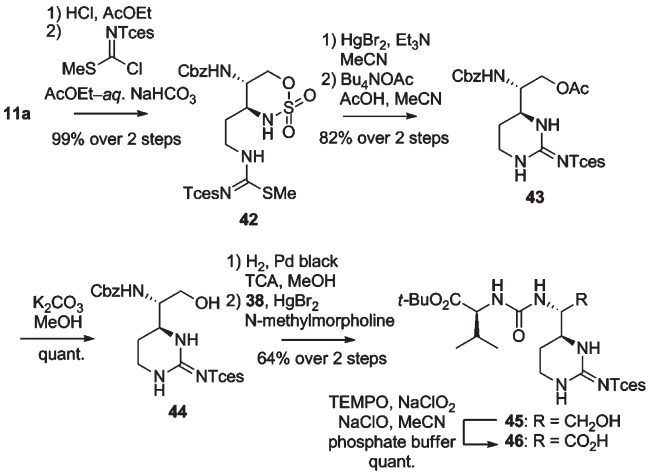
SCHEME 7

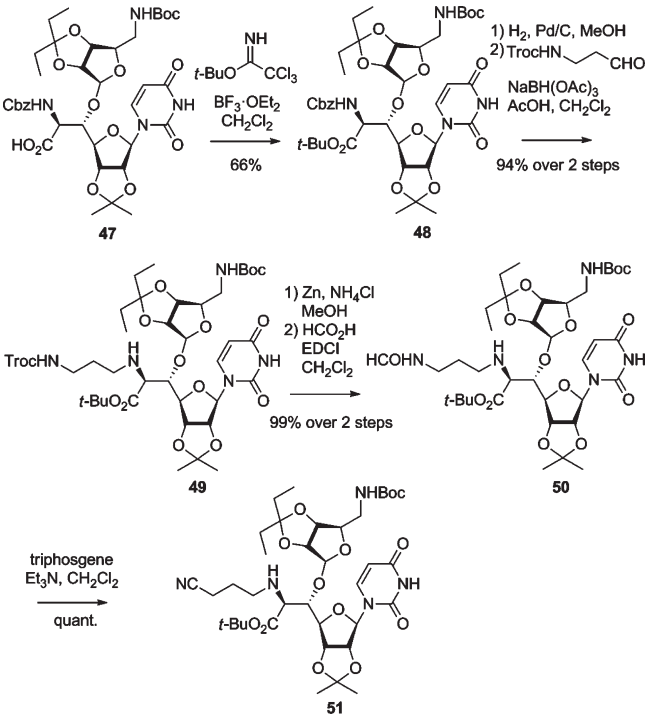


two steps. Finally, the alcohol **45** was oxidized to the carboxylic acid **46**. In this reaction scheme, it turned out that the primary alcohol in **44** did not have to be protected with a TBDPS group; consequently, the number of steps could be reduced to prepare **46**.

The isonitrile component **51** linked to the 6′-*N*-alkyl-5′-*β*-*O*-aminoribosyl-*C*-glycyluridine, a key structural feature of this class of natural products, was prepared from **47**, which was previously synthesized by our group.[30] In order to employ a final global deprotection at the last stage under acidic conditions to obtain the highly polar and base-sensitive target molecule, the carboxylic acid **47** was protected as a *t*-Bu ester by a conventional esterification (*t*-BuO(C=NH)CCl_3, $BF_3 \cdot OEt_2$) to give **48** in 66% yield (Scheme 8). Hydrogenolysis of the Cbz protecting group cleanly afforded the amine, which was then alkylated with *N*-2,2,2-trichloroethoxycarbonyl (Troc)-3-aminopropanal by reductive alkylation to give the secondary amine **49** in 94% yield over two steps. Upon removal of the Troc group of **49** with Zn, the corresponding amine derivative was treated with formic acid and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) in CH_2Cl_2 to selectively afford the terminal formamide **50**. After extensive efforts to dehydrate **50**, it was found that treating it with triphosgene and Et_3N in CH_2Cl_2 at −78 °C gave the isonitrile **51** in a clean and quantitative conversion.

With the carboxylic acid **46** and the isonitrile **51** in hand, we undertook the final assemblage by U4CR (Scheme 9). The U4CR in our synthetic strategy to the MRYs required the use of ammonia as an amine. Usually ammonium acetate or ammonium chloride is used; however, because of reactivity or side reactions, the yield was low.[31] In this study, 2,4-dimethoxybenzylamine was chosen as a "masked" ammonia, and the resulting 2,4-dimethoxybenzyl (DMB) group at the tertiary amide site after the U4CR can be removed by acid-catalyzed hydrolysis.[32] Compounds **46**, **51**, isovaleraldehyde, and 2,4-dimethoxybenzylamine were mixed in EtOH at room temperature; however, progress of the reaction was very slow, and only a trace amount of the Ugi products **52** was obtained after 72 h. Reaction without any solvent[33] at room temperature for 72 h provided the desired Ugi products in 54% yield as a mixture of diastereomers (1:1) at the α-position of the Leu residue after purification by silica gel column chromatography. The ^{1}H NMR analysis of the mixture **52** gave a rather complex spectrum because each diastereomer was observed as a mixture of rotamers. Therefore, the final deprotection of **52** was carried out with no further purification, and global deprotection (Zn, THF−aq NaH_2PO_4, then aq 80% TFA, quant over two steps) successfully afforded (−)-MRY D2 and *epi*-MRY D2 (**53**) after HPLC separation of the diastereomers. The ^{1}H NMR spectrum of the synthetic (−)-MRY D2 was in good agreement with that reported for the natural material.[11b] The newly formed stereogenic center at the Leu residue of each diastereomer was determined by conventional amino acid analysis[34] as shown in Scheme 10. Thus, (−)-MRY D2 or **53** was heated under reflux in 6 M aq HCl for 24 h, and the resulting mixture was treated with Marfey's reagent.[34] The reaction mixture was analyzed by reversed-phase HPLC (ODS, 10−60% MeCN−H_2O linear gradient containing 0.1% TFA) with an authentic material derived from L- or D-Leu. HPLC analysis of the reaction mixture obtained from the synthetic MRY D2 revealed the existence of a peak with the retention time of 36.5 min, which was completely matched to that of the authentic material derived from L-Leu (Supporting Information). These results revealed that the isomer matching with the natural product by the ^{1}H NMR spectrum

SCHEME 8



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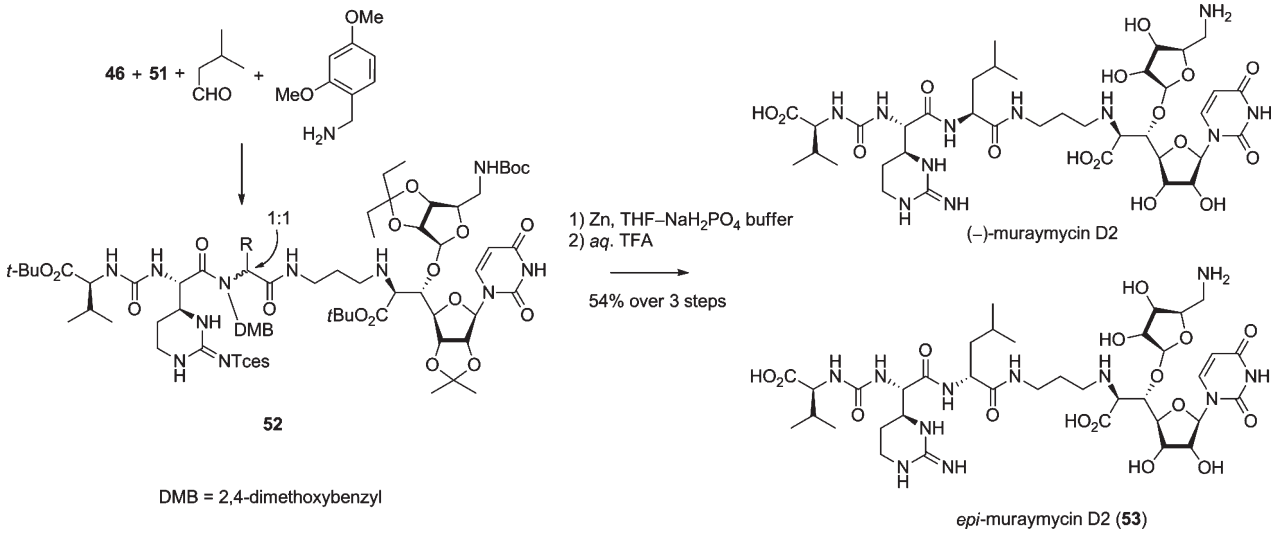
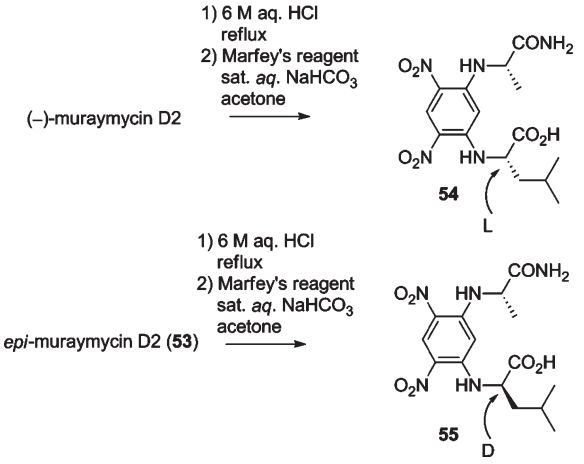
SCHEME 9



SCHEME 10



contained the L-Leu residue as reported.[11] By similar experiments with the epimer **53**, the Leu residue was unambiguously determined to be D-Leu.

Conclusions

The first total synthesis of MRY D2 and its epimer at the Leu residue has been accomplished and the details are described. By virtue of the multicomponent assemblage at a late stage of the synthesis and despite the challenges this poses because of the inherent labile nature of the MRYs due to potential epimerization, our approach provided ready access to a range of analogues simply by altering each component. This initial study has set the stage for the generation of novel antibacterial "lead" compounds based on MRYs.

Experimental Section

General Experimental Methods. NMR spectra are reported in parts per million (δ) relative to tetramethylsilane (0.00 ppm) as internal standard unless otherwise noted. Coupling constants (J) are reported in hertz (Hz). Abbreviations of multiplicity are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Data are presented as follows: chemical shift (multiplicity, integration, coupling constant). Assignments are based on $^1H-^1H$ COSY, HMBC, and HMQC NMR spectra.

(2*S*)-2-Benzyloxycarbonylamino-5-*tert*-butoxycarbonylamino-pentane-1-sulfamate (10). A suspension of Z-Orn(Boc)-OH (**7**, 50.0 g, 136 mmol) and $KHCO_3$ (27.3 g, 272 mmol) in DMF (1.4 L) were treated with MeI (17.0 mL, 272 mmol) at room temperature for 10 h. The resulting mixture was concentrated in vacuo. The residue was diluted with AcOEt (800 mL), which was washed with H_2O and saturated aq NaCl. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The resulting crude methyl ester **8** in EtOH (1.5 L) was treated with $LiBH_4$ (3.6 g, 164 mmol) at 0 °C for 24 h. The mixture was concentrated in vacuo, and the residue was diluted with AcOEt (800 mL), which was washed with 1 M aq HCl, saturated aq $NaHCO_3$, and saturated aq NaCl. The organic phase was dried (Na_2SO_4) and concentrated in vacuo to give alcohol **9**. A solution of sulfamoyl chloride in MeCN was prepared as follows. Formic acid (26.2 mL, 683 mmol) was added dropwise over 10 min to chlorosulfonyl isocyanate (59.5 mL, 683 mmol) at 0 °C, and the mixture was stirred for 10 min at the same temperature. Acetonitrile (1.5 L) was then added to the mixture, which was stirred at room temperature for an additional 8 h. A solution of **9** and Et_3N (96 mL, 690 mmol) in *N*,*N*′-dimethylacetamide (DMA) (100 mL) was added dropwise to the solution of sulfamoyl chloride in MeCN at 0 °C. The mixture was warmed to room temperature and stirred for 10 h. Saturated aq $NaHCO_3$ (30 mL) was added to the mixture, which was stirred for additional 1 h. The resulting mixture was concentrated in vacuo, and the residue was diluted with AcOEt (800 mL), which was washed with H_2O and saturated aq NaCl. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was crystallized from hexane−AcOEt to give **10** as a white solid (38.9 g, 66% over three steps): $[\alpha]^{22}_D$ −17.3 (*c* 1.08, MeOH); mp 100 °C (hexane−AcOEt); ^1H NMR (DMSO-d_6, 400 MHz) δ 7.48 (br s, 2H, SO_2NH_2), 7.34 (m, 6H, phenyl and N*H*-Cbz), 6.79 (br d, 1H, N*H*-Boc, $J_{NH,1}$ = 5.5 Hz), 5.01 (d, 2H, CH_2Ph, J = 12.0 Hz), 3.90 (d, 2H, H-1, $J_{1,2}$ = 5.5 Hz), 3.67 (m, 1H, H-2), 2.87 (d, 2H, H-5, $J_{5,4}$ = 6.0 Hz), 1.44 (m, 2H, H-3), 1.35 (m, 11H, H-4, ^{t}Bu); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 154.3, 154.0, 135.5, 126.8, 126.2, 126.1, 75.8, 68.5, 63.7, 48.0, 37.3, 26.7, 26.3, 24.3; FABMS-LR m/z 432 [(M + H)$^+$]; FABMS-HR calcd for $C_{18}H_{30}N_3O_7S$ 432.1805, found 432.1799.

(4*S*,5*S*)-5-Benzyloxycarbonylamino-4-(2-*tert*-butoxycarbonylamino)ethyl-2,2-dioxo-1,2,3-oxathiazinane (11a), (4*R*,5*S*)-5-Benzyloxycarbonylamino-4-(2-*tert*-butoxycarbonylamino)ethyl-2,2-dioxo-1,2,3-oxathiazinane (11b), 4-(3-*tert*-Butoxycarbonylamino)propyl-2,2-dioxo-1,2,3-oxathiazole (13), (5*S*,8*R*)-9-Benzyloxycarbonyl-8-*tert*-butoxycarbonylamino-2,2-dioxo-9-iminobicyclo[3,3,1]-1,2,3-oxathiazecane (14), and (4*S*)-4-(3-*tert*-Butoxycarbonylamino)propyl-2-oxazolidinone (15) (Entry 2, Table 1). A suspension of **10** (10.0 g, 23.3 mmol), MgO (2.8 g, 70 mmol), diacetoxyiodobenzene (12.0 g, 37.3 mmol) in CH_2Cl_2 were treated with bis[rhodium (α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] (1.11 g, 2.3 mmol) at 40 °C for 1.5 h. The insoluble portion was filtered off through a Celite pad, and the filtrate was concentrated in vacuo. The catalyst was removed by an amino silica gel column (6 × 20 cm, 25% AcOEt/hexane) and concentrated in vacuo. The residue was purified by silica gel column chromatography (6 × 20 cm, 0.3% MeOH/$CHCl_3$) to afford **11a** (1.57 g, 16%) as a white solid, **11b** (3.15 g, 32%) as white crystals, **13** (11 mg, 17%) as a white foam, **14** (4.3 mg, 4.5%) as a yellow foam, **9** (3 mg, 3.7%) as a white solid, and **15** (5.3 mg, 9.3%) as a white foam. Data for **11a**: $[\alpha]^{22}_D$ −28.8 (*c* 1.17, MeOH); mp 155−157 °C; ^{1}H NMR (acetone-d_6, 500 MHz) δ 7.40 (m, 5H, phenyl), 6.73 (d, 1H, N*H*-3, J = 8.6 Hz), 6.55 (br d, 1H, N*H*-Cbz, J = 10.3 Hz), 6.11 (br s, 1H, N*H*-Boc), 5.13 (s, 2H, CH_2Ph), 4.51 (dd, 1H, H-6a, $J_{6a,5}$ = 5.5, $J_{6a,6b}$ = 11.0 Hz), 4.43 (t, 1H, H-6b, $J_{6b,5}$ = $J_{6b,6a}$ = 11.0 Hz), 3.91 (ddd, 1H, H-4, $J_{5,6a}$ = 5.5, $J_{5,4}$ = 9.8, $J_{5,6b}$ = 11.0 Hz), 3.76 (dt, 1H, H-4, $J_{4,1'a}$ = 4.0, $J_{4,1'b}$ = $J_{4,5}$ = 9.8 Hz), 3.32 (m, 1H, H-2′a), 3.18 (m, 1H, H-2′b), 2.12 (m, 1H, 1′a), 1.75 (m, 1H, H-1′b), 1.43 (s, 9H, ^{t}Bu); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 156.2, 156.0, 137.1, 128.9, 128.4, 128.3, 78.1, 71.7, 66.4, 56.5, 47.8, 36.8, 28.8; FABMS-LR m/z 452 [(M + Na)$^+$]; FABMS-HR calcd for $C_{18}H_{28}N_3NaO_7S$ 452.1467, found 452.1448. Anal. Calcd for $C_{18}H_{27}N_3O_7S$: C, 50.34; H, 6.34; N, 9.78; S, 7.47. Found: C, 50.35; H, 6.28; N, 9.70; S, 7.56. Data for **11b**: $[\alpha]^{22}_D$ −30.4 (*c* 0.32, MeOH); mp 134−135 °C; ^{1}H NMR (CD_3OD, 500 MHz) δ 7.33 (m, 5H, phenyl), 5.11 (d, 1H, CH_2Ph, J = 12.6 Hz), 5.10 (d, 1H, CH_2Ph, J = 12.6 Hz), 4.84 (d, 1H, H-6a, $J_{6a,6b}$ = 10.3), 4.43 (d, 1H, H-6b, $J_{6b,6a}$ = 10.3 Hz), 3.88 (t, 1H, H-4, $J_{4,1'a}$ = $J_{4,1'b}$ = 5.2 Hz), 3.79 (s, 1H, H-5), 3.17 (m, 1H, H-2′a), 3.05 (m, 1H, H-2′b), 1.68 (m, 1H, H-1′a), 1.54 (m, 1H, H-1′b), 1.41 (s, 9H, ^{t}Bu); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 156.8, 156.7, 137.3, 129.4, 129.0, 128.6, 79.0, 77.0, 56.3, 45.4, 36.6, 31.5, 29.0; FABMS-LR m/z 452 [(M + Na)$^+$]; FABMS-HR calcd for $C_{18}H_{27}N_3NaO_7S$ 452.1467, found 452.1448. Data for **13**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.09 (s, 2H, H-5), 4.66 (br s, 1H, N*H*-Boc), 3.24 (dd, 2H, H-3′, $J_{3',2'}$ = 6.9, $J_{3'a,3'b}$ = 12.6 Hz), 2.66 (t, 2H, H-1′, $J_{1',2'}$ = $J_{1'a,1'b}$ = 6.9 Hz), 1.99 (dt, 2H, H-2′, $J_{2',3'}$ = $J_{2',1'}$ = 6.9, $J_{2'a,2'b}$ = 13.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.8, 156.7, 80.1, 39.6, 30.1, 29.3, 28.7, 26.3; ESIMS-LR m/z 301 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{10}H_{18}N_5NaO_5S$ 301.0829, found 301.0827. Data for **14**: $[\alpha]^{22}_D$ +57.4 (*c* 0.90, DMSO); ^{1}H NMR (CD_3CN, 400 MHz) δ 7.38 (m, 5H, phenyl), 6.46 (br d, 1H, N*H*-8, $J_{NH,8}$ = 9.2 Hz), 5.25 (d, 1H, CH_2Ph, J = 13.0 Hz), 5.13 (d, 1H, CH_2Ph, J = 13.0 Hz), 4.98 (dt, 1H, H-4a, $J_{4a,5}$ = $J_{4a,6b}$ = 2.5, $J_{4a,4b}$ = 12.0 Hz), 4.66 (d, 1H, H-4b, $J_{4b,4a}$ = 12.0 Hz), 4.22 (t, 1H, H-5, $J_{5,4b}$ = $J_{5,6}$ = 2.5 Hz), 2.63 (ddd, 1H, H-7b, $J_{7b,6b}$ = 5.8, $J_{7b,6a}$ = 8.6, $J_{7b,6a}$ = 14.3 Hz), 2.29 (ddd, 1H, H-6a, $J_{6a,7a}$ = 5.5, $J_{6a,7b}$ = 8.6, $J_{6a,6b}$ = 13.6 Hz), 1.89 (dd, 1H, H-6b, $J_{6b,7b}$ = 5.5, $J_{6b,6a}$ = 13.6 Hz), 1.64 (dd, 1H, H-7a, $J_{7a,6a}$ = 5.2, $J_{7a,6b}$ = 14.3 Hz), 1.37 (s, 9H, ^{t}Bu); ^{13}C NMR (CD_3CN, 125 MHz) δ 155.3, 136.8, 129.1, 129.0, 127.7, 80.2, 79.6, 68.4, 64.9, 43.1, 28.0, 22.8, 22.1; ESIMS-LR m/z 450 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{18}H_{25}N_3NaO_7S_1$ 450.1311, found 450.1305. Data for **15**: $[\alpha]^{22}_D$ −6.72 (*c* 0.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.71 (br s, 1H, N*H*-3), 4.61 (br s, 1H, N*H*-Boc), 4.49 (t, 1H, H-5a, $J_{5a,5b}$ = $J_{5a,4}$ = 13.0 Hz), 4.01 (dd, 1H, H-5b, $J_{5b,4}$ = 6.3, $J_{5b,5a}$ = 8.0 Hz), 3.90 (m, 1H, H-4), 3.14 (m, 2H, H-3′), 1.52 (m, 4H, H-1′and 2′), 1.43 (s, 9H, ^{t}Bu); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 156.2, 79.7, 70.3, 52.2, 39.9, 32.4, 28.5, 26.0; ESIMS-LR m/z 267 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{11}H_{20}N_2NaO_4$ 267.1315, found 267.1316.

(4*S*,5*S*)-5-Benzyloxycarbonylamino-4-(2-benzyloxycarbonylamino)ethyl-2,2-dioxo-1,2,3-oxathiazinane (12). Compound **11a** (50 mg, 0.12 mmol) was treated with 4 M HCl in AcOEt for 1 h. The resulting solution was concentrated in vacuo. A suspension of the residue in AcOEt (3 mL) was treated with saturated aq $NaHCO_3$ (3 mL) and benzyl chloroformate (18.3 μL, 0.13 mmol), and the resulting biphasic layers were vigorously stirred at room temperature for 1 h. The organic phase was washed with H_2O and saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was crystallized from $CHCl_3$ to afford **12** (41 mg, 76% over two steps) as colorless prisms. A part of the material was recrystallized from hexane−AcOEt for an analytical sample: $[\alpha]^{22}_D$ −27.8 (*c* 0.46, MeOH); mp 144 °C (hexane−AcOEt); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.59 (br d, 1H, N*H*-3, $J_{NH,4}$ = 10.0 Hz), 7.43 (d, 1H, N*H*-5, $J_{NH,5}$ = 8.2 Hz), 7.30 (m, 11H, phenyl and N*H*-2′), 5.07 (s, 2H, CH_2Ph), 5.00 (s, 2H, CH_2Ph), 4.37 (dd, 1H, H-6a, $J_{6a,5}$ = 4.5, $J_{6a,6b}$ = 11.0 Hz), 4.18 (t, 1H, H-6b, $J_{6b,5}$ = $J_{6b,6a}$ = 11.0 Hz), 3.60 (dd, 1H, H-5, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 11.0 Hz), 3.43 (m, 1H, H-4), 3.10 (ddd, 1H, H-2′a, $J_{2'a,1'a}$ = 4.6, $J_{2'a,1'b}$ = 8.6, $J_{1'a,1'b}$ = 17.0 Hz), 2.96 (dt, 1H, H-2′b, $J_{2'b,1'a}$ = $J_{2'b,1'b}$ = 7.6, $J_{2'b,2'a}$ = 17.0 Hz), 1.84 (m, 1H, H-1′a), 1.50 (m, 1H, H-1′b); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 156.2, 156.0, 137.4, 136.8, 128.6, 128.6, 128.1, 128.0, 71.4, 66.1, 65.4, 56.2, 47.6, 36.9, 30.6; FABMS-LR m/z 464 [(M + H)$^+$]; FABMS-HR calcd for $C_{21}H_{26}N_3O_7S$ 464.1492, found 464.1484. Anal. Calcd for $C_{21}H_{25}N_3O_7S\cdot{}^1/_2H_2O$: C, 53.89; H, 5.49; N, 8.98; S, 6.85. Found: C, 53.74; H, 5.28; N, 8.86; S 6.98.

(4*S*,5*S*)-5-Benzyloxycarbonylamino-4-[2-[*S*-methyl-*N*-(2,2,2-trichloroethoxysulfonyl)isothioureido]]ethyl-2,2-dioxo-1,2,3-oxathiazinane (42). Compound **11a** (100 mg, 0.23 mmol) was treated with 4 M HCl in AcOEt (10 mL) at room temperature for 3 h. The mixture was concentrated in vacuo. A suspension of the residue in AcOEt (10 mL) was treated with saturated aq $NaHCO_3$ (10 mL) and *S*-methyl-*N*-(2,2,2-trichloroethoxysulfonyl)carbonchloroimidothioate (97.3 mg, 0.30 mmol) at room temperature for 1 h. The organic phase was washed with H_2O, saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (2 × 2 cm, 2.4% acetone/$CHCl_3$) to afford **42** (163 mg, 99% over two steps) as a white foam: $[\alpha]^{22}_D$ −19.9 (*c* 1.02, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.33 (br t, 1H, N*H*-isothiourea, $J_{NH,2'}$ = 5.6 Hz), 7.64 (br d, 1H, N*H*-3, $J_{NH,3}$ = 10.0 Hz), 7.47 (d, 1H, N*H*-5, $J_{NH,5}$ = 8.8 Hz), 7.34 (m, 5H, phenyl), 5.03 (d, 2H, CH_2Ph, J = 12.8 Hz), 4.67 (s, 2H, CH_2CCl$_3$), 4.38 (dd, 1H, H-6a, $J_{6a,5}$ = 5.2, $J_{6a,6b}$ = 11.8 Hz), 4.20 (t, 1H, H-6b, $J_{6b,5}$ = $J_{6b,6a}$ = 11.8 Hz), 3.60 (dd, 1H, H-5, $J_{5,6a}$ = 5.2, $J_{5,6b}$ = 11.8 Hz), 3.45 (m, 2H, H-4 and H-1′a), 3.33 (m, 1H, H-1′b), 1.98 (m, 1H, H-2′a), 1.62 (m, 1H, H-2′b); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 168.0, 156.3, 137.1, 129.0, 128.5, 128.4, 128.1, 94.8, 78.0, 71.7, 66.3, 56.8, 47.7, 40.0, 29.5, 14.8; FABMS-LR m/z 613 [(M + H)$^+$]; FABMS-HR calcd for $C_{17}H_{24}Cl_3N_4O_8S_3$ 612.9823, found 612.9828.

(4*S*)-4-(2-Acetoxy-1*S*-benzyloxycarbonylaminoethyl)-2-(2,2,2-trichloroethoxysulfonyl)iminotetrahydropyrimidine (43). Compound **42** (1.03 g, 1.68 mmol) in AcOEt (15 mL) was treated with saturated aq $NaHCO_3$ (15 mL) and $HgBr_2$ (725 mg, 2.0 mmol) at room temperature for 2 h. The insoluble portion was filtered off through a Celite pad, and the filtrate was partitioned between AcOEt and 1 M aq HCl. The organic phase was washed with saturated aq $NaHCO_3$, H_2O, and saturated aq NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue in MeCN (20 mL) was treated with AcOH (106 μL, 1.84 mmol) and tetrabutylammonium acetate

(1.01 g, 3.36 mmol) at room temperature for 4 h. The resulting mixture was concentrated in vacuo. The residue was suspended in AcOEt (15 mL) and 0.4 M aq HCl (15 mL), and the resulting biphasic layers were vigorously stirred for 1 h. The organic phase was washed with saturated aq $NaHCO_3$ and saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (3 × 12 cm, 40% AcOEt/hexane) to afford **43** (750 mg, 82% over two steps) as a white foam: $[\alpha]^{22}_D$ −0.62 (*c* 1.03, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.81 (br d, 2H, N*H*-1 and 3, $J_{NH\text{-}1,6} = J_{NH\text{-}3,4}$ = 12.0 Hz), 7.50 (br d, 1H, N*H*-Cbz, *J* = 12.0 Hz), 7.34 (m, 5H, phenyl), 5.02 (d, 2H, CH_2Ph, *J* = 13.0 Hz), 4.56 (s, 2H, CH_2CCl$_3$), 4.17 (dd, 1H, H-2′a, $J_{2'a,1'}$ = 3.0, $J_{2'a,2'b}$ = 11.0 Hz), 3.99 (dd, 1H, H-2′b, $J_{2'b,1'}$ = 3.0, $J_{2'b,2'a}$ = 11.0 Hz), 3.76 (m, 1H, H-1′), 3.47 (m, 1H, H-4), 3.23 (m, 2H, H-6), 1.96 (s, 3H, OAc), 1.74 (m, 2H, H-5); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 170.6, 156.6, 153.8, 137.2, 128.6, 128.1, 127.9, 95.0, 77.3, 65.8, 63.7, 52.0, 49.4, 36.4, 20.8, 20.5; FABMS-LR *m*/*z* 545 [(M + H)$^+$]; FABMS-HR calcd for $C_{18}H_{24}Cl_3N_4O_7S$ 545.0431, found 545.0424.

(4*S*)-4-(1*S*-Benzyloxycarbonylamino-2-hydroxyethyl)-2-(2,2,2-trichloroethoxysulfonyl)iminotetrahydropyrimidine (44). A solution of **43** (53.2 mg, 0.098 mmol) in MeOH (20 mL) was treated with K_2CO_3 (138 mg, 1.00 mmol) at 0 °C for 45 min. The resulting mixture was neutralized by AcOH (114 μL, 2.0 mmol) and concentrated in vacuo. The residue was partitioned between AcOEt and saturated aq NaCl, and the organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (1 × 6 cm, 1% MeOH/$CHCl_3$) to afford **44** (49.0 mg, quant) as a white foam: $[\alpha]^{22}_D$ −4.43 (*c* 1.15, MeOH); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.81 (br s, 1H, N*H*-6), 7.65 (br s, 1H, N*H*-4), 7.31 (m, 5H, phenyl), 7.26 (br d, 1H, N*H*-Cbz, $J_{NH,1'}$ = 9.0 Hz), 5.01 (s, 2H, CH_2Ph), 4.93 (br s, 1H, OH), 4.56 (s, 2H, CH_2CCl$_3$), 3.53 (m, 1H, H-1′), 3.49 (m, 2H, H-4 and H-2′), 3.24 (m, 1H, H-6a), 3.19 (m, 1H, H-6b), 1.72 (m, 1H, H-5a), 1.67 (m, 1H, H-5b); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 156.6, 153.9, 137.2, 128.7, 128.1, 128.0, 95.1, 77.4, 65.8, 61.3, 54.8, 50.4, 37.0, 21.1; FABMS-LR *m*/*z* 503 [(M + H)$^+$]; FABMS-HR calcd for $C_{16}H_{22}Cl_3N_4O_6S$ 503.0326, found 503.0324.

Ureido Alcohol (45). A mixture of **44** (252 mg, 0.50 mmol), $Pd(OH)_2$ (250 mg), and trichloroacetic acid (1.63 g, 10.0 mmol) in MeOH (10 mL) was vigorously stirred under H_2 atmosphere at room temperature for 35 min. The mixture was neutralized with $NaHCO_3$ (1.26 g), the insoluble was filtered off through Celite pad, and the filtrate was concentrated in vacuo. The residue was semipurified by silica gel column chromatography (2 × 2 cm, 10% MeOH/$CHCl_3$) to afford the amine, which was immediately used to the next step. A mixture of the amine, *N*-methylmorpholine (340 μL, 3.1 mmol) and (*S*)-*tert*-butyl *N*-(*S*-methylthiocarbonyl)valinate (**38**, 370 mg, 1.50 mmol) in AcOEt (10 mL) was treated with $HgBr_2$ (540 mg, 1.50 mmol) at room temperature for 3 h. The insoluble was filtered off through Celite pad, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (0.5 × 5 cm, 2% MeOH/$CHCl_3$) to afford **45** (181 mg, 64% over two steps) as a white foam: $[\alpha]^{22}_D$ −3.19 (*c* 3.30, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.83 (br s, 1H, N*H*-6), 7.61 (br s, 1H, N*H*-4), 6.27 (br d, 1H, N*H*-2-Val, *J* = 5.2 Hz), 6.26 (br d, 1H, N*H*-1′, *J* = 3.6 Hz), 4.96 (br t, 1H, OH, *J* = 6.9 Hz), 4.56 (s, 2H, CH_2CCl$_3$), 3.86 (dd, 1H, H-2-Val, $J_{2,NH}$ = 6.8, $J_{2,3}$ = 11.4 Hz), 3.65 (m, 1H, H-2′a), 3.55 (ddd, 1H, H-1′, $J_{1',4}$ = 4.6, $J_{1',2'a}$ = 11.4, $J_{1',2'b}$ = 16.5 Hz), 3.42 (m, 1H, H-2′b), 3.39 (m, 1H, H-4-*epi*-Cpm, $J_{4,1'}$ = 4.6 Hz), 3.29 (m, 1H, H-6a), 3.19 (dd, 1H, H-6b, $J_{6b,5}$ = 4.5, $J_{6b,6a}$ = 11.2 Hz), 1.95 (dd, 1H, H-3-Val, $J_{3,4}$ = 8.6, $J_{3,2}$ = 11.4 Hz), 1.72 (m, 2H, H-5), 1.32 (s, 9H, ^{t}Bu), 0.85 (d, 3H, H-4a-Val, $J_{4a,3}$ = 8.6 Hz), 0.82 (d, 3H, H-4b-Val, $J_{4b,3}$ = 8.6 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 172.0, 158.1, 153.7, 95.1, 80.4, 77.3, 60.9, 58.7, 52.3, 49.8, 36.6, 30.5, 27.9, 20.5, 19.3, 17.9; FABMS-LR *m*/*z* 591 [(M + Na)$^+$]; FABMS-HR calcd for $C_{18}H_{32}Cl_3N_5NaO_7S$ 590.0986, found 590.0981.

Ureido Carboxylic Acid (46). A mixture of **45** (83.1 mg, 0.146 mmol) and 2,2,6,6-tetramethyl-1-piperidinyloxy radical (2.28 mg, 0.015 mmol) in MeCN (2 mL) and phosphate buffer (pH 6.7, 0.67 M, 1.2 mL) was treated with $NaClO_2$ (39.6 mg, 0.53 mmol) and 5% aq NaClO (592 μL, 0.53 mmol) at room temperature for 15 min and at 40 °C for 10 min. The resulting mixture was partitioned between AcOEt and saturated aq $Na_2S_2O_3$, and the organic phase was washed with 1 M aq HCl and saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (1 × 3 cm, 4% MeOH/$CHCl_3$ containing 0.1% AcOH) to afford **46** (94.0 mg, quant) as a white foam: $[\alpha]^{22}_D$ −1.16 (*c* 0.83, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.83 (br s, 1H, N*H*-3), 7.69 (br s, 1H, N*H*-5), 6.58 (br d, 1H, N*H*-2-*epi*-Cpm, $J_{NH,2}$ = 9.0 Hz), 6.40 (br d, 1H, N*H*-2-Val, $J_{NH\text{-}2}$ = 8.7 Hz), 4.55 (s, 1H, CH_2CCl$_3$), 4.25 (t, 1H, H-2-Val, $J_{2,NH}$ = $J_{2,3}$ = 8.7 Hz), 3.94 (dd, 1H, H-2-*epi*-Cpm, $J_{2,3}$ = 5.0, $J_{2,NH}$ = 9.0 Hz), 3.70 (m, 1H, H-3-*epi*-Cpm, $J_{3,2}$ = 5.0 Hz), 3.30 (m, 1H, H-5a-*epi*-Cpm), 3.19 (m, 1H, H-5b-*epi*-Cpm), 1.95 (dt, 1H, H-3-Val, $J_{3,4a} = J_{3,4b}$ = 6.8, $J_{3,2}$ = 13.8 Hz), 1.68 (m, 2H, H-4-*epi*-Cpm), 1.39 (s, 9H, ^{t}Bu), 0.83 (t, 6H, H-4a and 4b-Val, $J_{4a,3} = J_{4b,3}$ = 6.8 Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 172.4, 171.9, 158.7, 153.6, 95.1, 80.3, 77.3, 58.8, 56.3, 53.5, 38.23, 30.6, 27.9, 22.8, 19.3, 18.1; FABMS-LR (negative mode) *m*/*z* 580 [(M − H)$^-$]; FABMS-HR calcd for $C_{18}H_{29}Cl_3N_5O_8S$ 580.0802, found 580.0790.

***tert*-Butyl 6-Benzyloxycarbonylamino-5-*O*-[5-*tert*-butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-*ribo*-pentofuranosyl]-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-β-D-*glycelo*-L-*talo*-heptofuranuronate (48).** Compound **47**[26a] (1.65 g, 2.09 mmol) in CH_2Cl_2 (23 mL) was treated with *t*-BuOC(NH)CCl_3 (1.17 mL, 6.6 mmol) and $BF_3\cdot OEt_2$ (66.0 μL, 0.52 mmol) at 0 °C for 8 h. $BF_3\cdot OEt_2$ (66.0 μL, 0.52 mmol) was further added to the mixture, which was stirred for an additional 10 h. The reaction mixture was quenched by saturated aqueous $NaHCO_3$ (10 mL), and the whole mixture was extracted by AcOEt. The organic phase was washed with saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by neutral silica gel column chromatography (3 × 15 cm, 33% AcOEt/hexane) to afford **48** (1.38 g, 66%) as a white foam: $[\alpha]^{22}_D$ +18.5 (*c* 3.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.44 (br s, 1H, N*H*-3), 7.31 (m, 6H, phenyl and H-6), 5.68 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.57 (s, 1H, H-1′), 5.54 (br d, 1H, N*H*-Cbz, $J_{NH,6'}$ = 6.3 Hz), 5.43 (br d, 1H, N*H*-Boc, $J_{NH,5''}$ = 9.2 Hz), 5.18 (d, 1H, CH_2Ph, *J* = 12.0 Hz), 5.07 (s, 1H, H-1″), 5.00 (d, 1H, CH_2Ph, *J* = 12.0 Hz), 4.93 (m, 1H, H-2′), 4.80 (m, 1H, H-3′), 4.53 (br s, 2H, H-6′, H-3″), 4.48 (d, 1H, H-2″, $J_{2'',3''}$ = 9.7 Hz), 4.32 (d, 1H, H-5′, $J_{5',4'}$ = 8.0 Hz), 4.21 (m, 1H, H-4″), 4.16 (m, 1H, H-4′), 3.23 (m, 1H, H-5″a), 3.06 (m, 1H, 5″b), 1.47 (m, 25H, ^{t}Bu, acetonide, and CH_2CH$_3$), 1.30 (s, 3H, acetonide), 0.77 (t, 6H, CH_2CH_3, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.8, 163.5, 156.3, 156.2, 150.1, 143.1, 136.3, 128.6, 128.4, 116.5, 115.0, 112.3, 102.6, 94.9, 87.1, 86.8, 86.5, 84.1, 83.4, 82.2, 81.1, 79.4, 67.3, 55.0, 43.4, 29.4, 28.9, 28.5, 28.1, 27.1, 25.5, 8.5, 7.4; FABMS-LR *m*/*z* 847 [(M + H)$^+$]; FABMS-HR calcd for $C_{41}H_{59}N_4O_{15}$ 847.3977, found 847.3978.

***tert*-Butyl 5-*O*-[5-*tert*-Butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-*ribo*-pentofuranosyl]-6-*N*-[3-(2,2,2-trichloroethoxycarbonylamino)propyl]amino-6-deoxy-2,3-*O*-isopropylidene-1-(uracil-1-yl)-β-D-*glycelo*-L-*talo*-heptofuranuronate (49).** A mixture of **48** (115 mg, 0.13 mmol) and 10% Pd/C (40 mg) in MeOH (2 mL) was vigorously stirred under H_2 atmosphere at room temperature for 30 min. The catalyst was filtered off through a Celite pad, and the filtrate was concentrated in vacuo to give a crude amine. A solution of the amine and 3-(2,2,2-trichloroethoxycarbonyl)aminopropanal (33 mg, 0.13 mmol) and AcOH (80 μL, 1.3 mmol) in CH_2Cl_2 (2 mL)

was treated with $NaBH(OAc)_3$ (85 mg, 0.39 mmol) at room temperature for 30 min. The reaction was quenched by saturated aqueous $NaHCO_3$ (500 μL), and the whole mixture was partitioned between AcOEt and saturated aq $NaHCO_3$. The organic phase was washed with saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by neutral silica gel column chromatography (2 × 2 cm, 60% AcOEt/hexane) to afford **49** (119 mg, 94% over two steps) as a white foam: $[\alpha]^{22}_D$ +38.6 (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.67 (br s, 1H, N*H*-3), 7.21 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.98 (br s, 1H, N*H*-Troc), 5.75 (br s, 1H, N*H*-Boc), 5.68 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.46 (s, 1H, H-1′), 5.17 (d, 1H, H-2′, $J_{2',3'}$ = 5.7 Hz), 4.95 (s, 1H, H-1″), 4.84 (t, 1H, H-3′, $J_{3',2'}$ = $J_{3',4'}$ = 5.7 Hz), 4.75 (d, 1H, CH_2CCl$_3$, *J* = 13.0 Hz), 4.69 (d, 1H, CH_2CCl$_3$, *J* = 13.0 Hz), 4.55 (m, 2H, H-4′ and 3″, $J_{4',3'}$ = 5.7 Hz), 4.49 (m, 1H, H-2″), 4.22 (m, 1H, H-4″), 4.08 (m, 1H, H-5′), 3.33 (d, 2H, H-8′, $J_{8'a,8'b}$ = 5.2 Hz), 3.26 (m, 1H, 5″a), 3.23 (s, 1H, H-6′), 3.05 (d, 1H, 5″b, $J_{5''b,5''a}$ = 6.9 Hz), 2.90 (m, 1H, H-10′a), 2.33 (m, 1H, H-10′b), 1.70 (m, 1H, H-9′a), 1.56 (m, 1H, H-9′b), 1.55 (s, 4H, CH_2CH$_3$), 1.51 (s, 9H, ^{t}Bu), 1.44 (s, 12H, ^{t}Bu and acetonide), 1.37 (s, 3H, acetonide), 0.76 (m, 6H, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.0, 162.9, 156.1, 154.5, 149.9, 143.8, 115.9, 114.8, 112.8, 102.3, 96.7, 95.8, 89.0, 86.7, 84.8, 82.6, 82.0, 81.8, 81.5, 79.0, 74.4, 62.5, 45.2, 43.3, 38.7, 29.3, 28.8, 28.4, 28.2, 26.8, 25.1, 8.4, 7.3; ESIMS-LR *m*/*z* 946 [(M + H)$^+$]; ESIMS-HR calcd for $C_{39}H_{61}Cl_3N_5O_{15}$ 944.3222, found 944.3230.

***tert*-Butyl 5-*O*-[5-*tert*-Butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-*ribo*-pentofuranosyl]-6-deoxy-6-*N*-(3-formylaminopropyl)amino-2,3-*O*-isopropylidene-1-(uracil-1-yl)-β-D-*glycelo*-L-*talo*-heptofuranuronate (50).** A mixture of **49** (28.9 mg, 0.031 mmol) and NH_4Cl (50.0 mg, 0.93 mmol) in MeOH (1 mL) was treated with activated Zn powder (85% purity, 33.3 mg, 0.51 mmol) at room temperature for 2 h. The insoluble portion was filtered off through a Celite pad, and the filtrate was concentrated in vacuo. A mixture of the residue and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 35 mg, 0.18 mmol) in CH_2Cl_2 (1 mL) at 0 °C was treated with formic acid (10.0 μL, 0.25 mmol) for 15 h. The mixture was partitioned between AcOEt and H_2O, and the organic phase was washed with saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by neutral silica gel column chromatography (2 × 4 cm, 66% AcOEt/hexane containing 3% MeOH) to afford **50** (30.4 mg, 99% over two steps) as a white foam: $[\alpha]^{22}_D$ +30.7 (*c* 1.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.67 (br s, 1H, N*H*-3), 7.21 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.98 (br s, 1H, N*H*-Troc), 5.75 (br s, 1H, N*H*-Boc), 5.68 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.46 (s, 1H, H-1′), 5.17 (d, 1H, H-2′, $J_{2',3'}$ = 5.7 Hz), 4.95 (s, 1H, H-1″), 4.84 (t, 1H, H-3′, $J_{3',2'}$ = $J_{3',4'}$ = 5.7 Hz), 4.75 (d, 1H, CH_2CCl$_3$, *J* = 13.0 Hz), 4.69 (d, 1H, CH_2CCl$_3$, *J* = 13.0 Hz), 4.55 (m, 2H, H-4′ and 3″, $J_{4',3'}$ = 5.7 Hz), 4.49 (m, 1H, H-2″), 4.22 (m, 1H, H-4″), 4.08 (m, 1H, H-5′), 3.33 (d, 2H, H-8′, $J_{8'a,8'b}$ = 5.2 Hz), 3.26 (m, 1H, 5″a), 3.23 (s, 1H, H-6′), 3.05 (d, 1H, H-5″b, $J_{5''b,5''a}$ = 6.9 Hz), 2.90 (m, 1H, H-10′a), 2.33 (m, 1H, H-10′b), 1.70 (m, 1H, H-9′a), 1.56 (m, 1H, H-9′b), 1.55 (s, 4H, CH_2CH$_3$), 1.51 (s, 9H, ^{t}Bu), 1.44 (s, 12H, ^{t}Bu and acetonide), 1.37 (s, 3H, acetonide), 0.76 (m, 6H, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.1, 162.9, 156.1, 154.5, 149.9, 143.8, 116.0, 114.8, 112.8, 102.3, 96.7, 95.8, 89.0, 86.7, 84.8, 82.6, 82.0, 81.8, 81.5, 79.0, 74.4, 62.5, 45.2, 43.3, 38.7, 29.3, 28.8, 28.4, 28.2, 26.8, 25.1, 8.4, 7.3; ESIMS-LR *m*/*z* 798 [(M + H)$^+$]; ESIMS-HR calcd for $C_{37}H_{60}N_5O_{14}$ 798.4137, found 798.4142.

***tert*-Butyl 5-*O*-[5-*tert*-Butoxycarbonylamino-5-deoxy-2,3-*O*-(3-pentylidene)-β-D-*ribo*-pentofuranosyl]-6-deoxy-6-(3-isocyanopropyl)amino-2,3-*O*-isopropylidene-1-(uracil-1-yl)-β-D-*glycelo*-L-*talo*-heptofuranuronate (51).** A mixture of **50** (20 mg, 0.025 mmol) and Et_3N (62.0 μL, 0.45 mmol) in CH_2Cl_2 (2 mL) was treated with triphosgene (22.0 mg, 0.075 mmol) at −78 °C for 20 min. The mixture was partitioned between AcOEt and saturated aq $NaHCO_3$, and the organic phase was washed with saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo to give **51** (19.5 mg, quant) as a white foam: $[\alpha]^{22}_D$ +26.2 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.68 (br s, 1H, N*H*-3), 7.22 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.81 (br s, 1H, N*H*-Boc), 5.67 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.47 (s, 1H, H-1′), 5.14 (d, 1H, H-2′, $J_{2',3'}$ = 6.4 Hz), 4.97 (s, 1H, H-1″), 4.77 (dd, 1H, H-3′, $J_{3',2'}$ = 6.4, $J_{3',4'}$ = 5.6 Hz), 4.51 (m, 3H, H-4′, 2″ and 3″), 4.22 (m, 1H, H-4″), 4.07 (m, 1H, H-5′), 3.50 (m, 2H, H-10′), 3.20 (m, 2H, H-6′, 5″a), 3.09 (ddd, 1H, H-5″b, $J_{5''b,NH}$ = 4.0, $J_{5''b,4''}$ = 7.2, $J_{5''b,5''a}$ = 15.1 Hz), 2.91 (dt, 1H, H-8′a, $J_{8'a,9'a}$ = 5.7, $J_{8'a,9'b}$ = $J_{8'a,8'b}$ = 12.0 Hz), 2.44 (dt, 1H, H-8′b, $J_{8'b,9'a}$ = 6.0, $J_{8'b,9'b}$ = $J_{8'b,8'a}$ = 12.0 Hz), 1.77 (m, 2H, H-9′), 1.56 (s, 4H, CH_2CH$_3$), 1.51 (s, 9H, ^{t}Bu), 1.44 (s, 9H, ^{t}Bu), 1.35 (s, 3H, acetonide), 1.24 (s, 3H, acetonide), 0.75 (m, 6H, CH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 162.9, 156.1, 155.4, 149.8, 143.7, 115.9, 114.7, 112.8, 102.3, 96.5, 88.5, 86.8, 86.6, 84.9, 82.7, 82.0, 81.9, 79.0, 61.5, 45.7, 44.0, 43.1, 39.2, 29.7, 29.3, 28.7, 28.4, 28.2, 27.0, 25.2, 8.4, 7.2; ESIMS-LR *m*/*z* 802 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{37}H_{57}N_5NaO_{13}$ 802.3851, found 802.3824.

(−)-Muraymycin D2 and *epi*-Muraymycin D2 (53). Carboxylic acid **46** (33.0 mg, 0.052 mmol), isovaleraldehyde (19.5 μL, 0.13 mmol), and 2,4-dimethoxybenzylamine (19.2 μL, 0.13 mmol) in EtOH (1 mL) were concentrated in vacuo. The residue was coevaporated with EtOH (1 mL), and this was repeated 3 times. The residue and the isonitrile **51** (20.9 mg, 0.026 mmol) in EtOH (1 mL) were concentrated in vacuo, and the resulting syrup was kept at room temperature for 72 h. The mixture was diluted with AcOEt, and the solution was washed with H_2O and saturated aq NaCl, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by neutral silica gel column chromatography (0.5 × 2 cm, 66% AcOEt/hexane) to afford **52** (22.0 mg, 54%, ESIMS-LR *m*/*z* 1621 [(M + Na)$^+$]) as a white foam. Compound **52** (8.7 mg, 5.6 mmol) in THF (1 mL) and 1 M aq NaH_2PO_4 (500 μL) was treated with Zn (5.7 mg, 0.088 mmol) at room temperature for a week. After the mixture was concentrated in vacuo, the residue was suspended in AcOEt. The resulting insoluble was filtered off through a short silica gel pad, and the filtrate was concentrated in vacuo. The residue was treated with 80% aq TFA at room temperature for 8 h. After the mixture was concentrated in vacuo, the residue was purified by HPLC (YMC J′sphere ODS M80, 4.6 × 150 mm, 0.1% TFA, 23% MeOH−H_2O, 7.2 min for **53**, 20.0 min for muraymycin D2) to afford (−)-muraymycin D2 (2.6 mg, 52%) and **53** (2.4 mg, 48%) as a white foam. Data for muraymycin D2: $[\alpha]^{22}_D$ −3.33 (*c* 0.32, H_2O); ^{1}H NMR (D_2O, 500 MHz) δ 7.72 (d, 1H, H-6, J_{6-5} = 8.0 Hz), 5.89 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.82 (s, 1H, H-1′), 5.23 (s, 1H, H-1″), 4.61 (d, 1H, H-5′, $J_{5',6'}$ = 3.5 Hz), 4.45 (t, 1H, H-2′, $J_{2',3'}$ = $J_{2',1'}$ = 3.7 Hz), 4.41 (d, 1H, H-2-*epi*-Cpm, $J_{2,3}$ = 7.5 Hz), 4.33 (m, 1H, H-3′), 4.30 (m, 1H, H-3′), 4.27 (m, 1H, H-2-Leu), 4.16−4.17 (m, 3H, H-2″, 3″ and 4″), 3.99 (s, 1H, H-6′), 3.92 (d, 1H, H-2-Val, $J_{2,3}$ = 5.2 Hz), 3.95 (dd, 1H, H-3-*epi*-Cpm, $J_{3,4a}$ = 6.6, $J_{3,4b}$ = 12.3 Hz), 3.35 (m, 2H, H-5-*epi*-Cpm), 3.31 (m, 1H, H-5″a), 3.27 (t, 2H, H-10′, $J_{10',9'a}$ = $J_{10',9'b}$ = 6.0 Hz), 3.18 (m, 1H, H-8′), 3.14 (dd, 1H, H-5″b, $J_{5''b,4''}$ = 8.0, $J_{5''b,5''a}$ = 13.8 Hz), 2.11 (ddd, 1H, H-3-Val, $J_{3,4a}$ = 3.4, $J_{3,4b}$ = 6.3, $J_{3,2}$ = 12.6 Hz), 1.91 (m, 2H, H-4-*epi*-Cpm), 1.91 (m, 2H, H-9′), 1.67 (m, 1H, H-3a-Leu), 1.61 (m, 1H, H-4-Leu), 1.55 (m, 1H, H-3b-Leu), 0.94 (d, 6H, H-4-Val and H-5-Leu, *J* = 6.3 Hz), 0.87 (m, 3H, H-4-Val), 0.86 (d, 3H, H-4-Leu, $J_{5,4}$ = 5.3 Hz); ^{13}C NMR (D_2O, 125 MHz) δ 177.5, 174.9, 171.9, 170.9, 166.1, 159.1, 153.9, 151.4, 142.6, 109.0, 102.3, 91.9, 84.4, 79.0, 75.8, 74.8, 72.5, 71.9, 69.2, 63.6, 59.5, 55.7, 52.7, 49.5, 45.8, 42.5, 39.7, 36.0, 35.9, 30.2, 25.2, 24.4, 22.2, 20.6, 20.5, 18.7, 16.9; ESIMS-LR *m*/*z* 458 [(M + 2H)$^{2+}$]; ESIMS-HR calcd for

$C_{37}H_{61}N_{11}O_{16}$ 915.4298, found 915.4337. Data for **32**: $[\alpha]^{22}_{D}$ +3.25 (*c* 0.37, H_2O); ^{1}H NMR (D_2O, 500 MHz) δ 7.73 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.90 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.84 (s, 1H, H-1′), 5.21 (s, 1H, H-1″), 4.62 (s, 1H, H-5′), 4.43 (s, 1H, H-2′), 4.35 (m, 3H, H-3′,4′ and H-2-*epi*-Cpm), 4.19 (m, 4H, H-2″,3″,4″ and H-2-Leu), 4.00 (m, 1H, H-2-Val), 3.98 (s, 1H, H-6′), 3.89 (m, 1H, H-3-*epi*-Cpm), 3.36 (m, 4H, H-5″ and H-5-*epi*-Cpm), 3.20 (m, 3H, H-10′ and H-8′a), 3.17 (m, 1H, H-8′b), 2.15 (m, 1H, H-3-Val), 1.92 (m, 3H, H-9′a and H-4-*epi*-Cpm), 1.84 (m, 1H, H-9′b), 1.61 (m, 4H, H-3 and H-4-Leu), 0.95 (d, 6H, H-4-Val and H-5-Leu, *J* = 8.0 Hz), 0.93 (m, 6H, H-4-Val and H-4-Leu); ^{13}C NMR (D_2O, 125 MHz) δ 177.5, 175.0, 172.3, 170.8, 166.1, 159.2, 153.7, 151.3, 142.6, 108.9, 102.2, 91.8, 84.4, 79.1, 75.7, 74.9, 72.6, 71.9, 69.0, 63.5, 59.6, 55.8, 52.9, 49.5, 45.2, 42.4, 39.5, 35.7, 35.5, 29.9, 25.0, 24.5, 22.3, 20.6, 20.3, 18.7, 17.0; ESIMS-LR *m*/*z* 458 [$(M + 2H)^{2+}$]; ESIMS-HR calcd for $C_{37}H_{61}N_{11}O_{16}$ 915.4298, found 915.4343.

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Supporting Information Available: NMR data for ^{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.