^{1}H NMR δ 7.82 (d, **26** and **27**, J = 8.4 Hz, 2 H), 7.40–7.23 (complex, **26** and **27**, 7 H), 6.93 (s, **26**) and 6.25 (s, **27**, total 1 H), 3.81 (t, **27**, J = 6.0 Hz) and 3.60 (t, **26**, J = 6.3 Hz, total 2 H), 2.68 (t, **27**, J = 6.0 Hz), 2.48 and 2.45 (2 s superimposed on t, **26** and **27**, total 5 H), δ 1.7 (br s, **26** and **27**, 1 H); mass spectrum, m/z (relative intensity, %) 398 (20 M^+), 243 (17, $M^+ - ArSO_2^{\bullet}$), 213 (38), 183 (48), 157 (63, $PhSe^+$), 155 (50, $ArSO_2^+$), 91 (100, $C_7H_7^+$); exact mass calcd for $C_{17}H_{18}O_4SSe$ 398.0091, found 398.0103. Inclusion of triethylamine did not improve the yield.

4-Pentynoic Acid. The reaction of selenenyl sulfonate **1** (1.00 mmol) with 4-pentynoic acid (98 mg, 1.00 mmol) and triethylamine (0.139 mL, 1.00 mmol) was carried out as in the case of 4-pentenoic acid. Preparative TLC of the crude product in 50% dichloromethane–hexane afforded 41 mg (16%) of the products **28** and **29** in the ratio of 3:1 (NMR integration), with NMR and IR spectra as reported in the literature.[36]

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

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Electrochemical Oxidation of Proline Derivatives: Total Syntheses of Bulgecinine and Bulgecin C

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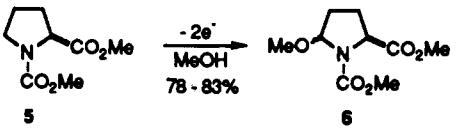
The influence of structure on the efficiency of the electrochemical C-5 oxidation of (2*S*,4*S*)-hydroxyproline carbamate esters is presented. Optimum methoxylation was observed with (2*S*,4*S*)-4-acetoxy-1,2-pyrrolidinedicarboxylic acid 2-methyl 1-(2-(trimethylsilyl)ethyl) ester (**19**). The corresponding C-5 methoxy derivative **20** was converted into bulgecinine (**4**) via a stereospecific radical homologation to incorporate the C-5 hydroxymethyl substituent. Bulgecin C (**1c**) was prepared via a β-stereoselective glycosidation reaction using a 2-azido-2-deoxy-α-D-glucopyranosyl trichloroacetimidate derivative, regiospecific C-4′ sulfation, and deprotection.

The bulgecins A (**1a**), B (**1b**), and C (**1c**), SQ-28504 (**2**), and SQ-28546 (**3**) are potent β-lactam synergists found in the culture broth of *Pseudomonas acidophila*, *Pseudomonas mesoacidophila*,[1] and *Chromobacterium violaceum*.[2] These natural products mediate, in concert with β-lactams, the development of bulges in the cell wall of Gram-negative bacteria. These curious morphological changes are accompanied by an increased sensitivity of the organism to inhibition and as a result, bacteria are killed at lower β-lactam concentrations. However, none of these glycopeptide sulfates exhibit antibacterial activities when administered alone. In consequence of these unusual biological effects and structural novelty, the bulgecins have been the subject of synthetic investigations. The bulgecin aglycon, bulgecinine (**4**), has been synthesized from D-glucose,[3] D-glucuronic acid,[4] pyroglutamic acid,[5] and an L-allylglycine derivative.[6] Additionally, Shiba and coworkers have reported the syntheses of bulgecin A (**1a**), 6-deoxybulgecin A, and 5-dehydroxymethylbulgecin A.[7]

Scheme I



5 **6**

Herein we report studies on the electrochemical oxidation of several proline derivatives, the use of radical chemistry to stereoselectively functionalize C-5 of proline, and experimental details on the first total synthesis of bulgecin C (**1c**).[8]

Electrochemical Oxidations of Proline Derivatives. Shono and co-workers have reported that carbamates including the proline derivative **5** may be regioselectively oxidized by electrolysis in methanol to provide the corresponding carbinolamine ether **6** (Scheme I).[9] This methodology should be applicable for the concise conversion of commercial (4*R*)-4-hydroxyproline (**7**) into bulgecinine (**4**) via anodic oxidation and subsequent homologation at C-5. The amino acid **7** was smoothly converted into the (4*S*)-ester **9** by protection[10] and esterification using the excellent Mitsunobu procedure[11] (Scheme II). However, much to our disappointment, the anodic oxidation of **9** proceeded to give a legion of products that may have contained the desired ether **10** (≤5%). This poor conversion stands in stark contrast to successful anodic oxidations of proline derivatives lacking a 4-substituent.[12]

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(3) Wakamiya, T.; Yamanoi, K.; Nishikawa, M.; Shiba, T. *Tetrahedron Lett.* **1985**, *26*, 4759.
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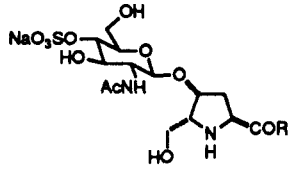
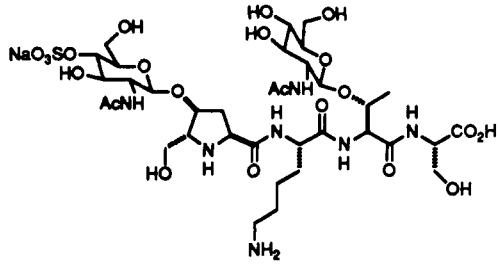
(10) Greene, T. W. *Protective Groups in Organic Synthesis*; J. Wiley and Sons: New York, 1981.
(11) Mitsunobu, O. *Synthesis* **1981**, 1.

0022-3263/91/1956-2787$02.50/0

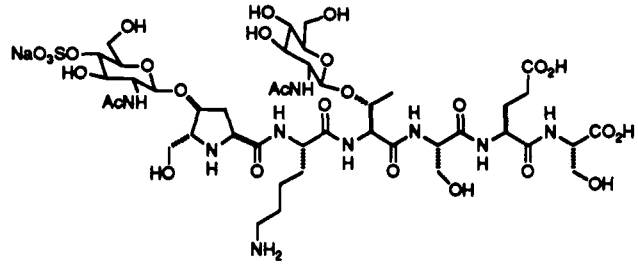


1

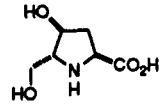
a R = $NHCH_2CH_2SO_3H$
b R = $NHCH_2CH_2CO_2H$
c R = OH



2



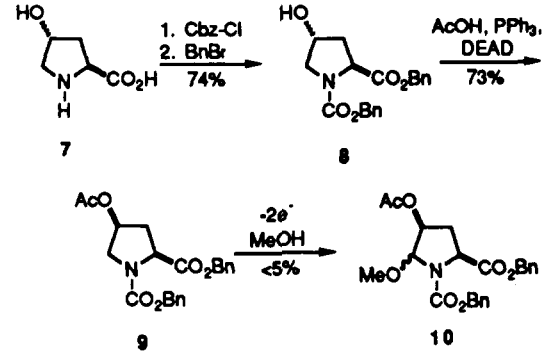
3



4

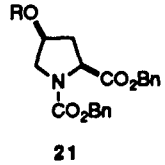
Thus, in order to optimize the reaction, we examined the electrochemical oxidation of several 4-substituted prolines, **9**, **11**, **13**, **15**, **17**, and **19**, in which the protecting groups were systematically varied. The substrates for electrochemical oxidations were all easily prepared from commercial 4(*R*)-hydroxyproline (**7**). Mitsunobu reaction of **8** with formic acid gave **21a** (55%), and this was readily transesterified to provide the alcohol **21b** (92%). Pivaloylation and methylation of **21b** gave the ester **11** (100%) and methyl ether **13** (31%), respectively. In the second case, partial epimerization gave a second methyl ether product **23** (25%). Selective methanolysis of **8** gave **24e**, and this was directly esterified under Mitsunobu conditions to produce **15** (53%). The methyl and TEOC carbamates **17** (46%) and **19** (63%) were respectively prepared from **22b** and **24f** again using the Mitsunobu reaction to ensure clean 4*S* stereochemistry. All the NMR spectra for these proline derivatives showed signal duplication due to hindered inversion of the carbamate residues. Thus in order to be certain that **9**, **11**, **13**, **15**, **17**, **19**, and **21a** were all diastereoisomerically pure, we undertook the syntheses of the corresponding (4*R*)-trans derivatives **24a**, **24b**, **24c**, **24d**, and **24g**. Direct acylation of **8** gave the acetate **24a** (85%), formate **24b** (91%), and

Scheme II



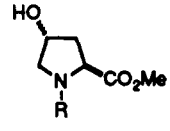
7 8 9 10

pivaloate **24c** (81%). Alternatively methylation of **8** gave only **24d** (66%). Examination of this material unequivocally established the identities of the two (4*S*)-methyl ethers **13** and **23**. The TEOC protected system **24g** was readily prepared from **22a** by N-protection using 2-(trimethylsilyl)ethyl azidoformate[14] (82%) and acetylation (94%). Comparisons of compounds with the 4*R* and 4*S* stereochemistries clearly established the stereochemical purity of all the substrates used for anodic oxidations.



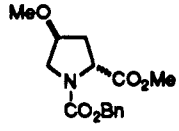
21

a R = HCO
b R = H

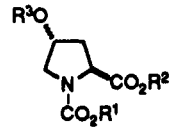


22

a R = H_2Cl
b R = CO_2Me



23



24

a $R^1 = R^2 = Bn$, $R^3 = Ac$
b $R^1 = R^2 = Bn$, $R^3 = HCO$
c $R^1 = R^2 = Bn$, $R^3 = t\text{-}BuCO$
d $R^1 = R^2 = Bn$, $R^3 = Me$
e $R^1 = Bn$, $R^2 = Me$, $R^3 = H$
f $R^1 = CH_2CH_2SiMe_3$, $R^2 = Me$, $R^3 = H$
g $R^1 = CH_2CH_2SiMe_3$, $R^2 = Me$, $R^3 = Ac$

The electrochemical oxidation results are summarized in Table I. The poor oxidation yield of **9** (entry 1) was originally conjectured to be caused by the methanolysis of the 4-*O*-acetate. However, the anodic oxidation of the more stable 4-*O*-pivaloate **11** afforded only 10% of a methoxylated product that may have been **12** (entry 2), while the oxidation of the 4-methoxy derivative **13** produced very little of the 4,5-dimethoxy compound **14** (<5%, entry 3). That the methanolysis of the benzyl ester did not contribute to the low oxidation yields was demonstrated by the low conversion of the methyl ester **15** to **16** (19%, entry 4). The workup conditions in entry 4 included an acetylation step to reprotect any hydrolyzed 4-*O*-acetate, further insuring that methanolysis was not a significant factor. These results clearly show that methanolysis of the 2- or 4-protecting group was not a major cause of the poor yields. Nor was the oxidation of the

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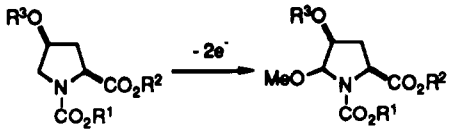
Table I. Anodic Oxidation of Proline Derivatives

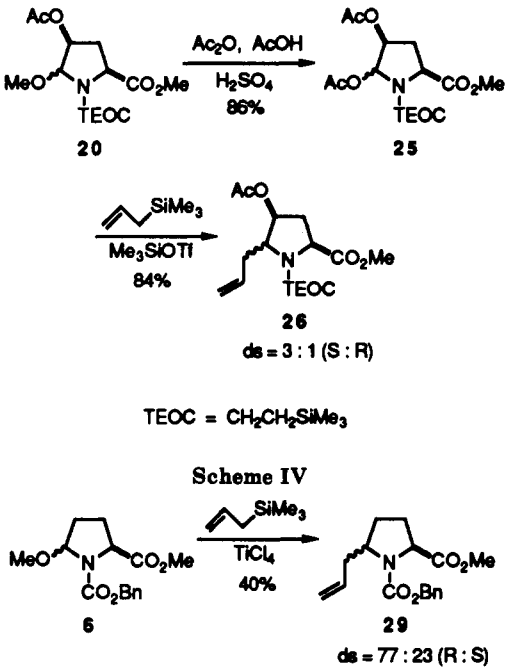


entry	compd	R^1	R^2	R^3	compd	yield (%)
1	9	Bn	Bn	Ac	10	<5
2	11	Bn	Bn	Piv	12	<10
3	13	Bn	Bn	Me	14	<5
4	15	Bn	Me	Ac	16	<19
5	17	Me	Me	Ac	18a/18b	52
6	19	2-TMS-Et	Me	Ac	20	66

various isolated functional groups on the pyrrolidine ring a likely cause of the poor yields because there are many reported examples showing the compatibility of this procedure with ether linkages, various carbamates, and esters.[12] One possible explanation that could account for the low yields is that the anodic oxidation at the electrode surface is sensitive to steric congestion.[13] Consistent with this postulate we found that switching to sterically less demanding nitrogen-protecting groups resulted in superior yields of methoxylated derivatives. The *O*-methyl carbamate **17** was converted in good yield (52%) to the methoxylated compounds **18a** and **18b** (entry 5). Similarly, the *O*-2-(trimethylsilyl)ethyl carbamate **19** was smoothly and cleanly oxidized in good yield (66%) to give the 5-methoxy derivative **20** (entry 6). Presumably in the more sterically congested systems **9**, **11**, **13**, and **15**, competitive electrochemical oxidations at benzylic centers took place, resulting in complex reaction mixtures. The successful oxidations of **17** and **19** are fully in accord with Thaning and Wistrand's studies on the anodic methoxylation of 4(*R*)- and 4(*S*)-acetoxyprolineamides.[15] For the subsequent synthesis of bulgecinine (**4**), compound **20** with the more easily removed TEOC group was employed to protect the nitrogen.

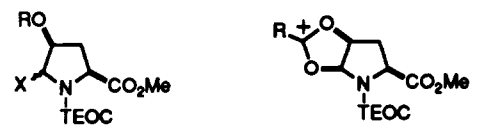
C-5 Alkylation of Carbinolamine 20 and Synthesis of Bulgecinine (4). We anticipated that it should be possible to stereoselectively homologate ether **20** by reaction with a carbon-centered nucleophile under Lewis acidic conditions.[15,16] Additionally we hoped that the process would proceed with excellent trans-stereochemical control as a result of neighboring group participation via acetoxonium ion formation.[17] In a related study Thaning and Wistrand showed that the stereoselectivity of such displacement reactions on the proline ring system depended on the stereochemistry of the C4-acetate. Selective trans allylation was observed only with the (4*R*)-acetate.[15] Although **20** was slow to react with carbon nucleophiles, the derived acetate **25** was easily homologated using excess allyltrimethylsilane in the presence of trimethylsilyl trifluoromethanesulfonate. Unfortunately the product **26** (84%) was formed as a mixture of isomers with the undesired (5*S*)-cis compound as the major component (3:1). The 2,5-trans stereochemistry of the minor isomer was assigned on the basis of the small coupling constant between H-4 and H-5.[15,16] Alternative carbon-centered nucleophiles were also examined. Propargyltrimethylsilane[16,18] and trimethylsilyl cyanide respectively gave **27a**

Scheme III



Scheme IV

(15%) and **27b** (25%). Again both these substances were produced as mixtures of diastereoisomers (~1:1). It is clear from these results that the acetoxonium ion **28a** is not an important intermediate on the reaction coordinate.



27

a R = Ac, X = CH=C=CH$_2$
b R = Ac, X = CN
c R = PhCO, X = OMe
d R = PhCO, X = OAc
e R = PhCO, X = CH$_2$CH=CH$_2$

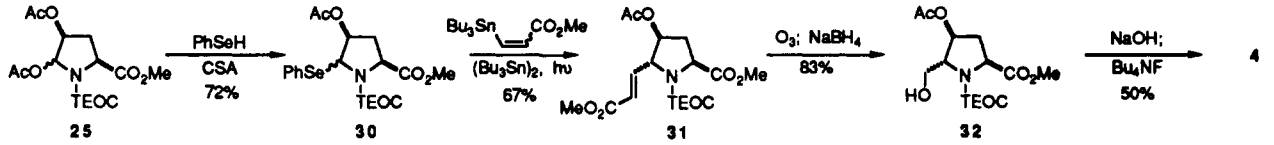
28

a R = Me
b R = Ph

In order to try to salvage the approach, **20** was converted via **27c** into the benzoate **27d** (61%). Since the benzoyloxonium cation **28b** should be lower in energy than **28a**,[19] higher trans diastereoselectively may be observed. This was indeed the case since reaction of **27d** with allyltrimethylsilane and trimethylsilyl trifluoromethanesulfonate gave **27e**. However, the selectivity had only increased from 1:3 to 1:1. It is clear from all these results that the intermediacy of the acyloxonium intermediates **28** are of little consequence. Indeed the nucleophilic substitution

(15) Thaning, M.; Wistrand, L.-G. *Helv. Chim. Acta* **1986**, *69*, 1711.
(16) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200. Schinzer, D. *Synthesis* **1988**, 263.
(17) Structurally related acetoxonium ions are presumably involved in the β-specific kinetic N-glycosidation technology of Vorbrüggen. See: Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234.
(18) Klaver, W. J.; Moolenaar, M. J.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1988**, *44*, 3805.
(19) Sato, S.; Nunomura, S.; Nakano, T.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1988**, *29*, 4097.

Scheme V

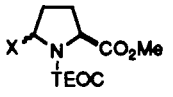


TEOC = $CH_2CH_2SiMe_3$

of both **25** and **27d** closely follow the stereochemical outcome observed on the substitution reactions of prolines lacking C-4 oxygenation[12] and 4(*S*)-acetoxyprolineamides.[15] Such transformations are exemplified in Scheme IV.

Since the nucleophilic substitution reactions of **25** proved unrewarding, we examined a complementary radical strategy. Reaction of acetate **25** with PhSeH smoothly provided selenide **30** (Scheme V). Irradiation of **30** with hexabutyldistannane and methyl (*E*)- or (*Z*)-2-(tributylstannyl)acrylate[20,21] cleanly gave adduct **31** as a single diastereoisomer in 67% yield. The trans-2,5 stereochemistry was indicated by the small coupling constant between H-4 and H-5[16] and the *E* geometry from the large *J* value. Ozonolysis with a sodium borohydride workup gave **32** (83%), and this substance was deprotected to provide bulgecinine (**4**) (50%). The material exhibited mp, $[\alpha]_D$, and ^1H and ^{13}C NMR spectra in agreement with data published for authentic material.[22]

The stereospecificity of the above free-radical addition reaction is undoubtedly due to steric approach control where the C4 substituent is exerting a strong influence toward trans addition. But does the C2 substituent, which adopts an axial position to avoid occupying the plane of the carbamate, play a role in determining the stereochemical outcome of this free radical addition? To test for this possible influence, the free-radical addition reaction was repeated with the desacetoxy derivative **33d**. This

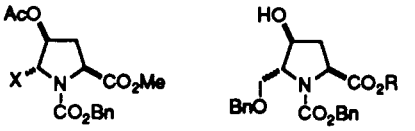


33

a X = H
b X = OMe
c X = OAc
d X = SePh
e X = (E)-MeO_2CCH=CH

selenide **33d** was prepared from (*S*)-proline via the carbamate **33a**, electrochemical oxidation to produce **33b**, and acetate **33c**. On irradiation with hexabutyldistannane and methyl (*Z*)-2-tributylstannylacrylate **33d** gave the desacetoxy compound **33e** as a 1:3 mixture of cis:trans isomers. Evidently, the axially disposed C2 substituent does provide a significant influence in determining the stereochemical outcome of this radical addition. It would appear therefore that the excellent stereochemical control in the radical conversion of **30** into **31** is the result of steric approach control by both the acetate and methyl ester residues. In contrast, the conversion of **25** into **26** results in low stereoselectivity since steric approach control, which favors the 5*R* stereochemistry, and stereoelectronics, which favors pseudoaxial allyl transfer, are mismatched.

Preparation of Bulgecin C (1c). Although the electrochemical oxidation of 4-hydroxyproline derivatives proceeded best with the TEOC protecting group, we were concerned as to the ease of deprotection after glycosidation and sulfation. Ideally global debenzylation would be the best strategy to reveal **1c** at the end of a synthesis. Thus alkene **31** was converted into the Cbz protected analogue **34a**[23] by cleavage of the TEOC group with trifluoroacetic acid followed by reprotection. Subsequent ozonolysis with a sodium borohydride workup and benzylation using benzyl bromide and silver(I) oxide in dichloromethane gave **34c** (88%). Zemplen methanolysis of **34c** gave **35a** (100%) whereas titanium tetraisopropoxide mediated transesterification in benzyl alcohol[24] gave **35b** (82%). Both these reactions resulted in concomitant cleavage of the 4-acetate residue.



34 **35**

a X = (E)-MeO_2CCH=CH
b X = CH_2OH
c X = CH_2OBn

a R = Me
b R = Bn

The corresponding glycosidating reagent **42** was prepared from 3,4,6-tri-*O*-acetyl-D-glucal via **36** using Schmidt methodology[25] (Scheme VI). Sequential benzylation of **36** and selective deprotection gave the diol **38**. Selective benzylation in the presence of bis(tributyltin) oxide,[26] C-4 benzoylation, and deprotection gave **41** as a mixture of anomeric alcohols. Reaction of **41** with trichloroacetonitrile in the presence of DBU[25] gave both the α-**42** and β-**43** trichloroacetimidates.

The pure α-trichloroacetimidate **42** was allowed to react with alcohol **35a** in the presence of boron trifluoride etherate to produce both the desired β-glycoside **44** (42%) and the α-anomer **45** (13%) (Scheme VII). Both the ^1H and ^{13}C NMR spectra of **44** and **45** were complex on account of signal duplication due to the proline carbamate residue. Nonetheless the two anomers were easily distinguished by comparisons of the anomeric carbons in the ^{13}C NMR spectra. Thus the double peak for **44** was observed at 100.9 and 100.5 and for **45** at 98.7 and 97.3.[27] Additionally the stereochemical assignment was confirmed by the conversion of **44** into bulgecin C (**1c**) (vide infra). The azide residue was cleanly reduced to directly produce the acetamide derivative **46** (80%) by reaction with thiolacetic acid.[28] Presumably this reaction involves azide reduction and subsequent acetylation with the byproduct diacetyl disulfide. The same glycosidation and acetylation tech-

(20) Baldwin, J. E.; Kelly, D. R. *J. Chem. Soc., Chem. Commun.* **1985**, 682. Russel, G. A.; Ngoviwatchai, P. *Tetrahedron lett.* **1985**, *26*, 4975.
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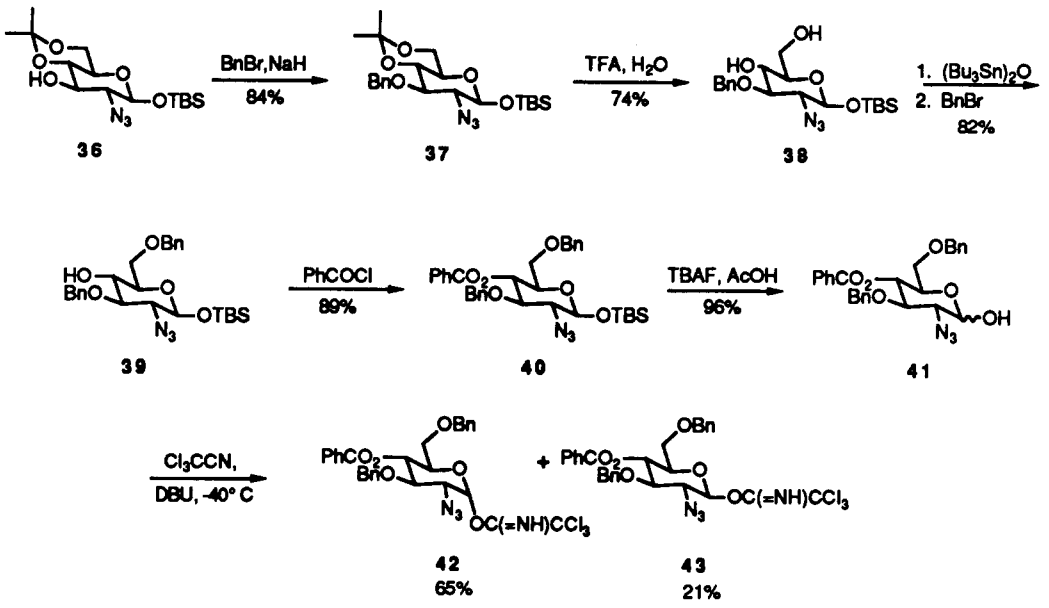
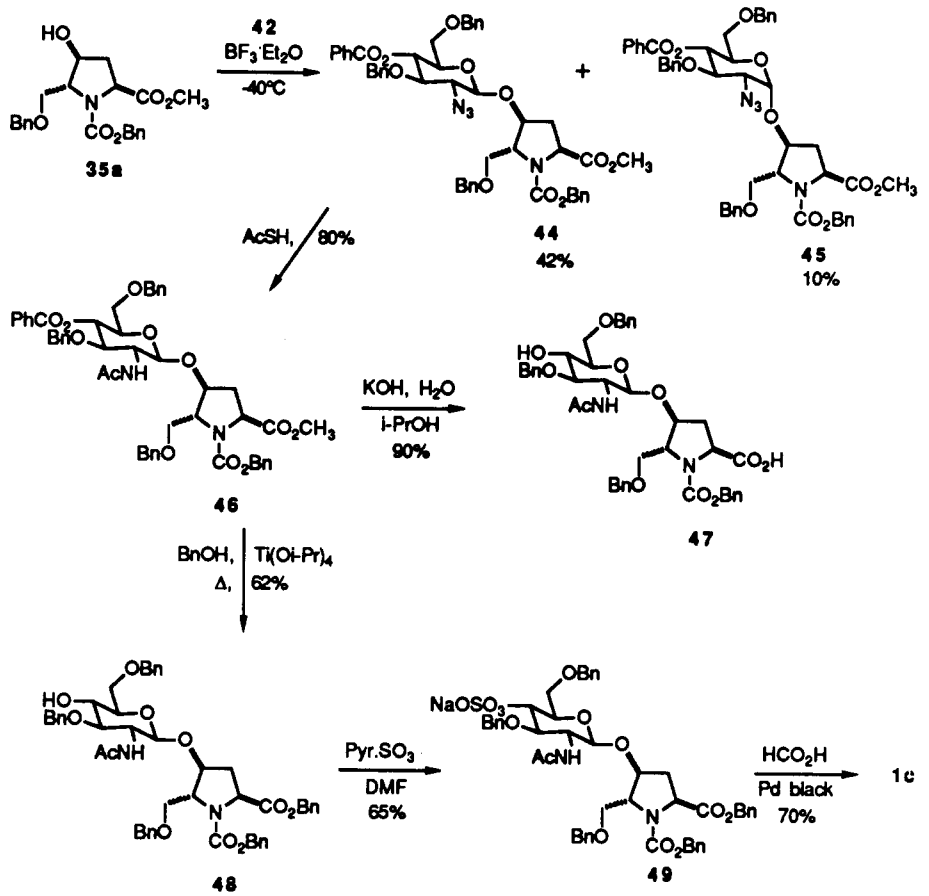
Scheme VI



Scheme VII



nologies were successful in converting alcohol **35b** into **50** (41% overall). Hydrolysis of diester **46** using aqueous potassium hydroxide in 2-propanol gave the hydroxy acid **47** (90%). In contrast, titanium tetraisopropoxide catalyzed transesterification gave the hydroxybenzyl ester **48** (62%). The same alcohol **48** (74%) was obtained from **50** by selective saponification using methanolic aqueous potassium hydroxide. All of these hydrolytic transformations proceeded without epimerization of the proline C-2 ester substituent. Sulfation of **48** using the pyridine–sulfur trioxide complex in DMF[29] gave the corresponding 4′-*O*-sulfate, and this was most conveniently isolated as the sodium salt **49**. The final global debenzylation, however, proved to be more challenging than originally anticipated. Attempted hydrogenolyses over palladium black, or palladium on carbon or barium sulfate at 1–3 atm of hydrogen were very slow. In addition mass recovery was poor and product isolation difficult. Presumably all these difficulties were the result of catalyst poisoning by the sulfate residue.

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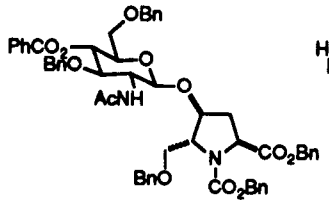
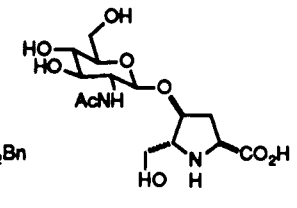
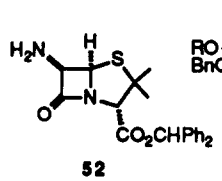
In contrast to **49**, the des-sulfate **47** was cleanly and rapidly hydrogenolyzed over palladium black to produce **51** (89%) as a crystalline solid. This substance showed identical data (mp, $[\alpha]_D$, and ^{13}C NMR spectrum) with that published for a sample of **51** prepared from bulgecin C (**1c**).[22] Although direct hydrogenolysis of **49** proved unacceptable, transfer hydrogenation using formic acid and palladium black[30] cleanly gave bulgecin C (**1c**) (70%). Much to our delight the product, $[\alpha]^{22}_D$ +6° (c = 0.51, 1 M AcOH in H_2O), was identical with an authentic sample of bulgecin C (**1c**), $[\alpha]_D$ +2.9° (c = 0.6, 1 M AcOH in H_2O) as judged by TLC behavior and spectroscopic data (IR, ^1H NMR, ^{13}C NMR). It should be noted that both the ^1H and ^{13}C NMR spectra showed considerable variations with concentration. Thus comparisons were made at identical concentrations.



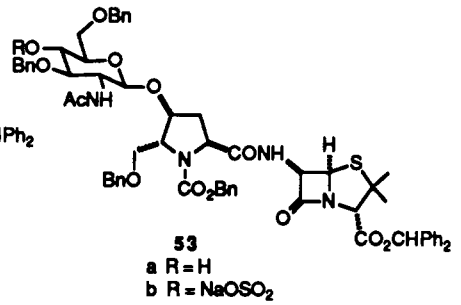
50



51



52



53
a R = H
b R = $NaOSO_2$

In addition to completing the synthesis of bulgecin C, we examined the synthesis of the penicillin bulgecin hybrid **53b**. Thus benzhydryl 6-aminopenicillanate (**52**) was converted into **53b** (54%) via amide formation with **47** under Shiori conditions[31] and sulfation. Unfortunately all attempts to deprotect **53b** by global hydrogenolysis resulted in destruction of the β-lactam ring system. However carboxylic acid **47** should be useful for the preparation of alternative bulgecin analogues.

Experimental Section

General Procedures. All reactions were carried out under an atmosphere of dry N_2 at room temperature in oven-dried glassware unless otherwise noted. Reaction temperatures were recorded as bath temperatures. Melting points were determined on a Reichert hot stage apparatus and appear uncorrected. Unless noted to the contrary ^1H and ^{13}C NMR spectra were recorded on a Varian XL400 spectrometer using $CDCl_3$ as solvent with Me_4Si (δ 0.0) or $CDCl_3$ (δ 77.0) as an internal reference. Elemental analyses were determined by G. D. Searle and Co., Skokie, IL. Flash chromatography was carried out on Merck silica gel 60, 230–400 mesh ASTM; eluants are given in parentheses. Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica gel 60 F_{254} plates.

Solvents for chromatography were distilled at atmospheric pressure prior to use. Hexanes refer to the ACS reagent boiling range 35–60 °C. Anhydrous THF, Et_2O, PhH, and PhMe were distilled from Na/benzophenone ketyl; CH_2Cl_2, Et_3N, pyridine, and MeCN from CaH_2; DMF from BaO; and MeOH from $Mg(OMe)_2$. Organic solutions were dried over $MgSO_4$ and rotary evaporated at or below 40 °C. Reported yields refer to chromatographically and spectroscopically homogeneous material.

(2*S*,4*R*)-4-Hydroxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (8). To a vigorously stirred solution of **7** (10.0 g, 76.3 mmol) and K_2CO_3 (21 g, 153 mmol) in H_2O (50 mL) was added $PhCH_2OCOCl$ (10.9 mL, 76.3 mmol) in dioxane (11 mL) at 10 °C. The mixture was stirred overnight and extracted with CH_2Cl_2 (2 × 100 mL), and the aqueous layer was acidified with solid $NaHSO_4$ and extracted with Et_2O (3 × 200 mL). The combined Et_2O extracts were dried and evaporated to give a thick syrup (16.5 g), which was homogeneous by TLC (R_f = 0.2, 1:10:89 AcOH–H_2O–*n*-BuOH). Without further purification, the syrup was dissolved in DMF (50 mL) along with K_2CO_3 (8.6 g, 62 mmol), $PhCH_2Br$ (9.3 mL, 78 mmol), and NaI (93 mg, 0.6 mmol), and the mixture was vigorously stirred for 16 h. The reaction mixture was evaporated, and the residue mixed with Et_2O. After extracting with H_2O and brine, the organic layer was dried and evaporated. The syrupy residue was chromatographed (1:4–1:0 Et_2O–CH_2Cl_2), giving **8** (20 g, 74%) as a syrup: $[\alpha]_D$ = −60° (c = 3.0, $CHCl_3$); IR (neat) 3440, 2950, 1745, 1700, 1420, 1360, 1280, 1190, 1170, 1125, 1085, 1005, 770, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.18 (m, 10 H), 5.20, 5.13 (AB q, 0.8 H, J = 12 Hz), 5.12, 4.98 (2 s, 2 H), 5.01, 4.98 (AB q, 1.2 H, J = 12.4 Hz), 4.53 (m, 1 H, J = 8 Hz), 4.40 (m, 1 H), 3.59 (m, 2 H), 2.95 (d, 0.6 H, J = 3.2 Hz), 2.85 (d, 0.4 H, J = 4.4 Hz), 2.25 (m, 1 H), 2.02 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.5, 172.3, 155.0, 154.6, 136.3, 136.1, 135.4, 135.2, 128.5, 128.4, 128.32, 128.28, 128.2, 128.1, 128.00, 127.95, 127.91, 127.8, 127.7, 69.9, 69.1, 67.19, 67.17, 66.9, 66.8, 58.0, 57.8, 55.1, 54.5, 39.0, 38.2; HRMS (EI) calcd for $C_{20}H_{21}NO_5$ (M + H^+) 356.1500, found (M + H^+) 356.1539. Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.40; H, 5.91; N, 4.06.

(2*S*,4*S*)-4-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (9). To a stirred solution of AcOH (1.8 mL, 31 mmol) and diethyl azodicarboxylate (4.9 mL, 31 mmol) in Et_2O (30 mL) were added **8** (10 g, 28 mmol) and Ph_3P (8.3 g, 31 mmol) in Et_2O (30 mL) at 5 °C. After 16 h, the reaction mixture was filtered and evaporated. The residue was chromatographed (0:1–3:47 Et_2O–CH_2Cl_2), giving **9** (8.2 g, 73%) as an oil: $[\alpha]_D$ = −65° (c = 2.6, $CHCl_3$); IR (neat) 2960, 1745, 1715, 1420, 1355, 1250, 1220, 1120, 1070, 1020, 745, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.18 (m, 10 H), 5.21 (m, 1 H), 5.19 (d, 1 H, J = 12.4 Hz), 5.16 (d, 1 H, J = 12.4 Hz), 5.093, 5.086 (2 s, 2 H), 4.62 (dd, 0.5 H, J = 2.4, 9.2 Hz), 4.53 (dd, 0.5 H, J = 2.0, 9.2 Hz), 3.79, 3.78 (2 t, 1 H, J = 12.4 Hz), 3.67, 3.62 (2 d, 1 H, J = 12.4 Hz), 2.43 (m, 1 H), 2.33 (d, 1 H, J = 12.8 Hz), 1.79, 1.77 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.2, 170.9, 170.2, 170.1, 154.5, 154.1, 136.2, 135.6, 135.4, 128.5, 128.4, 128.3, 128.24, 128.16, 128.01, 127.97, 127.91, 127.86, 127.8, 72.6, 71.6, 67.2, 67.1, 66.8, 66.7, 57.9, 57.6, 52.5, 52.2, 36.2, 35.2, 20.6; MS (EI) m/z 397 ($M^{\bullet+}$). Anal. Calcd for $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.31; H, 6.05; N, 3.50.

(2*S*,4*R*)-4-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (24a). To **8** (0.3 g, 0.85 mmol), DMAP (65 mg, 0.53 mmol), and AcOH (100 μL, 1.8 mmol) in CH_2Cl_2 (1 mL) was added DCC (0.34 g, 1.7 mmol) in CH_2Cl_2 (0.5 mL). After 10 min, the reaction mixture was diluted with Et_2O and extracted with 0.5 M $NaHSO_4$, brine, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated. The residue was chromatographed (1:3–2:1 Et_2O–hexanes), giving **24a** (0.29 g, 85%) as an oil: $[\alpha]_D$ = −46° (c = 3.3, $CHCl_3$); IR (neat) 2960, 1745, 1715, 1420, 1360, 1240, 1195, 1170, 1130, 1070, 1020, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.18 (m, 10 H), 5.27 (m, 1 H), 5.23, 5.15 and 5.17, 5.13 (2 AB q, 2 H, J = 12.4 Hz), 5.05, 5.00 (2 s, 2 H), 4.55, 4.48 (2 t, 1 H, J = 8 Hz), 3.78, 3.66 (m, 2 H), 2.41 (m, 1 H), 2.20 (m, 1 H), 2.03, 2.02 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.9, 171.7, 170.3, 170.2, 154.6, 154.1, 136.2, 136.1, 135.3, 135.1, 128.5, 128.4, 128.3, 128.2, 128.1, 128.03, 127.97, 127.8, 72.5, 71.7, 67.24, 67.22, 67.0, 66.9, 57.9, 57.6, 52.5, 52.1, 36.5, 35.5, 20.9; HRMS (EI) calcd for $C_{22}H_{23}NO_6$ ($M^{\bullet+}$) 397.1526, found ($M^{\bullet+}$) 397.1530. Anal. Calcd for $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.34; H, 5.87; N, 3.49.

(2*S*,4*S*)-4-(Formyloxy)-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (21a). To **8** (4.8 g, 13 mmol), Ph_3P (3.6 g, 13 mmol), and 96% HCO_2H (1.0 mL, 27 mmol) in THF (8 mL) was added diethyl azodicarboxylate (2.1 mL, 13 mmol) in THF (2 mL), maintaining the temperature at 23–28 °C. After 16 h the solvent was evaporated and the residue was dissolved

(30) El Amin, B.; Anantharamaiah, G. M.; Royer, G. P.; Means, G. E. *J. Org. Chem.* **1979**, *44*, 3442.
(31) Yamada, S.-I.; Kasai, Y.; Shioiri, T. *Tetrahedron Lett.* **1973**, 1595.

in Et_2O and hexanes added to the cloud point. After the mixture was filtered, the filtrate was evaporated, and the residue was chromatographed (0:1–1:24 Et_2O–CH_2Cl_2), giving **21a** (2.8 g, 55%) as an oil: $[\alpha]_D$ = −60° (*c* = 2.7, $CHCl_3$); IR (neat) 2950, 1755, 1715, 1420, 1350, 1165, 1120, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54 (s, 1 H), 7.40–7.26 (m, 10 H), 5.33 (t, 1 H, *J* = 4.8 Hz), 5.23, 5.15 (AB q, 1 H, *J* = 12.4 Hz), 5.19, 5.15 (AB q, 1 H, *J* = 12.4 Hz), 5.10 (s, 1 H), 5.13, 5.05 (AB q, 1 H, *J* = 12 Hz), 4.63, 4.54 (2 dd, 1 H, *J* = 1.6, 9.2 Hz), 3.81, 3.80 (2 t, 1 H, *J* = 12 Hz), 3.69, 3.64 (2 d, 1 H, *J* = 12 Hz), 2.45 (m, 1 H), 2.33 (d, 1 H, *J* = 14 Hz); ^{13}C NMR ($CDCl_3$) δ 171.0, 170.8, 159.9, 159.8, 154.4, 154.1, 136.2, 135.5, 135.3, 128.42, 128.35, 128.3, 128.2, 128.02, 127.95, 127.9, 127.8, 72.2, 71.2, 67.24, 67.16, 67.0, 66.8, 57.8, 57.6, 52.4, 52.1, 36.3, 35.2; HRMS (EI) calcd for $C_{21}H_{21}NO_6$ ($M^{\bullet+}$), 383.1369, found ($M^{\bullet+}$) 383.1333. Anal. Calcd for $C_{21}H_{21}NO_6$: C, 65.79; H, 5.52; N, 3.65. Found: C, 65.69; H, 5.72; N 3.63.

(2*S*,4*R*)-4-(Formyloxy)-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (24b). To **8** (0.3 g, 0.85 mmol), DMAP (65 mg, 0.53 mmol), and 96% HCO_2H (64 μL, 1.8 mmol) in CH_2Cl_2 (1 mL) was added dicyclohexylcarbodiimide (0.34 g, 1.7 mmol) in CH_2Cl_2 (0.5 mL). After 10 min, the reaction mixture was diluted with Et_2O and extracted with 0.5 M $NaHSO_4$, brine, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated and the residue was chromatographed (1:3–2:1 Et_2O–hexanes), giving **24b** (0.3 g, 91%) as an oil: $[\alpha]_D$ = −45° (*c* = 2.6, $CHCl_3$); IR (neat) 2960, 1755, 1715, 1420, 1360, 1160, 1125, 1070, 750, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97 (s, 1 H), 7.40–7.18 (m, 10 H), 5.40 (m, 1 H), 5.23, 5.17 and 5.16, 5.15 (2 AB q, 2 H, *J* = 12.4 Hz), 5.05, 5.00 (2 s, 2 H), 4.56, 4.50 (2 t, 1 H, *J* = 8.0 Hz), 3.84–3.67 (m, 2 H), 2.50–2.40 (m, 1 H), 2.30–2.18 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 171.8, 171.6, 160.00, 159.97, 154.5, 154.0, 136.1, 136.0, 135.3, 135.1, 128.5, 128.42, 128.36, 128.3, 128.13, 128.05, 128.0, 127.9, 127.8, 72.1, 71.4, 67.6, 67.3, 67.1, 67.0, 57.8, 57.5, 52.4, 51.9, 36.4, 35.4; HRMS (EI) calcd for $C_{21}H_{21}NO_6$ ($M^{\bullet+}$) 383.1369, found ($M^{\bullet+}$) 383.1368. Anal. Calcd for $C_{21}H_{21}NO_6$: C, 65.79; H, 5.52; N, 3.65. Found: C, 65.64; H, 5.55; N, 3.61.

(2*S*,4*S*)-4-Hydroxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (21b). To **21a** (2.6 g, 6.8 mmol) in $PhCH_2OH$ (6 mL) was added $LiOCH_2Ph$ in $PhCH_2OH$ (0.33 M; 300 μL). After 30 min, the formate was consumed and the solution was chromatographed (Et_2O), giving **21b** (2.2 g, 92%) as an oil: $[\alpha]_D$ = −17° (*c* = 0.7, $CHCl_3$); IR (neat) 3450, 2960, 1750, 1700, 1420, 1355, 1200, 1170, 1120, 1090, 970, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.20 (m, 10 H), 5.21 (d, 1 H, *J* = 12.4 Hz), 5.15 (d, 1 H, *J* = 12.4 Hz), 5.055 (d, 1 H, *J* = 12.4 Hz), 5.049 (d, 1 H, *J* = 12 Hz), 4.49, 4.42 (2 dd, 1 H, *J* = 1.6, 9.6 Hz), 4.35 (m, 1 H), 3.74–3.55 (m, 2 H), 3.34 (d, 0.5 H, *J* = 8.8 Hz), 3.30 (d, 0.5 H, *J* = 8.4 Hz), 2.30 (m, 1 H), 2.12 (t, 1 H, *J* = 13.2 Hz); ^{13}C NMR ($CDCl_3$) δ 174.03, 173.95, 154.9, 154.2, 136.3, 136.2, 135.1, 134.9, 128.5, 128.4, 128.34, 128.28, 128.2, 128.1, 128.0, 127.9, 127.81, 127.75 70.9, 69.9, 67.4, 67.3, 67.2, 58.2, 57.8, 55.8, 55.5, 38.6, 37.7; MS (EI) *m*/*z* 355 ($M^{\bullet+}$), 337 ($M - H_2O^{\bullet+}$). Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.39; H, 6.20; N, 3.93.

(2*S*,4*S*)-4-(Pivaloyloxy)-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (11). To **21b** (0.3 g, 0.85 mmol) and DMAP (0.13 g, 1.0 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise pivaloyl chloride (126 μL, 1 mmol), maintaining the temperature at 0–2 °C with an ice bath. The mixture was stirred at 0 °C for 1 h and evaporated, and the residue was chromatographed (1:4–63:37 Et_2O–hexanes) to give **11** (0.37 g, 100%) as an oil: $[\alpha]_D$ = −35° (*c* = 1.4, $CHCl_3$); IR (neat) 2980, 1755, 1720, 1420, 1350, 1290, 1155, 1070, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.22 (m, 10 H), 5.27 (m, 1 H), 5.24–5.00 (m, 4 H), 4.65, 4.55 (2 dd, 1 H, *J* = 1.6, 9.6 Hz), 3.81 (m, 1 H), 3.65, 3.59 (2 d, 1 H, *J* = 12.8 Hz), 2.47 (m, 1 H), 2.34, 2.32 (2 d, 1 H, *J* = 14.4 Hz), 1.11, 1.10 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 177.8, 177.7, 171.0, 170.7, 154.5, 154.2, 136.3, 136.2, 135.4, 135.3, 128.5, 128.41, 128.35, 128.3, 128.2, 128.0, 127.93, 127.87, 127.8, 72.4, 71.3, 67.21, 67.17, 67.0, 66.8, 58.0, 57.8, 52.8, 52.5, 38.4, 36.3, 35.3, 26.7; HRMS (EI) calcd for $C_{25}H_{29}NO_6$ ($M^{\bullet+}$) 439.1996, found ($M^{\bullet+}$) 439.2270. Anal. Calcd for $C_{25}H_{29}NO_6$: C, 68.32; H, 6.65; N, 3.19. Found: C, 68.59; H, 6.81; N, 3.42.

(2*S*,4*R*)-4-(Pivaloyloxy)-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (24c). To **8** (0.3 g, 0.85 mmol) and DMAP (0.13 g, 1.0 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise pivaloyl chloride (126 μL, 1 mmol), maintaining the temperature at 0–2 °C with an ice bath. The reaction mixture was stirred at 0 °C for 1 h and evaporated, and the residue was chromatographed (25–63% Et_2O–hexanes) to give **24c** (0.3 g, 81%) as an oil: $[\alpha]_D$ = −43° (*c* = 3.3, $CHCl_3$); IR (neat) 2990, 1730, 1720, 1420, 1360, 1290, 1190, 1160, 1130, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.18 (m, 10 H), 5.26 (m, 1 H), 5.23, 5.17 and 5.19, 5.13 (2 AB q, 2 H, *J* = 12 Hz), 5.07, 4.99 (2 s, 2 H), 4.55, 4.46 (2 t, 1 H, *J* = 8 Hz), 3.82–3.61 (m, 2 H), 2.39 (m, 1 H), 2.21 (m, 1 H), 1.16, 1.14 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 177.8, 177.7, 171.9, 171.7, 154.7, 154.1, 136.3, 136.1, 135.3, 135.1, 128.5, 128.42, 128.37, 128.3, 128.2, 128.1, 128.01, 127.98, 127.79, 127.75, 72.3, 71.5, 67.2, 67.1, 66.9, 58.0, 57.7, 52.5, 52.1, 38.6, 36.6, 35.5, 26.89, 26.86; HRMS (EI) calcd for $C_{25}H_{29}NO_6$ ($M^{\bullet+}$) 439.1996, found ($M^{\bullet+}$) 439.2020. Anal. Calcd for $C_{25}H_{29}NO_6$: C, 68.32; H, 6.65; N, 3.19. Found: C, 68.12; H, 6.67; N, 3.15.

(2*S*,4*S*)-4-Methoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (13). To **21b** (1.7 g, 4.8 mmol) and MeI (3 mL, 48 mmol) in DMF (3 mL) under N_2 was added portionwise over 2 h a suspension of 60% NaH in oil (192 mg, 4.8 mmol) in DMF (2 mL), maintaining the temperature at 0 °C with an oil bath. The reaction mixture was allowed to stir another 1 h at 0 °C before evaporating the solvent. The residue was mixed with Et_2O and extracted with H_2O and brine. After being dried, the organic layer was evaporated to leave an oil: TLC analysis (Et_2O) showed two components of equal intensity (R_f 0.62 and 0.50). Chromatography (1:3–1:0 Et_2O–hexanes) gave the less polar, epimerized product **23** (0.45 g, 25%) as an oil: $[\alpha]_D$ = +51° (*c* = 1.6, $CHCl_3$); IR (neat) 2950, 1750, 1710, 1420, 1360, 1170, 1125, 1100, 1005, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.18 (m, 10 H), 5.22, 5.15 (AB q, 0.8 H, *J* = 12.4 Hz), 5.15, 5.04, 4.99 (3 s, 3.2 H), 4.51, 4.46 (2 t, 1 H, *J* = 7.6 Hz), 3.96 (m, 1 H), 3.78–3.58 (m, 2 H), 3.29, 3.27 (2 s, 3 H), 2.36 (m, 1 H), 2.05 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.4, 172.2, 154.8, 154.2, 136.3, 136.2, 135.5, 135.2, 128.4, 128.34, 128.27, 128.2, 128.1, 128.02, 127.96, 127.89, 127.82, 127.77, 127.7, 78.5, 77.8, 67.1, 67.0, 66.8, 66.7, 57.9, 57.7, 56.6, 51.5, 51.3, 36.2, 35.0; HRMS (EI) calcd for $C_{21}H_{23}NO_5$ ($M^{\bullet+}$) 369.1577, found ($M^{\bullet+}$) 369.1584. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.42; H, 6.32; N, 3.80. Further elution gave the more polar **13** (0.56 g, 31%) as an oil: $[\alpha]_D$ = −48° (*c* = 1.4, $CHCl_3$); IR (neat) 2950, 1760, 1715, 1450, 1420, 1360, 1195, 1170, 1100, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.28 (m, 10 H), 5.29–5.08 (m, 4 H), 4.60, 4.52 (2 dd, 1 H, *J* = 2.4, 8.8 Hz), 3.97 (m, 1 H), 3.68 (m, 2 H), 3.21, 3.18 (2 s, 3 H), 2.4 (d, 1 H, *J* = 13.6 Hz), 2.24 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 171.6, 171.3, 154.8, 154.4, 136.5, 136.4, 135.8, 135.6, 128.4, 128.3, 128.2, 128.1, 128.05, 128.01, 127.93, 127.87, 127.85, 127.8, 78.9, 77.9, 67.04, 67.00, 66.8, 66.7, 57.8, 57.6, 56.29, 56.28, 51.8, 51.6, 35.7, 34.5; HRMS (EI) calcd for $C_{21}H_{23}NO_5$ ($M^{\bullet+}$) 369.1577, found ($M^{\bullet+}$) 369.1579. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.17; H, 6.28; N 3.69.

(2*S*,4*R*)-4-Methoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (24d). To **8** (5.3 g, 15 mmol) and MeI (9.3 mL, 150 mmol) in DMF (10 mL) under N_2 was added portionwise a suspension of 60% NaH in oil (600 mg, 15 mmol) in DMF (5 mL), maintaining the temperature at 0–2 °C with an ice bath. The reaction mixture was stirred for an additional 50 min at 0 °C, aqueous $NaHSO_4$ (0.5 M; 3 mL) was added, and the solvent was evaporated. The residue was mixed with Et_2O and extracted with H_2O, 0.5 M $NaHSO_4$, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated and the residue was chromatographed (1:1–4:1 Et_2O–hexanes), giving **24d** (3.6 g, 66%) as an oil: $[\alpha]_D$ = −48° (*c* = 2.6, $CHCl_3$); IR (neat) 2950, 1755, 1715, 1460, 1420, 1360, 1195, 1170, 1125, 1100, 1010, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.16 (m, 10 H), 5.23, 5.15 (AB q, 0.8 H, *J* = 12.4 Hz), 5.15, 5.04, 4.99 (3 s, 3.2 H), 4.51, 4.46 (2 t, 1 H, *J* = 8 Hz), 3.96 (m, 1 H), 3.78–3.58 (m, 2 H), 3.29, 3.27 (2 s, 3 H), 2.36 (m, 1 H), 2.05 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.5, 172.2, 154.8, 154.2, 136.4, 136.2, 135.5, 135.3, 128.5, 128.4, 128.3, 128.24, 128.16, 128.04, 127.9, 127.83, 127.79, 127.7, 78.6, 77.9, 67.1, 67.0, 66.8, 66.7, 58.0, 57.7, 56.6, 51.5, 51.3, 36.3, 35.0; HRMS (EI) calcd for $C_{21}H_{23}NO_5$ ($M^{\bullet+}$) 369.1577, found ($M^{\bullet+}$) 369.1569. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.12; H, 6.25; N, 3.76.

(2*S*,4*S*)-4-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-Phenylmethyl Diester (15). To **8** (6.85 g, 19.3 mmol) in MeOH (40 mL) was added NaOMe in MeOH (2.4 M; 1 mL).

After 8 h, the solution was diluted with Et_2O and extracted with 1 M $NaHSO_4$, brine, 10% $NaHCO_3$, and brine. The organic layer was dried with $MgSO_4$, and the solvents were evaporated. Chromatography of the residue (1:2–1:1 EtOAc–CH_2Cl_2) gave **24e** (4.9 g, 91%) as an oil. ^1H NMR ($CDCl_3$) showed OCH_3 singlets at 3.75 and 3.55 and no acetate methyl signals. The crude ester **24e** (17.6 mmol), Ph_3P (4.74 g, 17.6, mmol), and AcOH (1.51 mL, 26.4 mmol) were dissolved in THF (25 mL). To this solution was added diethyl azodicarboxylate (2.92 mL, 17.6 mmol) in THF (10 mL) while maintaining the temperature at 25 °C. After 18 h, the reaction mixture was filtered through silica gel (1:1 Et_2O–hexanes) and the eluate evaporated. Chromatography of the residue (1:1–4:1 Et_2O–hexanes) gave **15**[23] (3 g, 53%) as an oil.

(2*S*,4*R*)-4-Hydroxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Di(methyl ester) (22b). To a stirred suspension of **22a** (15 g, 83 mmol) in CH_2Cl_2 (100 mL) at 10 °C was dropwise added Et_3N (23 mL, 165 mmol) and, after 5 min, MeOCOCl (6.4 mL, 83 mmol). The ice bath was removed, the mixture stirred at room temperature for 30 min, diluted with CH_2Cl_2, and extracted with brine. After being dried, the organic layer was evaporated and the residue chromatographed (1:9–4:1 EtOAc–Et_2O), giving **22b** (14 g, 83%) as an oil: $[\alpha]_D$ = −85° (*c* = 3.0, $CHCl_3$); IR (neat) 3460, 2980, 1755, 1715, 1695, 1465, 1400, 1210, 1180, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.50–4.43 (m, 2 H), 3.75, 3.74, 3.71, 3.67 (4 s, 6 H), 3.65–3.50 (m, 3 H), 2.34–2.25 (m, 1 H), 2.10–2.00 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 173.2, 173.1, 155.6, 155.3, 69.7, 68.9, 57.8, 57.5, 55.0, 54.4, 52.7, 52.6, 52.2, 39.0, 38.2; HRMS (EI) calcd for $C_8H_{13}NO_5$ ($M^{\bullet+}$) 203.0794, found ($M^{\bullet+}$) 203.0813. Anal. Calcd for $C_8H_{13}NO_5$: C, 47.29; H, 6.45; N, 6.89. Found: C, 47.02; H, 6.42; N, 6.83.

(2*S*,4*S*)-4-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Di(methyl ester) (17). To **22b** (10 g, 49.3 mmol), Ph_3P (13.3 g, 49.3 mmol), and AcOH (5.65 mL, 98.5 mmol) in THF (15 mL) was added diethyl azodicarboxylate (7.75 mL, 49.3 mmol) in THF (10 mL) at 25–30 °C. After 16 h, the reaction mixture was filtered through silica (200 g) and eluted with 0:1–1:4 Et_2O–CH_2Cl_2. The eluate was evaporated and the residue was chromatographed (1:1–1:0 Et_2O–hexanes), giving **17** (5.5 g, 46%) as an oil: $[\alpha]_D$ = −50° (*c* = 3.0, $CHCl_3$); IR (neat) 2960, 1745, 1715, 1455, 1395, 1245, 1220, 1120, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.28–5.20 (m, 1 H), 4.54, 4.46 (2 dd, 1 H, *J* = 2, 9.2 Hz), 3.74, 3.73, 3.69 (3 s, 6 H), 3.82–3.70 (m, 1 H), 3.62, 3.58 (2 d, 1 H, *J* = 12.4 Hz), 2.50–2.30 (m, 2 H), 1.994, 1.987 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.9, 171.7, 170.1, 170.0, 155.1, 154.8, 72.6, 71.6, 57.7, 57.4, 52.6, 52.4, 52.2, 51.9, 36.4, 35.3, 20.8; HRMS (EI) calcd for $C_{10}H_{15}NO_6$ ($M^{\bullet+}$) 245.0899, found ($M^{\bullet+}$), 245.0928. Anal. Calcd for $C_{10}H_{15}NO_6$: C, 48.98; H, 6.17; N, 5.71. Found: C, 48.87; H, 6.11; N, 5.74.

(2*S*,4*R*)-4-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (24g). To **24f** (500 mg, 1.7 mmol), Et_3N (289 μL, 2.1 mmol), and DMAP (25 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) was added Ac_2O (196 μL, 2.1 mmol) at 0 °C. After 15 min, the mixture was diluted with Et_2O and extracted with H_2O, 1 M $NaHSO_4$, H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated, and the residue was chromatographed (1:1 Et_2O–hexanes) to give **24g** (530 mg, 94%) as an oil: $[\alpha]_D$ = −44° (*c* = 1.5, $CHCl_3$); IR (neat) 2980, 1755, 1715, 1430, 1365, 1250, 1215, 870, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.25 (m, 1 H), 4.38, 4.20 (2 dt, 1 H, *J* = 2.8, 8 Hz), 4.16 (m, 2 H), 3.733, 3.726, 3.711, 3.705 (4 s on m, 4.5 H), 3.60 (d, 0.5 H, *J* = 12 Hz), 2.37 (m, 1 H), 2.18 (m, 1 H), 2.028, 2.022 (2 s, 3 H), 0.99, 0.92 (2 t, 2 H, *J* = 8 Hz), 0.004, 0.000 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.7, 172.6, 170.3, 170.2, 155.0, 154.5, 72.6, 71.7, 63.9, 63.8, 57.6, 57.4, 52.3, 52.2, 52.0, 36.5, 35.5, 20.9, 17.63, 17.57, −1.6, −1.7; HRMS (EI) calcd for $C_{14}H_{25}NO_6Si$ (M − Me^+) 316.1216, found (M − Me^+) 316.1222. Anal. Calcd for $C_{14}H_{25}NO_6Si$: C, 50.73; H, 7.60; N, 4.23. Found: C, 50.66; H, 7.62; N, 4.19.

(2*S*,4*S*,5*RS*)-5-Methoxy-4-(pivaloyloxy)-1,2-pyrrolidinedicarboxylic Acid 1,2-Bis(phenylmethyl ester) (12). The acetate **11** (2.2 g, 5 mmol) and Et_4NOTs (240 mg, 0.8 mmol) in MeOH (10 mL) were electrolyzed (0.5 A) in an ice bath. After 2 h, the solution was diluted with CH_2Cl_2 and extracted with H_2O and brine. The organic layer was dried and evaporated, and the residue chromatographed (Et_2O–hexanes) to give crude **12** (240 mg, 10%) as an oil: ^1H NMR ($CDCl_3$) δ 7.40–7.22 (m, 10 H), 5.30–4.92 (m, 6 H), 4.64, 4.56 (2 d, 1 H, *J* = 10.0, 9.6 Hz), 3.53, 3.37 (2 s, 3 H), 2.79–2.63 (m, 1 H), 2.21, 2.19 (2 d, 1 H, *J* = 14.4, 14.8 Hz), 1.11, 1.09 (2 s, 9 H).

(2*S*,4*S*,5*R*)- and (2*S*,4*S*,5*S*)-4-Acetoxy-5-methoxy-1,2-pyrrolidinedicarboxylic Acid 1,2-Di(methyl ester) (18a and 18b). A stirred solution of **17** (2.94 g, 12 mmol) and Et_4NOTs (500 mg, 1.7 mmol) in MeOH (20 mL) was electrolyzed (carbon rods; 0.5 A) while being cooled in an ice bath. After passing 27 Faradays, the reaction solution was evaporated and the resulting residue dissolved in CH_2Cl_2 (2 mL) containing DMAP (105 mg, 0.9 mmol). To this solution was added Et_3N and Ac_2O in 12-mmol portions until reacetylation was complete. The reaction mixture was chromatographed (3:2–1:0 Et_2O–hexanes), giving the methoxy derivatives (1.7 g, 52%) as an oil. Upon addition of Et_2O, the 5*R* isomer crystallized. Recrystallization from CH_2Cl_2–Et_2O gave 5*R* isomer **18a** (490 mg): mp 108–109 °C; $[\alpha]_D$ = −55° (*c* = 1.7, $CHCl_3$); IR (KBr) 2980, 1765, 1745, 1720, 1460, 1400, 1385, 1250, 1205, 1090, 1065, 790, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.14, 5.00 (2 s, 1 H), 4.99, 4.96 (2 d, 1 H, *J* = 4.4 Hz), 4.53, 4.47 (2 d, 1 H, *J* = 10.0 Hz), 3.79, 3.74, 3.73, 3.72, 3.52, 3.45 (6 s, 9 H), 2.72–2.58 (m, 1 H), 2.23, 2.19 (2 d, 1 H, *J* = 14.8 Hz), 2.03, 2.01 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.6, 171.2, 170.1, 169.9, 155.2, 154.8, 92.5, 91.9, 75.6, 74.6, 57.9, 57.7, 57.2, 56.6, 52.9, 52.7, 52.2, 33.3, 32.1, 20.8, 20.7; HRMS (EI) calcd for $C_{11}H_{17}NO_7$ (M − OMe^+) 244.0821, found (M − OMe^+) 244.0832. Anal. Calcd for $C_{11}H_{17}NO_7$: C, 48.00; H, 6.23; N, 5.09. Found: C, 47.94; H, 6.18; N, 5.09. Careful chromatography (1:9–3:7 EtOAc–benzene) gave the 5*S* isomer **18b** (190 mg) as an oil: $[\alpha]_D$ = −102° (*c* = 3.3, $CHCl_3$); IR (neat) 2960, 1760, 1740, 1720, 1450, 1385, 1370, 1305, 1240, 1200, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45, 5.36 (2 d, 1 H, *J* = 4.4 Hz), 4.85–4.72 (m, 1 H), 4.39, 4.33 (2 t, 1 H, *J* = 9.2 Hz), 3.78, 3.76, 3.74, 3.72, 3.51, 3.45 (6 s, 9 H), 2.75–2.61 (m, 1 H), 2.28–2.15 (m, 1 H), 2.12 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.5, 171.3, 170.3, 170.2, 155.3, 155.2, 85.5, 85.1, 71.4, 70.7, 56.0, 55.5, 54.9, 53.0, 52.4, 30.9, 29.9, 20.7; HRMS (EI) calcd for $C_{11}H_{17}NO_7$ ($M^{\bullet+}$) 275.1005, found ($M^{\bullet+}$) 275.0999. Anal. Calcd for $C_{11}H_{17}NO_7$: C, 48.00; H, 6.23; N, 5.09. Found: C, 47.73; H, 6.26; N, 5.04.

(2*S*,4*S*,5*RS*)-4-Acetoxy-5-methoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (20). A stirred solution of **19**[23] (10.1 g, 30.5 mmol) and Et_4NOTs (1.0 g, 3.3 mmol) in MeOH (50 mL) was electrolyzed (carbon rod electrodes; 0.5 A) while being cooled in an ice bath. After passing 5 Faradays, the solvent was evaporated. To the residue dissolved in CH_2Cl_2 (20 mL) was added DMAP (373 mg, 3.1 mmol) followed by Et_3N and Ac_2O (1:1) until the material was reacetylated. The solution was extracted with H_2O, 1 M $NaHSO_4$, H_2O, 10% $NaHCO_3$, and brine. The organic layer was dried, evaporated, and chromatographed (1:3–29:31 Et_2O–hexanes) to give **20** (7.3 g, 66%) as an oil: $[\alpha]_D$ = −51° (*c* = 2.1, $CHCl_3$); IR (neat) 2960, 1765, 1750, 1715, 1410, 1350, 1240, 1200, 1180, 1080, 1060, 860, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.44, 5.37 (2 d, 0.4 H, *J* = 4.4 Hz), 5.15, 5.01 (2 s, 0.6 H), 4.99, 4.97 (2 d, 0.6 H, *J* = 4.8 Hz), 4.79 (m, 0.4 H), 4.52, 4.47 (2 d, 0.6 H, *J* = 9.2 Hz), 4.38, 4.32 (2 t, 0.4 H, *J* = 8.8 Hz), 4.22 (m, 2 H), 3.76, 3.74, 3.73, 3.51, 3.46 (5 s, 6 H), 2.66 (m, 1 H), 2.20 (m, 1 H), 2.12, 2.03, 2.01, (3 s, 3 H), 1.10–0.95 (m, 2 H), 0.05, 0.04, 0.03 (3 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.8, 171.4, 170.2, 170.0, 155.0, 154.7, 92.5, 91.9, 85.4, 85.0, 75.8, 74.8, 71.5, 7.09, 64.5, 64.4, 64.3, 64.1, 57.8, 57.2, 56.7, 56.1, 55.6, 54.9, 54.8, 52.4, 52.2, 52.1, 33.4, 32.2, 31.0, 29.9, 20.9, 20.8, 20.7, 17.8, 17.7, −1.57, −1.63; HRMS (EI) calcd for $C_{15}H_{27}NO_7Si$ ($M^{\bullet+}$) 361.1557, found ($M^{\bullet+}$) 361.1573. Anal. Calcd for $C_{15}H_{27}NO_7Si$: C, 49.85; H, 7.53; N, 3.88. Found: C, 49.66; H, 7.59; N, 3.73.

(2*S*,4*S*,5*RS*)-4,5-Diacetoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (25). The ether **20** (2.0 g, 5.5 mmol), Ac_2O (10 mL, 110 mmol), AcOH (20 mL), and concentrated H_2SO_4 (4 drops) in CH_2Cl_2 (20 mL) were stirred at 0 °C for 2 h. The solution was poured onto ice and extracted with CH_2Cl_2. The combined organic layers were extracted with H_2O, 10% $NaHCO_3$ and brine. After being dried, the organic layer was evaporated, and chromatographed (1:2–2:1 Et_2O–hexanes) to give **25** (1.9 g, 86%) as an oil: $[\alpha]_D$ = −7° (*c* = 1.6, $CHCl_3$); IR (neat) 2960, 1775, 1725, 1410, 1375, 1345, 1230, 1200, 1060, 1020, 860, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.69 (br s, 0.1 H), 6.64 (d, 0.2 H, *J* = 4.3 Hz), 6.53, 6.49 (2 s, 0.7 H), 5.18 (ddd, 0.3 H, *J* = 4.4, 7.1, 11.2 Hz), 5.03 (d, 0.7 H, *J* = 4.0 Hz), 4.60, 4.54 (2 d, 0.7 H, *J* = 10.0 Hz), 4.36–4.13 (m, 2.3 H), 3.79, 3.75, 3.74 (3 s, 3 H), 2.70–2.56 (m, 1.3 H), 2.31, 2.28 (2 d, 0.7 H, *J* = 14.0 Hz), 2.12, 2.06, 2.03, 2.02 (4 s, 6 H), 1.08–0.90 (m, 2 H), 0.04, 0.03 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.4, 171.1, 169.7, 169.6, 169.4,

169.3, 169.0, 168.8, 153.8, 85.3, 84.2, 76.0, 74.9, 64.9, 64.6, 64.4, 58.0, 57.9, 55.7, 52.4, 52.34, 52.26, 33.8, 32.7, 30.4, 20.9, 20.8, 20.7, 20.4, 17.6, -1.7; HRMS (EI) calcd for $C_{16}H_{27}NO_8Si$ (M - Me^+) 374.1271, found (M - Me^+) 374.1251. Anal. Calcd for $C_{16}H_{27}NO_8Si$: C, 49.34; H, 6.99; N, 3.60. Found: C, 49.41; H, 7.13; N, 3.50.

(2*S*,4*S*,5*RS*)-4-Acetoxy-5-allyl-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (26). Me_3SiOTf (503 μL, 2.6 mmol) was added to a solution of **25** (1.0 g, 2.6 mmol) and allyltrimethylsilane (2.3 mL, 14.7 mmol) in CH_2Cl_2 (2.3 mL) at -78 °C in a flask that had been previously silylated with hexamethyldisilazane. After 15 min, the solution was quenched with 10% $NaHCO_3$ (3 mL) and diluted with CH_2Cl_2. The organic layer was dried, evaporated, and chromatographed (7:13–11:9 Et_2O–hexanes) to give **26** (810 mg, 84%) as an oil: $[\alpha]_D$ = -10° (*c* = 2.1, $CHCl_3$); IR (neat) 2960, 1745, 1710, 1645, 1410, 1355, 1240, 1210, 1180, 1110, 1050, 860, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.86–5.72 (m, 1 H), 5.28–4.97 (m, 3 H), 4.52, 4.44 (2 d, 0.2 H, *J* = 9.0 Hz), 4.41 (dd, 0.8 H), 4.28–4.01 (m, 3 H), 3.75, 3.74, 3.73 (3 s, 3 H), 2.84–2.14 (m, 4 H), 2.02, 2.00, 1.97 (3 s, 3 H), 1.10–0.90 (m, 2 H), 0.05, 0.03 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.4, 169.9, 134.6, 133.4, 133.2, 118.4, 118.3, 116.7, 72.3, 71.9, 63.8, 63.5, 63.3, 59.7, 58.54, 58.47, 56.9, 52.2, 52.13, 52.06, 34.6, 34.2, 33.44, 33.41, 21.0, 20.9, 20.8, 17.7, -1.6; HRMS (EI) calcd for $C_{17}H_{29}NO_6Si$ (M - $C_3H_5^+$) 330.1373, found (M - $C_3H_5^+$) 330.1355. Anal. Calcd for $C_{17}H_{29}NO_6Si$: C, 54.96; H, 7.87; N, 3.77. Found: C, 54.96; H, 8.09; N, 3.68.

(2*S*,4*S*,5*RS*)-5-Acetoxy-5-allenyl-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27a). To **25** (140 mg, 0.36 mmol) and propargyltrimethylsilane (160 μL, 1 mmol) in CH_2Cl_2 (750 μL) at -78 °C was added Me_3SiOTf (8 μL, 0.04 mmol). After 1.5- and 2.75-h intervals, additional Me_3SiOTf (16 and 40 μL) was added. After 4 h, the reaction mixture was diluted with CH_2Cl_2 and brine. The organic layer was dried, evaporated, and chromatographed (1:2–7:3 Et_2O–hexanes) to give **27a** (20 mg, 15%) as an oil: IR (neat) 2960, 1960, 1750, 1705, 1410, 1345, 1220, 1045, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.40–5.05 (m, 2 H), 4.92–4.66 (m, 4 H), 4.62–4.12 (m, 2 H), 3.76, 3.75, 3.72 (3 s, 3 H), 2.58–2.48 (m, 1 H), 2.30–2.20 (m, 1 H), 2.05, 2.03, 1.98 (3 s, 3 H), 1.10–0.90 (m, 2 H), 0.04, 0.03, 0.02 (3 s, 9 H); HRMS (EI) calcd for $C_{16}H_{24}NO_6Si$ (M - Me^+) 354.1373, found (M - Me^+) 354.1358.

(2*S*,4*S*,5*R*)- and (2*S*,4*S*,5*S*)-4-Acetoxy-5-cyano-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27b). To **25** (130 mg, 0.33 mmol) and Me_3SiCN (133 μL, 1.0 mmol) in CH_2Cl_2 (300 μL) at -78 °C was added Me_3SiOTf (8 μL, 0.04 mmol). After 30 min, the reaction mixture was quenched with 10% $NaHCO_3$ and then diluted with CH_2Cl_2. The organic layer was dried, evaporated, and chromatographed (1:2–2:1 Et_2O–hexanes) to give the 5*R* isomer of **27b** (30 mg, 25%) as an oil [IR (neat) 2970, 2260, 1745, 1715, 1410, 1345, 1210, 1055, 840, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.40–5.35 (m, 1 H), 4.70, 4.64 (2 s, 1 H), 4.64, 4.55 (2 d, 1 H, *J* = 8.8 Hz), 4.38–4.20 (m, 2 H), 3.76, 3.75 (2 s, 3 H), 2.70–2.65 (m, 1 H), 2.49, 2.46 (2 d, 1 H, *J* = 14.8, 14.4 Hz), 1.12, 0.99 (2 m, 2 H), 0.06, 0.04 (2 s, 9 H)] and the 5*S* isomer of **27b** (37 mg, 31%): IR (neat) 2960, 2260, 1710, 1410, 1215, 1045, 840, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.26 (dt, 1 H), 5.07, 5.02 (2 d, 1 H, *J* = 6.0 Hz), 4.47, 4.42 (2 t, 1 H, *J* = 7.6 Hz), 4.35–4.15 (m, 2 H), 3.80, 3.73 (2 s, 3 H), 2.75–2.60 (m, 1 H), 2.42–2.30 (m, 1 H), 2.15 (s, 3 H), 1.15–0.95 (m, 2 H), 0.06, 0.04 (2 s, 9 H); HRMS (EI) calcd for $C_{15}H_{24}N_2O_6Si$ ($M^{\cdot+}$) 356.1404, found ($M^{\cdot+}$) 356.1423.

(2*S*,4*S*,5*RS*)-4-(Benzoyloxy)-5-methoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27c). To **20** (3.5 g, 9.7 mmol) in MeOH (30 mL) was added NaOMe in MeOH (1.2 M; 1.0 mL). After 30 min, aqueous $NaHSO_4$ (1 M; 2 mL) was added and the solubiton was evaporated. The residue was mixed with Et_2O, and the organic layer was extracted with brine. After being dried, the organic layer was evaporated and the residue was chromatographed (1:3 Et_2O–hexanes) to give the 4-hydroxy compound (2.4 g) as an oil. This was dissolved in CH_2Cl_2 (3 mL) along with DMAP (1.25 g, 9.38 mmol), and the temperature of the resulting solution was maintained at 10–15 °C as PhCOCl (1.21 mL, 10.5 mmol) was added. After 2 h, the mixture was diluted with CH_2Cl_2 and extracted with H_2O, 1 M $NaHSO_4$, H_2O, 10% $NaHCO_3$, and brine. After the organic layer was dried, the solvent was evaporated and the residue was chromatographed (1:3 Et_2O–hexanes) to give **27c** (2.8 g, 68%) as an oil: $[\alpha]_D$ = -22° (*c* = 1.8, $CHCl_3$); IR (neat) 2980, 1765, 1725, 1605, 1590, 1410, 1305, 1275, 1180, 1110, 1075, 860, 840, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10–7.40 (m, 5 H), 5.55, 5.49 (2 d, 0.4 H, *J* = 4.4 Hz), 5.31, 5.28 (2 d, 0.6 H, *J* = 4.0 Hz), 5.29, 5.12 (2 s, 0.6 H), 5.08–4.98 (m, 0.4 H), 4.61, 4.56 (2 dd, 0.6 H, *J* = 1.0, 10.1 Hz), 4.44, 4.38 (2 t, 0.4 H, *J* = 8.8 Hz), 4.31–4.17 (m, 2 H), 3.78, 3.72, 3.68, 3.57, 3.52, 3.46 (6 s, 6 H), 2.84–2.71 (m, 1 H), 2.45–2.30 (m, 1 H), 1.10–0.82 (m, 2 H), 0.05, 0.04, 0.031, 0.029 (4 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.82, 171.79, 171.6, 171.5, 165.9, 165.8, 165.7, 165.5, 155.0, 154.6, 133.3, 129.8, 129.7, 129.39, 129.35, 129.3, 128.4, 128.3, 92.7, 92.1, 85.8, 85.3, 75.9, 75.0, 71.9, 71.3, 64.5, 64.4, 64.34, 64.26, 64.1, 58.0, 57.9, 57.3, 56.8, 56.3, 55.8, 55.0, 54.9, 52.4, 52.3, 52.2, 33.6, 32.4, 31.2, 30.1, 17.8, 17.6, -1.6; HRMS (EI) calcd for $C_{20}H_{29}NO_7Si$ (M - Me^+) 408.1479, found (M - Me^+) 408.1460. Anal. Calcd for $C_{20}H_{29}NO_7Si$: C, 56.72; H, 6.90; N, 3.31. Found: C, 56.38; H, 7.00; N, 3.24.

(2*S*,4*S*,5*R*)-4-(Benzoyloxy)-5-acetoxy-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27d). To **27c** (2.0 g, 4.7 mmol), AcOH (17 mL), and Ac_2O (8.5 mL, 90 mmol) in CH_2Cl_2 (17 mL) at 0 °C was added concentrated H_2SO_4 (4 drops). After 3 h, the solution was poured onto ice and the mixture was extracted with CH_2Cl_2. The combined extracts were washed with H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic extract was evaporated and the residue was chromatographed (3:7–2:3 Et_2O–hexanes) to give **27d** (1.9 g, 90%) as an oil. Crystallization with 30% Et_2O–hexanes, followed by a recrystallization from benzene–hexanes gave a single isomer of **27d** (0.71 g, 34%): mp 97–98 °C; $[\alpha]_D$ = +8° (*c* = 1.7, $CHCl_3$); IR (KBr) 2970, 1765, 1750, 1725, 1720, 1410, 1275, 1205, 1180, 1115, 950, 875, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.99 (t, 2 H, *J* = 7.0 Hz), 7.57 (t, 1 H, *J* = 7.0 Hz), 7.44 (t, 2 H, *J* = 7.0 Hz), 6.69, 6.62 (2 s, 1 H), 5.34, 5.32 (2 d, 1 H, *J* = 4 Hz), 4.68, 4.61 (2 d, 1 H, *J* = 10.0 Hz), 4.32–4.17 (m, 2 H), 3.66, 3.61 (2 s, 3 H), 2.80–2.68 (m, 1 H), 2.42 (t, 1 H, *J* = 14.0 Hz), 2.08 (s, 3 H), 1.10–0.95 (m, 2 H), 0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.3, 171.0, 168.9, 168.7, 164.9, 164.8, 153.8, 153.7, 133.4, 129.83, 129.80, 129.0, 128.3, 85.4, 84.3, 76.1, 75.1, 64.6, 64.5, 58.1, 58.0, 52.34, 52.30, 34.0, 32.9, 20.84, 20.81, 17.6, 17.5, -1.7; HRMS (EI) calcd for $C_{21}H_{29}NO_8Si$ (M - Me^+) 436.1428, found (M - Me^+) 436.1422. Anal. Calcd for $C_{21}H_{29}NO_8Si$: C, 55.86; H, 6.47; N, 3.10. Found: C, 55.83; H, 6.57; N, 3.13.

(2*S*,4*S*,5*RS*)-5-Allyl-4-(benzoyloxy)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27e). To **27d** (149 mg, 0.33 mmol) and allyltrimethylsilane (300 μL, 1.9 mmol) in CH_2Cl_2 (300 μL) at -78 °C was added Me_3SiOTf (64 μL, 0.33 mmol). After 5 min, the solution was quenched with brine and 10% Na_2CO_3 and then diluted with CH_2Cl_2. The organic layer was dried and evaporated to leave an oil. ^1H NMR of the crude product (>80% pure) indicated a 1:1 ratio of diastereoisomers by comparison with authentic **27e** (vide infra).

(2*S*,4*S*,5*R*)- and (2*S*,4*S*,5*S*)-5-Allyl-4-(benzoyloxy)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (27e). To **26** (800 mg, 2.2 mmol) in MeOH (10 mL) was added NaOMe in MeOH (1 M; 250 μL). After 1 h, the solution was quenched with aqueous $NaHSO_4$ (1.0 M; 1 mL) and evaporated. The residue was dissolved in Et_2O and H_2O, and the organic layer was washed with H_2O and brine and dried. Evaporation gave the 4-hydroxy compound (620 mg) as an oil. This was dissolved in CH_2Cl_2 (5 mL) along with Et_3N (810 μL, 5.7 mmol) and DMAP (69 mg, 0.57 mmol). After the mixture was cooled to 0 °C, PhCOCl (660 μL, 5.7 mmol) was added, and the solution was stirred at room temperature. After 16 h, the mixture was diluted with CH_2Cl_2 and extracted with H_2O, 1 M $NaHSO_4$, 10% $NaHCO_3$, and brine. The organic extract was dried and evaporated. Chromatography of the residue (1:3–1:1 Et_2O–hexanes) gave the less polar 5*R* isomer as an oil that crystallized. Recrystallization from hexane gave (5*R*)-**27e** (120 mg, 15%): mp 85–86 °C; $[\alpha]_D$ = -17° (*c* = 1.2, $CHCl_3$); IR (KBr) 2980, 1765, 1705, 1410, 1350, 1275, 1200, 1185, 1115, 1065, 1035, 865, 835, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05–7.40 (m, 5 H), 5.90–5.78 (m, 1 H), 5.32, 5.29 (2 d, 1 H, *J* = 4.0 Hz), 5.20–5.10 (m, 2 H), 4.60, 4.52 (2 d, 1 H, *J* = 10.0 Hz), 4.30–4.12 (m, 3 H), 3.68, 3.64 (2 s, 3 H), 2.78–2.62 (m, 1 H), 2.59 (ddd, 1 H, *J* = 4.0, 10.0, 15.6 Hz), 2.40 (d, 1 H, *J* = 15.6 Hz), 2.36–2.24 (m, 1 H), 1.20–0.93 (m, 2 H), 0.04, 0.03 (2

s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.2, 171.7, 165.8, 165.6, 155.0, 154.7, 133.5, 133.3, 133.2, 129.8, 129.7, 128.4, 128.3, 118.6, 118.51, 118.47, 90.2, 77.1, 76.1, 64.2, 63.9, 63.6, 58.8, 58.6, 52.3, 52.2, 37.1, 36.1, 34.9, 33.7, 17.81, 17.78, -1.5; HRMS (EI) calcd for $C_{22}H_{31}NO_6Si$ (M - Me^+) 418.1686, (M - $C_3H_5^+$) 392.1529, found (M - Me^+) 418.1719, (M - $C_3H_5^+$) 392.1514. Anal. Calcd for $C_{22}H_{31}NO_6Si$: C, 60.95; H, 7.21; N, 3.23. Found: C, 60.63; H, 7.24; N, 3.14. The more polar 5*S* isomer was isolated as an oil that crystallized. Recrystallization from hexane gave (5*S*)-**27e** (280 mg, 34%): mp 69-71 °C; $[\alpha]_D$ = +34° (*c* = 1.3, $CHCl_3$); IR (melt) 2960, 1760, 1715, 1410, 1270, 1200, 1180, 1110, 855, 840, 715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.00 (d, 2 H, *J* = 8.0 Hz), 7.58 (t, 1 H, *J* = 8.0 Hz), 7.46 (t, 2 H, *J* = 8.0 Hz), 5.84-5.72 (m, 1 H), 5.58-5.48 (br s, 1 H), 5.02 (dd, 1 H, *J* = 2.0, 20.0 Hz), 4.95 (d, 1 H, *J* = 10.0 Hz), 4.62-4.50 (br s, 1 H), 4.24-4.18 (m, 3 H), 3.65, 3.633, 3.626 (3 br s, 3 H), 3.00, 2.75 (2 br s, 1 H), 2.60-2.30 (m, 3 H), 1.03 (br s, 2 H), 0.04 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.3, 165.3, 134.2, 133.3, 129.6, 129.5, 128.4, 117.3, 73.2 (broad), 72.7 (broad), 63.9 (broad), 61.0 (broad), 59.8 (broad), 57.8 (broad), 35.3 (broad), 34.0 (broad), 33.9 (broad), -1.6; HRMS (EI) calcd for $C_{21}H_{28}NO_6Si$ (M - Me^+) 418.1686, found (M - Me^+) 418.1663. Anal. Calcd for $C_{22}H_{31}NO_6Si$: C, 60.95; H, 7.21; N, 3.23. Found: C, 60.77; H, 7.43; N, 3.13.

(5*RS*,4*S*,2*S*)-4-Acetoxy-5-(phenylseleno)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (30). To Ph_2Se_2 in Et_2O (125 mL) under N_2 was portionwise added $LiAlH_4$ (1.37 g, 34.3 mmol). After the solution became colorless, the excess hydride was destoryed with 1 M $NaHSO_4$. The aqueous layer was removed with a pipette, and brine (25 mL) was added with vigorous stirring. Stirring was stopped, the aqueous layer was removed, and the remaining organic layer was dried under N_2. After rapid filtration, the solvent was removed in vacuo giving PhSeH as a yellow liquid (STENCH). Acetate **25** (9.5 g, 24.4 mmol) and camphorsulfonic acid (113 mg, 0.49 mmol) in CH_2Cl_2 (15 mL) were added to the PhSeH, and the mixture was stirred under N_2. After 3 h the odoriferous solution was chromatographed (1:4-3:2 Et_2O-hexanes), giving **30** (8.5 g, 72%) as a light yellow oil containing a mixture of diastereoisomers: $[\alpha]_D$ = -93.9° (*c* = 2.0, $CHCl_3$); IR (neat) 2960, 1750, 1715, 1405, 1355, 1230, 865, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.80-7.20 (m, 5 H), 5.95 (d, 0.5 H, *J* = 5.4 Hz), 5.83 (br s, 0.3 H), 5.38 (dd, 0.2 H, *J* = 4.5, 1.4 Hz), 5.32 (d, 0.2 H, *J* = 4.2 Hz), 5.14-5.02 (m, 0.8 H), 4.40-3.95 (m, 2.3 H), 3.82, 3.79 (2 br s, 2.4 H), 3.73, 3.70 (2 s on m, 1.3 H), 2.68-2.58 (m, 0.8 H), 2.44-2.28 (m, 1 H), 2.14 (t, 0.2 H, *J* = 15.0 Hz), 1.99, 1.97, 1.93, 1.89 (4 s, 3 H), 1.02-0.56 (m, 2 H), 0.04, 0.02, -0.02 (3 s, 9 H); HRMS (EI) calcd for $C_{20}H_{29}NO_6SeSi$ (M - $C_2H_3O^+$) 444.0745, found (M - $C_2H_3O^+$), 444.0370. Anal. Calcd for $C_{20}H_{29}NO_6SeSi$: C, 49.38; H, 6.01; N, 2.88. Found: C, 49.74; H, 6.24; N, 2.80.

(5*R*,4*S*,2*S*)-4-Acetoxy-5-[(*E*)-1-[2-(methoxycarbonyl)-ethenyl]]-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (31). Selenide **30** (4.55 g, 9.4 mmol), methyl (*E*)- and (*Z*)-2-(tributylstannyl)acrylate (7.22 g, 19.3 mmol) and Bu_6Sn_2 (0.98 mL, 1.94 mmol) in PhH (45 mL) were degased by alternatively evacuating the reaction flask until the solvent boiled and repressuring with nitrogen 10 times. The degassed solution was irradiated with a 250-W G.E. sunlamp for 4 h. The solution was chromatographed (2:3 Et_2O-hexanes) to give **31** (2.6 g, 67%) as an oil: $[\alpha]_D$ = -55.7° (*c* = 2.1, $CHCl_3$); IR (neat) 2960, 1735, 1715, 1415, 1350, 1250, 1175, 1050, 860, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.88, 6.84 (2 dd, 1 H, *J* = <1, 15.7 Hz), 5.98, 5.93 (2 dd, 1 H, *J* = 1.5, 15.7 Hz) 4.95 (t, 1 H, *J* = 4.8 Hz), 4.68, 4.62 (2 d, 1 H, *J* = 5.8 Hz), 4.62, 4.54 (2 d, 1 H, *J* = 9.4 Hz), 4.28-4.11 (m, 2 H), 3.761, 3.756, 3.75, 3.73 (4 s, 6 H), 2.52-2.40 (m, 1 H), 2.29 (app t, 1 H, *J* = 14.6 Hz), 2.03, 2.01 (2 s, 3 H), 0.98 (m, 2 H), 0.03, 0.01 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 171.7, 171.2, 170.1, 169.9, 166.1, 154.6, 154.4, 144.0, 143.3, 122.4, 122.2, 76.8, 64.8, 64.4, 64.3, 64.1, 58.50, 58.46, 52.3, 52.2, 51.8, 51.7, 34.1, 32.8, 20.9, 20.8, 17.7, 17.6, -1.6; HRMS (EI) calcd for $C_{18}H_{29}NO_8Si$ (M - Me^+) 400.1428, found (M - Me^+) 400.1420. Anal. Calcd for $C_{18}H_{29}NO_8Si$: C, 52.03; H, 7.04; N, 3.37. Found: C, 51.75; H, 7.05; N, 3.26.

(5*R*,4*S*,2*S*)-4-Acetoxy-5-(hydroxymethyl)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(2-(Trimethylsilyl)ethyl) Diester (32). Ozone was bubbled through a solution of **31** (2.6 g, 6.3 mmol) in MeOH-CH_2Cl_2 (1:1; 89 mL) at -78 °C until a faint blue color appeared. The excess ozone was purged with N_2 before $NaBH_4$ (2.4 g, 63 mmol) was added. The mixture was allowed to warm slowly up to 0 °C and, after 30 min, quenched with 1 M $NaHSO_4$ and extracted twice with Et_2O. The combined organic layers were washed with H_2O, 10% $NaHCO_3$, and brine and dried. Evaporation and chromatography of the residue (3:2 Et_2O-hexanes) gave **32** (1.9 g, 83%) as a colorless syrup: $[\alpha]_D$ = -51° (*c* = 1.4, $CHCl_3$); IR (neat) 3470, 2960, 1745, 1710, 1415, 1350, 1245, 1045, 855, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.18 (d, 0.3 H, *J* = 5.2 Hz), 5.05 (dt, 0.7 H, *J* = 5.2, 1.6), 4.56 (dd, 0.3 H, *J* = 1.2, 9.6 Hz), 4.49 (dd, 0.7 H, *J* = 1.6, 9.6 Hz), 4.26-4.10 (m, 2.7 H), 4.03-4.00 (m, 0.3 H), 3.95-3.84 (m, 1 H), 3.82-3.73 (m, 1 H), 3.75, 3.74 (2 s, 3 H), 2.83 (t, 0.7 H, *J* = 6 Hz), 2.63-2.53 (m, 1 H), 2.22 (d, 1 H, *J* = 14.4 Hz), 2.02, 2.00 (2 s, 3 H), 1.83 (dd, 0.3 H, *J* = 4.8, 6.8 Hz), 1.08-0.85 (m, 2 H), 0.04, 0.03 (3 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.8, 170.6, 170.2, 155.7, 155.0, 76.9, 75.3, 66.4, 65.6, 64.0, 62.4, 61.9, 59.2, 59.0, 52.1, 35.1, 34.2, 21.0, 20.8, 17.8, 17.6, -1.7; HRMS (EI) calcd for $C_{14}H_{24}NO_7Si$ (M - CH_3)$^+$ 346.1322, found 346.1320. Anal. Calcd for $C_{15}H_{27}NO_7Si$: C, 49.84; H, 7.53; N, 3.88. Found: C, 49.71; H, 7.71; N, 3.76.

Bulgecinine (4). Aqueous NaOH (3.0 M; 4.5 mL) was added to **32** (312 mg, 0.86 mmol) in MeOH (1.5 mL). After 1.5 h the solution was acidified to pH 2 with 1 M $NaHSO_4$ and extracted twice with EtOAc. The combined organic extracts were dried with $MgSO_4$ and evaporated to give the hydroxy acid (189 mg, 72%) as a thick syrup which was homogeneous by TLC (1:2:9 H_2O-AcOH-$CHCl_3$): ^{1}H NMR ($CDCl_3$) δ 5.20 (br s, 3 H), 4.48-3.95 (m, 5 H), 3.85-3.45 (m, 2 H), 2.45 (m, 1 H), 2.22 (m, 1 H), 1.00 (m, 2 H), 0.05, 0.03 (s, 9 H). The hydroxy acid was dissolved in THF (1 mL), and Bu_4NF in THF (1 M; 1.0 mL) was added. After 24 h, additional Bu_4NF (1 mL) was added and the solution volume was reduced by half under a stream of N_2. The reaction was complete after warming to 50-60 °C for 2 h. The solution was applied to a column of AG 50W-X4 sulfonic acid resin, and the resin was eluted with H_2O until the eluate was neutral. Subsequently the resin was eluted with 1.5 M NH_4OH, and the basic eluate was evaporated to give **4** (70 mg, 70% from the hydroxy acid) as a white solid. Recrystallization from H_2O-MeOH gave a white solid: mp 181-183 °C; $[\alpha]_D$ = -12° (*c* = 0.99, H_2O) [lit.[1] mp 182 °C, $[\alpha]_D$ = -13.1° (*c* = 0.95, H_2O)]; ^{1}H NMR (D_2O, sodium 3-(trimethylsilyl)propionate-*2,2,3,3-d*$_4$ standard) δ 4.39 (app q, 1 H, *J* = 4.4, 5.2, 5.4 Hz), 4.21 (dd, 1 H, *J* = 6.6, 8.8 Hz), 3.90 (dd, 1 H, *J* = 6.6, 14.8 Hz), 3.79-3.72 (m, 2 H), 2.67 (ddd, 1 H, *J* = 5.8, 9.0, 14.5 Hz), 2.16 (ddd, 1 H, *J* = 4.6, 6.3, 14.5 Hz); ^{13}C NMR (D_2O, CD_3OD standard) δ 174.8, 71.4, 67.7, 60.2, 58.9, 37.4. Anal. Calcd for $C_6H_{11}NO_4$: C, 44.72; H, 6.88; N, 8.69. Found: C, 44.53; H, 6.85; N, 8.51. The literature[1] values for ^{1}H NMR (D_2O) are δ 4.39 (ddd, 1 H, *J* = 4.2, 5.1, 5.8 Hz), 4.21 (dd, 1 H, *J* = 6.6, 9.0 Hz), 3.90 (dd, 1 H, *J* = 6.5, 14.0 Hz), 3.76 (m, 1 H, *J* = 4.2, 6.0, 6.5 Hz), 3.75 (m, 1 H, *J* = 6.0, 14.0 Hz), 2.66 (ddd, 1 H, *J* = 5.8, 9.0, 13.9 Hz), 2.16 (ddd, 1 H, *J* = 5.1, 6.6, 13.9 Hz); values for ^{13}C NMR (D_2O) are δ 174.4 (s), 71.3 (d), 67.6 (d), 60.1 (d), 58.8 (t), 37.3 (t).

(2*S*)-1,2-Pyrrolidinedicarboxylic Acid 1-(2-(Trimethylsilyl)ethyl) 2-Methyl Diester (33a). To a mixture of MeCN (25 mL) and proline methyl ester hydrochloride (9.5 g, 57.2 mmol) at 0 °C was added Et_3N (17.5 mL, 126 mmol), followed by 2-(trimethylsilyl)ethyl azidoformate (10.7 g, 57.2 mmol). The ice bath was removed the mixture was stirred 16 h. The mixture was diluted with Et_2O and extracted with H_2O, 3% HCl, H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated, and the residue chromatographed (1:3 Et_2O-hexanes) to give **33a** (10.8 g, 69%) as an oil: $[\alpha]_D$ = -52° (*c* = 1.0, $CHCl_3$); IR (neat) 2970, 1760, 1710, 1415, 1355, 1200, 1170, 860, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.37, 4.31 (2 dd, 1 H, *J* = 3.4, 8.8, 3.8, 8.6 Hz), 4.22-4.10 (m, 2 H), 3.74, 3.72 (2 s, 3 H), 3.64-3.40 (m, 2 H), 2.30-2.14 (m, 1 H), 2.05-1.84 (m, 3 H), 1.06-0.90 (m, 2 H), 0.04, 0.02 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 173.2, 155.2, 154.7, 63.7, 63.6, 63.5, 63.4, 63.3, 63.2, 59.0, 58.9, 58.8, 58.6, 52.2, 52.1, 52.04, 51.98, 46.6, 46.3, 30.9, 29.8, 29.7, 24.3, 23.4, 17.8, -1.5, -1.56, -1.63; HRMS (FAB) calcd for $C_{12}H_{23}NO_4Si$ ($M^{\bullet+}$) 273.1396, found ($M^{\bullet+}$) 273.1399. Anal. Calcd for $C_{12}H_{23}NO_4Si$: C, 52.72; H, 8.48; N, 5.12. Found: C, 52.86; H, 8.53; N, 5.11.

(2*S*,5*RS*)-5-Methoxy-1,2-pyrrolidinedicarboxylic Acid 1-(2-(Trimethylsilyl)ethyl) 2-Methyl Diester (33b). The proline derivative **33a** (4 g, 14.7 mmol) in MeOH (16 mL) cooled in an ice bath was electrolyzed (0.5 A) for 8 h. The reaction

solution was evaporated, and the residue was dissolved in Et_2O. After extraction with H_2O and 10% $NaHCO_3$, the organic layer was dried and evaporated. Chromatography of the residue (1:3–1:1 Et_2O–hexanes) gave **33b** (3.3 g, 74%) as an oil: $[\alpha]_D = -44°$ (c = 1.0, $CHCl_3$); IR (neat) 2970, 1750, 1710, 1175, 1075, 935, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.36, 5.33, 5.26, 5.21 (4 d, 1 H, J = 4.6, 5.0, 4.4, 4.5 Hz), 4.44–4.10 (m, 3 H), 3.80, 3.75, 3.73, 3.71 (4 s, 3 H), 3.45, 3.414, 3.407, 3.35 (4 s, 3 H), 2.54–1.74 (m, 4 H), 1.10–0.90 (m, 2 H), 0.04, 0.03 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.8, 172.7, 172.6, 155.3, 155.1, 155.0, 154.8, 89.5, 89.4, 88.9, 88.8, 88.7, 88.3, 88.1, 64.1, 63.9, 63.8, 63.7, 63.6, 63.5, 59.1, 58.92, 58.85, 58.8, 58.7, 56.2, 56.1, 55.6, 55.5, 55.24, 55.16, 54.8, 52.1, 52.0, 51.3, 50.9, 32.6, 32.0, 30.6, 30.0, 28.1, 28.0, 27.94, 27.87, 26.9, 26.8, 17.7, 17.6, 17.54, 17.47, -1.66, -1.70, -1.75, -1.78; HRMS (FAB) calcd for $C_{13}H_{25}NO_5Si$ ($M^{\bullet+}$) 303.1502, found ($M^{\bullet+}$) 303.1494. Anal. Calcd for $C_{13}H_{25}NO_5Si$: C, 51.46; H, 8.31; N, 4.62; Found: C, 51.61; H, 8.37; N, 4.60.

(2*S*,5*RS*)-5-Acetoxy-1,2-pyrrolidinedicarboxylic Acid 1-(2-(Trimethylsilyl)ethyl) 2-Methyl Diester (33c). To **33b** (3 g, 9.9 mmol), Ac_2O (16 mL, 176 mmol), and AcOH (33 mL) in CH_2Cl_2 (33 mL) at 0 °C was added concentrated sulfuric acid (7 drops). After 2 h, the solution was diluted with CH_2Cl_2 and ice water and stirred for 1 h. The organic layer was extracted with H_2O and 10% $NaHCO_3$, and dried. Evaporation of the solvent gave a mixture of the product, the 5-hydroxy compound, and Ac_2O. Reacetylation was accomplished by adding DMAP to this mixture. After 1 h, the reaction solution was concentrated at <1 mmHg, and the residue was chromatographed (3:7–1:1 Et_2O–hexanes) to give **33c** (1.55 g, 45%) as an oil. The data is for the major 5*R* isomer: $[\alpha]_D = -35°$ (c = 0.6, $CHCl_3$); IR (neat) 2980, 1720, 1410, 1210, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.58, 6.53 (2 d, 1 H, J = 4.9, 4.8 Hz), 4.49, 4.45 (2 d, 1 H, J = 9.2 Hz), 4.26–4.10 (m, 2 H), 3.75, 3.73 (2 s, 3 H), 2.48–1.92 (m, 4 H), 2.04, 2.03 (2 s, 3 H), 1.04–0.92 (m, 2 H), 0.031, 0.027 (s, 9 H); HRMS (FAB) calcd for $C_{14}H_{25}NO_6Si$ ($M^{\bullet+}$) 331.1451; found ($M^{\bullet+}$) 331.1458. Anal. Calcd for $C_{14}H_{25}NO_6Si$: C, 50.73; H, 7.60; N, 4.23. Found: C, 50.96; H, 7.67; N, 4.18.

(2*S*,5*RS*)-5-(Phenylseleno)-1,2-pyrrolidinedicarboxylic Acid 1-(2-(Trimethylsilyl)ethyl) 2-Methyl Diester (33d). To PhSeH (0.95 g, 6.0 mmol) in CH_2Cl_2 (2 mL) was added **33c** (0.5 g, 1.52 mmol) followed by (*S*)-camphorsulfonic acid (12 mg, 0.05 mmol). After 30 min, the odoriferous solution was chromatographed (3:17–1:3 Et_2O–hexanes) to give **33d** (400 mg, 62%) as an oil: $[\alpha]_D = -63°$ (c = 1.4, $CHCl_3$); IR (neat) 2960, 1750, 1705, 1410, 1345, 1175, 860, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.75–7.25 (m, 5 H), 5.64–5.52 (m, 1 H), 4.42–3.90 (m, 3 H), 3.80, 3.78, 3.72, 3.69 (4 s, 3 H), 2.55–1.90 (m, 4 H), 1.00–0.85 (m, 2 H), 0.030, 0.026 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.64, 172.56, 154.1, 153.4, 136.2, 135.8, 135.6, 129.04, 128.95, 128.20, 128.16, 127.9, 127.8, 64.4, 64.3, 64.1, 62.8, 61.9, 61.3, 60.8, 59.9, 59.6, 59.12, 59.10, 52.29, 52.24, 34.2, 33.9, 33.4, 32.8, 28.9, 28.7, 28.0, 27.8, 17.8, 17.6, -1.52, -1.55; MS (EI) m/z 386, 342, 272, 228, 200, 140. Anal. Calcd for $C_{18}H_{27}NO_4SeSi$: C, 50.46; H, 6.35; N, 3.27. Found: C, 50.63; H, 6.44; N, 3.23.

(2*S*,5*R*)-5-[(*E*)-1-[2-(Methoxycarbonyl)ethenyl]]-1,2-pyrrolidinedicarboxylic Acid 1-(2-(Trimethylsilyl)ethyl) 2-Methyl Diester (33e). Selenide **33d** (285 mg, 0.67 mmol), methyl (*Z*)-2-(tributylstannyl)acrylate (503 mg, 1.34 mmol), and Bu_6Sn_2 (71 μL, 0.14 mmol) in PhH (3.2 mL) under nitrogen were irradiated with a sunlamp (G.E. 250-W) for 8 h. The resultant solution was chromatographed (1:1 Et_2O–hexanes) to give the product (155 mg, 65%) as an oil. ^1H NMR indicated that the oil contained a 1:3 mixture of 5*S*:5*R* isomers. Careful chromatography gave **33e** as an oil: $[\alpha]_D = -90°$ (c = 0.9, $CHCl_3$); IR (neat) 2975, 1755, 1720, 1670, 1410, 1350, 1280, 1255, 1205, 1170, 860, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.85, 6.81 (2 t, 1 H, J = 6.0 Hz), 5.88, 5.82 (2 dd, 1 H, J = 1.3, 14.2 Hz), 4.73, 4.66 (2 t, 1 H, 6.8 Hz), 4.43, 4.37 (2 d, 1 H, J = 8.0, 7.4 Hz), 4.19–4.06 (m, 2 H), 3.74, 3.72, 3.71 (3 s, 6 H), 2.36–2.12 (m, 2 H), 2.10–1.92 (m, 1 H), 1.81–1.72 (m, 1 H), 1.00–0.88 (m, 2 H), 0.01, 0.00 (2 s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.8, 172.7, 166.7, 154.9, 154.4, 147.8, 147.2, 120.6, 120.4, 64.0, 63.8, 59.4, 59.3, 58.3, 57.9, 52.3, 52.2, 51.63, 51.55, 29.5, 28.6, 28.4, 27.2, 17.8, 17.7, -1.6; HRMS (FAB) calcd for $C_{16}H_{27}NO_6Si$ ($M^{\bullet+}$) 357.1608, found ($M^{\bullet+}$) 357.1598. Anal. Calcd for $C_{16}H_{27}NO_6Si$: C, 53.76; H, 7.61; N, 3.92; Found: C, 53.94; H, 7.71; N, 3.91.

(5*R*,4*S*,2*S*)-4-Acetoxy-5-[(*E*)-1-[2-(methoxycarbonyl)ethenyl]]-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (34a). To **31** (4.73 g, 11.4 mmol) in CH_2Cl_2 (4.7 mL) at 0 °C was added CF_3CO_2H (19 mL). After 5 min the ice bath was removed and the mixture was warmed up to room temperature. After 3.5 h, the solution was evaporated at <1 mmHg, the resulting syrupy trifluoroacetate salt was dissolved in CH_2Cl_2, and $PhCH_2OCOCl$ (1.7 mL, 11.4 mmol) and 10% aqueous $NaHCO_3$ were added with vigorous stirring. After 15 and 30 min, additional $PhCH_2OCOCl$ (0.8 mL, 5.7 mmol) was added. When the trifluoroacetate salt was consumed, the mixture was diluted with CH_2Cl_2, and the organic layer was separated, washed with brine, dried, evaporated, and chromatographed (30–40% EtOAc–hexanes) to give **34a** (3.8 g, 83%) as an oil: $[\alpha]_D = -75.7°$ (c = 1.4, $CHCl_3$); IR (neat) 2950, 1705, 1655, 1585, 1400, 1340, 1240, 1110, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.25 (m, 5 H), 6.86, 6.84 (2 dd, 1 H, J = 5.0, 15.0 Hz), 5.98, 5.85 (2 dd, 1 H, J = 1.0, 15.0 Hz), 5.23, 5.21, 5.06, 5.02 (4 d, 2 H, J = 12.0 Hz), 4.95 (d, 1 H, J = 4.4 Hz), 4.73, 4.64 (2 d, 1 H, J = 5.0 Hz), 4.66, 4.58 (2 d, 1 H, J = 8.0 Hz), 3.76, 3.74, 3.73, 3.58 (4 s, 6 H), 2.52–2.40 (m, 1 H), 2.30 (dd, 1 H, J = 1, 14.0 Hz), 2.03, 2.00 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.5, 171.0, 170.1, 169.9, 166.1, 165.9, 154.2, 154.0, 143.5, 142.9, 136.0, 135.8, 128.4, 128.3, 128.1, 128.04, 128.02, 122.5, 75.6, 67.53, 67.45, 65.0, 64.5, 58.6, 58.5, 52.4, 52.2, 51.7, 34.1, 32.9, 20.83, 20.75; HRMS (EI) calcd for $C_{20}H_{23}NO_8$ ($M^{\bullet+}$) 405.1424, found ($M^{\bullet+}$) 405.1448. Anal. Calcd for $C_{20}H_{23}NO_8$: C, 59.26; H, 5.72; N, 3.45. Found: C, 59.13; H, 5.75; N, 3.46.

(5*R*,4*S*,2*S*)-4-Acetoxy-5-(hydroxymethyl)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (34b). Ozone was bubbled through **34a** in MeOH and CH_2Cl_2 (1:1, 120 mL) at -78 °C until a faint blue color developed. The excess ozone was purged with N_2, $NaBH_4$ (3.18 g, 84.0 mmol) was added, and the mixture was stirred as it warmed slowly up to 0 °C. After 45 min at 0 °C, 1 M $NaHSO_4$ was carefully added to quench the reaction mixture, followed by H_2O to dissolve the salts. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic layer was evaporated and the residue was chromatographed (2:3–3:2 Et_2O–hexanes) to give **34b** (2.85 g, 97%) as an oil: $[\alpha]_D = -74.6°$ (c = 1.9, $CHCl_3$); IR (neat) 3460, 2950, 1715, 1405, 1345, 1230, 1210, 1110, 1040, 760, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.28 (m, 5 H), 5.25, 5.21, 5.12, 5.03 (4 d, 2 H, J = 12.4 Hz), 5.19, 5.08 (2 d, 1 H, J = 5.2 Hz), 4.59, 4.52 (2 d, 1 H, J = 1.0, 9.2 Hz), 4.13, 4.04 (2 dd, 1 H, J = 5.0 Hz), 3.96–3.72 (m, 2 H), 3.75, 3.58 (2 s, 3 H), 2.76, 1.96 (2 t, 1 H, J = 5.6 Hz), 2.58 (m, 1 H), 2.22 (d, 1 H, J = 14.4 Hz), 2.01, 1.99 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.7, 170.6, 170.3, 155.1, 154.6, 135.96, 135.92, 128.5, 128.4, 128.2, 128.1, 128.01, 127.97, 76.9, 75.3, 67.5, 67.4, 66.5, 65.7, 62.1, 61.9, 59.3, 59.1, 52.2, 52.1, 35.2, 34.2, 21.0, 20.8; HRMS (EI) calcd for $C_{17}H_{21}NO_7$ ($M^{\bullet+}$) 351.1318, found ($M^{\bullet+}$) 351.1315. Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 57.76; H, 6.15; N, 3.88.

(5*R*,4*S*,2*S*)-4-Acetoxy-5-((phenylmethoxy)methyl)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (34c). A mixture of **34b** (1.0 g, 2.85 mmol), $PhCH_2Br$ (620 μL, 5.71 mmol), and Ag_2O (660 mg, 2.85 mmol) in CH_2Cl_2 (10 mL) was heated to reflux for 10 h. At this time additional $PhCH_2Br$ (700 μL) and Ag_2O (664 mg) were added, and the reflux continued for 12 h. Evaporation of the slurry and chromatography (1:1 Et_2O–hexanes) gave **34c**[23] (1.15 g, 91%) as a syrup.

(5*R*,4*S*,2*S*)-4-Hydroxy-5-((phenylmethoxy)methyl)-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (35a). To **34c** (1.15 g, 2.61 mmol) in dry MeOH (2 mL) was added NaOMe in MeOH (1.4 M; 100 μL). After 1 h, Dowex 50W-X8 (300 mg, 1.53 mequiv) was added, and the mixture was stirred for 20 min. The resin was removed by filtration, and the filtrate was evaporated to give **35a** (1.05 g, 100%) as an oil. Chromatography (1:9 EtOAc–CH_2Cl_2) gave an analytical sample: $[\alpha]_D = -58°$ (c = 1.0, $CHCl_3$); IR (neat) 3470, 1755, 1705, 1410, 1350, 1210, 1125, 1090, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.20 (m, 10 H), 5.22, 5.16, 5.06, 4.98 (4 d, 2 H, J = 12.2 Hz), 4.55–4.35 (m, 3 H), 4.32, 4.28 (2 t, 1 H, J = 4.9 Hz), 4.22 (t, 0.5 H, J = <1 Hz), 4.14 (dd, 0.5 H, J = <1, 5.6 Hz), 3.82, 3.54 (2 s, 3 H), 3.72–3.33 (m, 3 H), 2.80–2.54 (m, 1 H), 1.95, 1.94 (2 d, 1 H, J = 13.9 Hz); ^{13}C NMR ($CDCl_3$) δ 176.0, 175.7, 154.8, 154.0, 138.0, 137.8, 136.1, 128.5, 128.39, 128.36, 128.10, 128.07, 127.9, 127.7, 127.6, 127.42,

127.38, 75.0, 74.0, 73.3, 73.2, 69.3, 68.8, 67.9, 67.4, 67.3, 67.2, 59.2, 58.8, 52.9, 52.5, 37.4, 36.3; HRMS (EI) calcd for $C_{22}H_{25}NO_6$ (M - $C_2H_3O_2^+$) 340.1550, found (M - $C_2H_3O_2^+$) 340.1554. Anal. Calcd for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 65.81; H, 6.43; N, 3.43.

(2*S*,4*S*,5*R*)-5-((Benzyloxy)methyl)-4-hydroxy-1,2-pyrrolidinedicarboxylic Acid Bis(phenylmethyl ester) (35b). Methyl ester **34c** (1.34 g, 3.04 mmol) and $Ti(O\text{-}iPr)_4$ (180 μL, 0.60 mmol) in $PhCH_2OH$ (18 mL) were heated to 110 °C. After 9 h, the solution was diluted with EtOAc and extracted with 10% HCl, H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic solution was evaporated, and the residue was further evaporated at <0.5 mmHg to remove the benzyl alcohol. Chromatography (1:1 Et_2O–hexanes) gave **35b** (1.16 g, 82%) as an oil: $[\alpha]_D$ = −51° (*c* = 1.4, $CHCl_3$); IR (neat) 3480, 2960, 1755, 1710, 1410, 1350, 1200, 1170, 1125, 1085, 735, 695 cm^{-1}; ^1H NMR ($CHCl_3$) δ 7.40–7.15 (m, 15 H), 5.30, 5.18, 5.17, 5.08, 5.06, 5.04, 5.02, 4.92 (8 d, 4 H, *J* = 12.3 Hz), 4.49, 4.46, 4.43, 4.41 (4 d, 2 H, *J* = 11.8 Hz), 4.47, 4.42 (2 dd, 1 H, *J* = 1.1, 10.1 Hz), 4.29, 4.26 (2 dd, 1 H, *J* = 1.8, 4.8 Hz), 4.22 (t, 0.5 H, *J* = 3.6 Hz), 4.13 (dd, 0.5 H, *J* = 2.2, 5.4 Hz), 3.69 (dd, 0.5 H, *J* = 2.9, 10.0 Hz), 3.64 (dd, 0.5 H, *J* = 5.0, 10.0 Hz), 3.56 (dd, 0.5 H, 2.8, 9.9 Hz), 3.48 (d, 0.5 H, *J* = 11.1 Hz), 3.43 (dd, 0.5 H, *J* = 5.7, 9.9 Hz), 3.30 (d, 0.5 H, *J* = 10.7 Hz), 2.59 (m, 1 H), 1.97, 1.94 (d, 1 H, *J* = 13.6 Hz); ^{13}C NMR ($CDCl_3$) δ 175.2, 175.1, 154.8, 154.0, 138.0, 137.8, 136.1, 135.0, 134.8, 128.6, 128.50, 128.47, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.57, 127.35, 75.0, 74.0, 73.3, 73.2, 69.4, 68.8, 68.0, 67.6, 67.44, 67.39, 67.3, 67.2, 59.4, 59.0, 37.5, 36.3; HRMS (EI) calcd for $C_{28}H_{29}NO_6$ ($M^{\cdot+}$) 475.1995, found: ($M^{\cdot+}$) 475.2014. Anal. Calcd for $C_{28}H_{29}NO_6$: C, 70.72; H, 6.15; N, 2.95. Found: C, 70.55; H, 6.19; N, 2.83.

***tert*-Butyldimethylsilyl 2-Azido-3-*O*-benzyl-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (37).** To **36**[25] (7.34 g, 20.5 mmol), $PhCH_2Br$ (7.30 mL, 61.3 mmol), and Bu_4NI (395 mg, 1.07 mmol) in THF (40 mL) at 0 °C was added portionwise 60% NaH in oil (1.23 g, 30.8 mmol). The mixture was slowly warmed to room temperature and, after 5 h, poured onto ice and extracted with Et_2O. The organic layer was washed with H_2O until neutral and brine. The organic layer was dried and evaporated, and the residue was chromatographed (1:19 Et_2O–hexanes) to give **37** (6.9 g, 84%) as an oil that crystallized: mp 38–40 °C; $[\alpha]_D$ = −43° (*c* = 3.4, $CHCl_3$); IR (neat) 2460, 2370, 2100, 1360, 1195, 1175, 1090, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.27 (m, 5 H), 4.84, 4.75 (AB q, 2 H, *J* = 11.6 Hz), 4.52 (d, 1 H, *J* = 7.2 Hz), 3.93–3.72 (m, 3 H), 3.42–3.30 (m, 2 H), 3.24 (dt, 1 H, *J* = 5.6, 10 Hz), 1.48, 1.42 (2 s, 6 H), 0.92 (s, 9 H), 0.14, 0.13 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.3, 128.3, 127.9, 127.7, 99.4, 97.4, 79.3, 74.50, 74.46, 68.6, 67.2, 62.1, 29.2, 25.5, 19.1, 17.9, −4.4, −5.2; HRMS (EI) $C_{22}H_{35}N_3O_5Si$ (M - Me^+) 434.2113, found (M - Me^+) 434.2097. Anal. Calcd for $C_{22}H_{35}N_3O_5Si$: C, 58.77; H, 7.85; N, 9.35. Found: C, 59.14; H, 7.89; N, 9.21.

***tert*-Butyldimethylsilyl 2-Azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (38).** To **37** (6.9 g, 15.4 mmol) in THF (70 mL) at 0 °C was added CF_3CO_2H (70 mL). After 15 min, the solution was diluted with Et_2O (200 mL) and washed with ice water (4–500 mL), carefully with 10% $NaHCO_3$, and brine. After being dried, the organic extract was evaporated and the residue was chromatographed (1:4–1:1 Et_2O–hexanes) to give **38** (4.64 g, 74%) as an oil: $[\alpha]_D$ = −34° (*c* = 1.6, $CHCl_3$); IR (neat) 3410, 2930, 2210, 2100, 1460, 1380, 1345, 1245, 1060, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.30 (m, 5 H), 4.98, 4.68 (AB q, 2 H, *J* = 11 Hz), 4.58 (d, 1 H, *J* = 7.6 Hz), 3.85, 3.75 (2 m, 2 H), 3.56 (dt, 1 H, *J* = 2.8, 9.6 Hz), 3.31 (m, 2 H), 3.21 (dd, 1 H, *J* = 10 Hz), 2.32 (d, 1 H, *J* = 2.8 Hz), 1.94 (t, 1 H, *J* = 6.4 Hz), 0.94 (s, 9 H), 0.17, 0.16 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.0, 128.7, 128.1, 128.0, 97.2, 82.3, 75.07, 74.96, 70.5, 68.3, 62.5, 25.5, 17.9, −4.3, −5.2; HRMS (EI) calcd for $C_{19}H_{31}N_3O_5Si$ (M - Bu^+) 352.1330, found (M - Bu^+) 352.1321. Anal. Calcd for $C_{19}H_{31}N_3O_5Si$ (409.561): C, 55.72; H, 7.63; N, 10.26. Found: C, 55.50; H, 7.69; N, 10.16.

***tert*-Butyldimethylsilyl 2-Azido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (39).** A solution of the diol **38** (4 g, 9.78 mmol) and $(Bu_3Sn)_2O$ (3.74 mL, 7.34 mmol) in PhMe (150 mL) was heated to reflux for 4 h (Dean–Stark trap). The temperature was lowered to 80 °C, and $PhCH_2Br$ (3.19 mL, 29.3 mmol) and Bu_4NBr (1.58 g, 4.89 mmol) were added. After 16 h, additional $PhCH_2Br$ (3.19 mL) and Bu_4NBr (1.58 g) were added, and after 24 h, the mixture was cooled, diluted with Et_2O, and extracted with 10% $NaHCO_3$ and brine. The organic layer was evaporated, and the residue was chromatographed (1:9–3:17 Et_2O–hexanes) to give **39** (4 g, 82%) as an oil: $[\alpha]_D$ = −27° (*c* = 1.3, $CHCl_3$): IR (neat) 3470, 2950, 2860, 2210, 2100, 1250, 1110, 1070, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.25 (m, 10 H), 4.92, 4.76 (AB q, 2 H, *J* = 11.2 Hz), 4.59, 4.55 (AB q, 2 H, *J* = 12 Hz), 4.53 (d, 1 H, *J* = 7.6 Hz), 3.71 (app d, 2 H, *J* = 4.8 Hz), 3.64 (dt, 1 H, *J* = 2.4, 9.6 Hz), 3.41 (m, 1 H), 3.32 (dd, 1 H, *J* = 7.6, 10 Hz), 3.21 (dd, 1 H, *J* = 8.8, 9.6 Hz), 2.62 (d, 1 H, *J* = 2.4 Hz), 0.94 (s, 9 H), 0.16 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.2, 137.7, 128.6, 128.4, 128.03, 127.95, 127.7, 127.6, 97.2, 82.3, 74.9, 74.0, 73.7, 71.9, 70.3, 68.1, 25.6, 18.0, −4.3, −5.2; HRMS (EI) calcd for $C_{26}H_{37}N_3O_5Si$ (M - Bu^+) 442.1799, found (M - Bu^+) 442.1795. Anal. Calcd for $C_{26}H_{37}N_3O_5Si$: C, 62.50; H, 7.46; N, 8.41. Found: C, 62.46; H, 7.60; N, 8.33.

***tert*-Butyldimethylsilyl 2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (40).** To **39** (4 g, 8.02 mmol), Et_3N (3.35 mL, 24.1 mmol), and DMAP (98 mg, 0.80 mmol) in CH_2Cl_2 (8 mL) at 0 °C was added portionwise PhCOCl (1.86 mL, 16.0 mmol). The ice bath was removed, and the mixture was stirred at room temperature. After 4 h, additional PhCOCl and Et_3N were added to consume the remaining starting material. The solution was poured onto ice and Et_2O, and the organic layer was washed with H_2O, 1 M $NaHSO_4$, H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic phase was evaporated and the residue was chromatographed (2:1 CH_2Cl_2–CCl_4) to give **40** (4.3 g, 89%) as an oil that solidified: mp 83–84 °C; $[\alpha]_D$ = −66.2° (*c* = 1.5, $CHCl_3$); IR (KBr) 2940, 2860, 2220, 2120, 1730, 1610, 1590, 1250, 1115, 1065, 860, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98–7.10 (m, 15 H), 5.25 (dd, 1 H, *J* = 8.8, 10 Hz), 4.75, 4.60 (AB q, 2 H, *J* = 11.2 Hz), 4.62 (d, 1 H, *J* = 7.2 Hz), 4.46 (s, 2 H), 3.70 (dt, 1 H, *J* = 4.8, 10 Hz), 3.58 (app d, 2 H, *J* = 4.4 Hz), 3.50 (m, 2 H), 0.96 (s, 9 H), 0.199, 0.192 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) δ 165.3, 137.8, 137.4, 133.3, 129.7, 129.5, 128.4, 128.20, 128.18, 128.1, 127.7, 127.50, 127.45, 97.2, 79.8, 74.7, 73.7, 73.5, 71.4, 69.7, 68.4, 25.6, 18.0, −4.3, −5.3; HRMS (EI) calcd for $C_{33}H_{41}N_3O_6Si$ (M - Bu^+) 546.2062, found (M - Bu^+) 546.2068. Anal. Calcd for $C_{33}H_{41}N_3O_6Si$: C, 65.65; H, 6.85; N, 6.96. Found: C, 65.48; H, 6.91; N, 6.89.

2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-D-glucopyranose (41). To **40** (2.3 g, 3.81 mmol) and AcOH (657 μL, 11.5 mmol) in THF (18 mL) was added Bu_4NF in THF (1.0 M; 7.7 mL). After 1 h, the reaction mixture was diluted with CH_2Cl_2 and extracted with H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic phase was evaporated, and the residue was chromatographed (3:7 EtOAc–hexanes) to give **41** (1.79 g, 96%) as a solid: mp 105–108 °C; $[\alpha]_D$ = −44° (*c* = 2.4, $CHCl_3$); IR (KBr) 3380, 2110, 1725, 1610, 1590, 1270, 1140, 1110, 1050, 740, 710, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05–7.10 (m, 15 H), 5.37 (t, 0.6 H, *J* = 4 Hz), 5.32, 5.24 (2 dd, 1 H, *J* = 9, 9 Hz), 4.77, 4.74 (2 d, 1 H, *J* = 4.6 Hz), 4.66 (dd, 0.4 H, *J* = 5.7, 8 Hz), 4.62, 4.59 (2 d, 1 H, *J* = 2.3 Hz), 4.49, 4.81 (app 2 s, 2 H), 4.32, 3.72 (2 m, 1 H), 4.16 (t, 0.6 H, *J* = 10 Hz), 3.91 (d, 0.4 H, *J* = 5.7 Hz), 3.62–3.46 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 165.24, 165.20, 137.19, 137.15, 137.1, 133.4, 129.8, 129.7, 129.3, 129.2, 128.5, 128.28, 128.25, 128.2, 128.1, 128.0, 127.9, 127.8, 127.74, 127.71, 96.1, 91.8, 80.1, 77.5, 75.0, 74.9, 73.6, 73.5, 71.5, 71.0, 69.1, 69.0, 66.9, 63.5; HRMS (EI) calcd for $C_{27}H_{27}N_3O_6$ (M - N_2^+) 461.1839, found (M - N_2^+) 461.1827. Anal. Calcd for $C_{27}H_{27}N_3O_6$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.34; H, 5.69; N, 8.63.

***O*-(2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl) Trichloroacetimidate (42) and *O*-(2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl) Trichloroacetimidate (43).** Alcohol **41** (1.62 g, 3.31 mmol) and CCl_3CN (6.6 mL, 66 mmol) in CH_2Cl_2 (10 mL) were stirred with 4-Å sieves for 3 h. The solution was cooled to −40 °C and DBU in CH_2Cl_2 (1.3 M; 495 μL) was added. At 45-, 90-, and 140-min intervals additional CCl_3CN (3.3 mL) was added. After a further 3 h, the solution was diluted with CCl_4 and filtered through silica (50 g; 2:3 EtOAc–hexanes). The eluate was evaporated, and the residue was chromatographed (1:9 EtOAc–hexanes) to give the α-anomer **42** (1.36 g, 65%) as an oil: $[\alpha]_D$ = +24° (*c* = 1.0, $CHCl_3$); IR (neat) 3350, 2220, 2100, 1725, 1675, 1600, 1580, 1500, 1455, 1255 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.78 (s, 1 H), 8.05–7.15 (m, 15 H), 6.50 (d, 1 H, *J* = 3.6 Hz), 5.57 (t, 1 H, *J* = 9.6 Hz), 4.78, 4.66 (AB

q, 2 H, J = 10.8 Hz), 4.47, 4.45 (AB q, 2 H, J = 11.6 Hz), 4.22 (ddd, 1 H, J = 2.8, 4.4, 9.6 Hz), 4.17 (t, 1 H, J = 9.2 Hz), 3.84 (dd, 1 H, J = 3.6, 10.4 Hz), 3.58 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 165.0, 160.5, 151.0, 137.5, 136.9, 133.4, 129.8, 129.3, 128.5, 128.29, 128.27, 128.2, 127.9, 127.7, 127.5, 94.5, 90.8, 77.6, 75.0, 73.5, 72.2, 70.6, 68.2, 62.6; MS (FAB) m/z 633 ($M^{\bullet+}$), 534, 472, 444, 276. Anal. Calcd. for $C_{29}H_{27}N_4O_6Cl_3$: C, 54.95; H, 4.28; N, 8.84. Found: C, 54.87; H, 4.36; N, 8.69. Further elution gave the β-anomer **43** (450 mg, 21%) as a solid: mp 123–125 °C (Et_2O/hexanes); $[\alpha]_D$ = –50° (c = 1.1, $CHCl_3$); IR (KBr) 2850, 2120, 1730, 1680, 1600, 1580, 1275, 1070, 805, 715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.79 (s, 1 H), 8.00–7.15 (m, 15 H), 5.74 (d, 1 H, J = 8.4 Hz), 5.40 (t, 1 H, J = 9.6 Hz), 4.78, 4.66 (AB q, 2 H, J = 11.2 Hz), 4.48 (s, 2 H), 3.86 (m, 1 H), 3.82 (t, 1 H, J = 8.4 Hz), 3.70 (t, 1 H, J = 9.6 Hz), 3.62 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 165.1, 161.0, 137.6, 137.0, 133.4, 129.8, 129.3, 128.4, 128.3, 128.2, 127.9, 127.7, 127.5, 96.6, 90.4, 80.1, 75.0, 74.9, 73.4, 70.7, 68.6, 65.4; MS (FAB) m/z 597, 517, 472, 444, 276. Anal. Calcd for $C_{29}H_{27}Cl_3N_4O_6$: C, 54.95; H, 4.28; N, 8.84; Found: C, 54.91; H, 4.34; N, 8.83.

(2*S*,4*S*,5*R*)-4-[(2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (44) and (2*S*,4*S*,5*R*)-4-[(2-Azido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (45). Trichloroacetimidate **42** (1.03 g, 1.63 mmol) and alcohol **35a** (649 mg, 1.63 mmol) in CH_2Cl_2 (3.5 mL) were stirred with 4-Å sieves for 4 h. The solution was cooled to –40 °C, and BF_3·Et_2O in CH_2Cl_2 (1.63 M; 100 μL) was added dropwise. After 50 min, the mixture was quenched with solid $NaHCO_3$, diluted with CH_2Cl_2, and allowed to warm up to room temperature. The mixture was centrifuged and the supernatant filtered through silica (1:4 Et_2O–CH_2Cl_2). The eluate was evaporated, and the residue was chromatographed (7:13 Et_2O–hexanes) to give the α-anomer **45** (159 mg, 10%) as an oil: $[\alpha]_D$ = +11° (c = 1.2, $CHCl_3$); IR (neat) 2960, 2100, 1750, 1710, 1600, 1580, 1420, 1345, 1260, 845, 795 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.10–7.10 (m, 25 H), 5.46 (q, 1 H, J = 8.8 Hz), 5.20, 5.09, 5.06, 5.04 (2 AB q, 2 H, J = 12.4 Hz), 5.02, 4.97 (2 d, 1 H, J = 3.6 Hz), 4.72–4.10 (m, 10 H), 3.96 (m, 1 H), 3.76, 3.61 (2 s, 3 H), 3.70–3.28 (m, 5 H), 2.57 (m, 1 H), 2.32 (t, 1 H, J = 13.2 Hz); ^{13}C NMR ($CDCl_3$) δ 171.9, 171.4, 165.0, 154.53, 154.45, 137.9, 137.7, 137.64, 137.61, 137.2, 136.4, 136.3, 133.3, 133.2, 129.83, 129.80, 129.5, 128.43, 128.39, 128.33, 128.31, 128.2, 128.1, 128.01, 127.98, 127.9, 127.82, 127.77, 127.72, 127.69, 127.61, 127.60, 127.42, 127.38, 98.7, 97.3, 82.9, 80.0, 77.6, 74.6, 74.3, 73.5, 73.4, 73.2, 73.1, 70.74, 70.65, 69.80, 69.76, 69.0, 68.4, 67.83, 67.80, 67.1, 67.0, 64.7, 63.4, 62.7, 62.5, 59.0, 58.9, 52.01, 51.95, 35.7, 35.0; HRMS (FAB) calcd for $C_{49}H_{50}N_4O_{11}$ ($M + H^+$) 871.3556, found ($M + H^+$) 871.3383. Anal. Calcd for $C_{49}H_{50}N_4O_{11}$: C, 67.57; H, 5.79; N, 6.43. Found: C, 67.86; H, 5.88; N, 6.41. Further elution gave the β-anomer **44** (600 mg, 42%) as an oil: $[\alpha]_D$ = –71° (c = 1.2, $CHCl_3$); IR (neat) 2870, 2220, 2110, 1720 (br), 1600, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.98–7.10 (m, 25 H), 5.22 (m, 1 H), 5.22, 5.17, 5.13, 5.04 (2 AB q, 2 H, J = 12.4 Hz), 4.73, 4.59 (AB q, 2 H, J = 11.2 Hz), 4.55–4.38 (m, 6 H), 4.36, 4.35 (2d, 1 H, J = 8 Hz), 4.30, 4.20 (2 dd, 1 H, J = 2.8, 6.4 Hz), 3.81–3.35 (m, 7 H), 3.70, 3.55 (2 s, 3 H), 2.51 (m, 1 H), 2.44 (d, 1 H, J = 12.8 Hz); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.5, 165.2, 154.6, 154.5, 138.1, 137.9, 137.63, 137.60, 137.2, 136.44, 136.40, 133.3, 129.7, 129.4, 128.5, 128.44, 128.40, 128.3, 128.22, 128.20, 128.15, 128.00, 127.96, 127.81, 127.75, 127.63, 127.58, 127.53, 127.49, 100.9, 100.5, 82.1, 80.6, 80.24, 80.15, 75.0, 74.9, 73.6, 73.5, 73.3, 73.2, 71.11, 71.06, 69.4, 69.3, 69.1, 68.4, 67.2, 67.0, 66.1, 66.0, 64.5, 63.9, 59.4, 59.2, 52.3, 52.1; HRMS (FAB) calcd for $C_{49}H_{50}N_4O_{11}$ ($M + H^+$) 871.3556, found ($M + H^+$) 871.3677. Anal. Calcd for $C_{49}H_{50}N_4O_{11}$: C, 67.57; H, 5.79; N, 6.43. Found: C, 67.36; H, 5.83; N, 6.36.

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid 2-Methyl 1-(Phenylmethyl) Diester (46). AcSH (1.97 mL) and **44** (600 mg, 0.69 mmol) were allowed to stand for 24 h. The solvent was evaporated, and the residue was chromatographed (Et_2O) to give **46** (489 mg, 80%) as a syrup: $[\alpha]_D$ = –42° (c = 1.2, $CHCl_3$); IR (neat) 3340, 2980, 2890, 1770, 1735, 1720, 1670, 1610, 1590, 1420, 1366, 1275, 1130, 1080, 750, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.00–7.10 (m, 25 H), 6.12, 6.06 (2 d, 1 H, J = 6.4 Hz), 5.31–5.24 (m, 1 H), 5.19, 5.13 (AB q, 2 H, J = 13.0 Hz), 5.13 (2 d, 0.5 H, J = 10.8 Hz), 5.07 (d, 0.5 H, J = 12.4 Hz), 5.01 (t, 1 H, J = 9.5 Hz), 4.6–4.3 (m, 8 H), 4.07, 4.01 (2 d, 1 H, J = 2.4, 5.7 Hz), 3.78–3.36 (m, 5 H), 3.70, 3.62 (2, s 3 H), 2.92–2.80 (m, 1 H), 2.60–2.48 (m, 1 H), 2.32, 2.30 (2 d, 1 H, J = 14.0 Hz), 1.93, 1.90 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 172.5, 172.24, 172.19, 172.0, 165.4, 154.6, 154.5, 138.3, 138.0, 136.6, 136.2, 133.0, 130.0, 129.7, 128.6, 128.4, 128.3, 128.2, 127.9, 127.7, 127.6, 127.54, 127.50, 127.4, 96.8, 96.3, 79.9, 79.8, 78.94, 78.91, 74.6, 74.4, 73.6, 73.5, 73.4, 73.3, 72.9, 72.7, 69.7, 69.2, 68.6, 67.4, 67.1, 64.0, 63.0, 59.7, 59.5, 59.3, 59.01, 58.96, 52.1, 36.1 34.9, 23.6, 23.5; HRMS (FAB) calcd for $C_{51}H_{54}N_2O_{12}$ ($M + H^+$) 887.3757, found ($M + H^+$) 887.3895. Anal. Calcd for $C_{51}H_{54}N_2O_{12}$: C, 69.00; H, 6.14; N, 3.16. Found: C, 68.94; H, 6.15; N, 3.16.

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid 1-Phenylmethyl Monoester (47). Aqueous KOH (3.95 M; 1 mL) was added to **46** (275 mg, 0.29 mmol) in iPrOH (1 mL), and the mixture was vigorously stirred. After 4 days, AG 50W-X4 ion exchange resin (1.5 g, 8 mequiv) was added, and the mixture was stirred for 1 h. The mixture was filtered, and the filtrate was evaporated to give the product (290 mg). Chromatography of an aliquot (100 mg) (1:200 AcOH–EtOAc) gave crude **47** (81 mg) as a syrup: $[\alpha]_D$ = –40° (c = 0.6, $CHCl_3$); IR (KBr) 3400, 2920, 1680, 1410, 1350, 1210, 1120, 1070, 740, 700 cm^{-1}; ^{1}H NMR (CD_3OD) δ 7.50–7.20 (m, 20 H), 5.15–4.75 (m, 6 H), 4.75–4.25 (m, 6 H), 4.18–4.05 (m, 1 H), 3.85–3.30 (m, 8 H), 2.70–2.50 (m, 1 H), 2.35–2.25 (m, 1 H), 1.91, 1.87 (2 s, 3 H); HRMS (FAB) calcd for $C_{43}H_{48}N_2O_{11}$ ($M + H^+$) 769.3336, found ($M + H^+$) 769.3310.

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-4-*O*-benzoyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)-methyl]-1,2-pyrrolidinedicarboxylic Acid Bis(phenylmethyl ester) (50). A CH_2Cl_2 (5 mL) solution of **35b** (1.65 g, 3.56 mmol) and **42** (2.85 g, 4.50 mmol) were stirred with 4-Å sieves. After 3 h, the mixture was cooled to –40 °C and BF_3·Et_2O in CH_2Cl_2 (1.63 M; 276 μL) was added dropwise over a 10-min period. After 45 min, the mixture was quenched with solid $NaHCO_3$ and diluted with CH_2Cl_2, and the mixture was allowed to warm up to room temperature. The mixture was centrifuged, and the supernatant was filtered through silica (1:4 Et_2O–CH_2Cl_2). The eluate was evaporated, and the residue was chromatographed (2:3–1:1 Et_2O–hexanes) to give a mixture of anomers (2.0 g, 59%) as a syrup. The syrup was dissolved in AcSH (5 mL) and allowed to stand for 48 h. After evaporation, chromatography (1:1–4:1 Et_2O–hexanes) gave **50** (1.4 g, 41% from **35b**) as a syrup: $[\alpha]_D$ = –44° (c = 1.6, $CHCl_3$); IR (KBr) 3440, 2880, 1755, 1730, 1710, 1675, 1410, 1350, 1270, 1120, 1070, 740, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.00–7.10 (m, 30 H), 5.62, 5.55 (2 d, 1 H, J = 6.4 Hz), 5.24–4.83 (m, 7 H), 4.64–4.28 (m, 8 H), 4.06–3.96 (m, 1 H), 3.75–3.35 (m, 5 H), 2.65–2.30 (m, 3 H), 1.85, 1.79 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 172.3, 172.1, 172.0, 171.4, 165.3, 154.6, 154.3, 138.12, 138.10, 138.06, 137.7, 136.4, 136.0, 135.8, 135.5, 133.1, 129.7, 128.7, 128.6, 128.58, 128.55, 128.3, 128.2, 128.2, 128.1, 127.97, 127.95, 127.9, 127.8, 127.7, 127.6, 127.43, 127.39, 96.22, 96.17, 95.71, 95.66, 79.4, 78.7, 74.6, 74.5, 73.4, 73.14, 73.06, 73.0, 72.5, 72.4, 69.2, 68.8, 68.3, 67.3, 67.13, 67.10, 67.06, 67.02, 66.98, 66.9, 63.82, 63.8, 62.7, 59.4, 59.34, 59.27, 59.25, 59.0, 36.1, 34.9, 23.6, 23.5; HRMS (FAB) calcd for $C_{57}H_{58}N_2O_{12}$ ($M + H^+$) 963.4040, found ($M + H^+$) 963.3690. Anal. Calcd for $C_{57}H_{58}N_2O_{12}$: C, 71.09; H, 6.07; N, 2.91. Found: C, 70.70; H, 6.13; N, 2.82.

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid Bis(phenylmethyl ester) (48). (1) Amide **46** (100 mg, 0.11 mmol) and $Ti(O\text{-}iPr)_4$ (44 μL, 0.15 mmol) in $PhCH_2OH$ (1 mL) were heated at 115 °C. After 24 h, the solution was chromatographed (1:1–1:0 Et_2O–hexanes) to give **48** (60 mg, 62%) as a syrup: $[\alpha]_D$ = –53° (c = 0.8, $CHCl_3$); IR (CCl_4) 3460, 1765, 1705, 1695, 1545, 1510, 1420, 1360, 1130, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40–7.18 (m, 25 H), 5.60, 5.57 (2 d, 1 H, J = 6.8 Hz), 5.23, 5.03 (AB q, 2 H, J = 12.4 Hz), 5.15, 5.11 (AB q, 2 H, J = 12.2 Hz), 4.96, 4.91 (2 d, 1 H, J = 8.4 Hz), 4.71, 4.70 (2 s, 2 H), 4.61–4.37 (m, 7 H), 4.03, 3.95 (2 dd, 1 H, J = 2.2, 5.8 Hz), 3.70–3.36 (m, 6 H), 2.63–2.38 (m, 2 H), 2.51, 2.49 (2 d, 1 H, J = 2.4 Hz), 2.32, 2.30 (2 d, 1 H, J = 13.6 Hz), 1.87, 1.81 (2 s, 3 H); ^{13}C NMR ($CDCl_3$) δ 172.04, 171.94, 171.4, 154.6, 154.4, 139.0, 138.20, 137.96, 136.5, 136.2, 136.0, 135.8, 128.6, 128.5, 128.42, 128.38,

128.2, 128.13, 127.98, 127.7, 127.6, 127.52, 127.46, 96.7, 96.1, 79.5, 79.2, 78.6, 74.5, 74.4, 73.7, 73.3, 73.2, 73.1, 70.3, 69.2, 68.5, 67.4, 67.1, 67.0, 66.9, 63.9, 62.9, 59.5, 59.2, 59.1, 58.8, 36.2, 35.0, 23.6, 23.5; HRMS (FAB) $C_{50}H_{54}N_2O_{11}$ (M + H^+) 859.3808, found (M + H^+) 859.3746. Anal. Calcd for $C_{50}H_{54}N_2O_{11}$: C, 69.91; H, 6.34; N, 3.26. Found: C, 69.68; H, 6.47; N, 3.19.

(2) Aqueous KOH (3.95 M; 120 μL) was added to **50** (220 mg, 0.23 mmol) in MeOH (2.9 mL). After 2 h, additional KOH solution (60 μL) was added and after a further 1 h MeOH (5 mL) and AG 50W-X4 ion exchange resin (1.5 g) were added. Filtration and evaporation gave an oil that was dissolved in EtOAc and dried. Evaporation and chromatography gave **48** (145 mg, 74%).

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-4-*O*-sulfo-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-[(benzyloxy)methyl]-1,2-pyrrolidinedicarboxylic Acid Bis(phenylmethyl ester) (49). To **48** (66 mg, 0.077 mmol) in DMF (200 μL) was added pyridine·SO_3 in DMF (1.0 M; 310 μL). After 50 min and 1 h, respectively, additional pyridine·SO_3 in DMF (310 μL) and H_2O (12 mg, 0.67 mmol) and Et_3N (86 μL, 0.62 mmol) in Me_2CO (1 mL) were added at 0 °C, and the mixture was chromatographed (Me_2CO) on the sodium form of AG 50W-X4 ion exchange resin (87 mmol). The product fractions were reapplied to the column three more times to insure complete exchange. Finally, the eluate was evaporated, and the residue was chromatographed (1:19–1:1 iPrOH–EtOAc), to give **49** (49 mg, 65%) as a syrup: $[\alpha]_D$ = +5° (*c* = 3.0, $CHCl_3$); IR (KBr) 3430, 1750, 1710, 1670, 1550, 1500, 1270, 1220, 1140, 1070, 1055, 805, 740, 700, 605 cm^{-1}; ^1H NMR (CD_3OD) δ 7.45–7.10 (m, 25 H), 5.18–4.95 (m, 6 H), 4.63–4.25 (m, 8 H), 4.15–4.00 (m, 2 H), 3.75–3.35 (m, 7 H), 2.60–2.45 (m, 1 H), 2.35–2.25 (m, 1 H), 1.87, 1.79 (2 s, 3 H); ^{13}C NMR (CD_3OD) δ 173.6, 173.4, 172.5, 172.1, 156.49, 156.47, 140.0, 139.8, 139.5, 139.4, 137.6, 137.5, 129.6, 129.5, 129.4, 129.30, 129.25, 129.20, 129.1, 128.9, 128.8, 128.7, 128.5, 99.9, 82.4, 81.5, 80.3, 78.5, 76.0, 75.84, 76.81, 74.3, 74.1, 71.0, 70.9, 69.9, 69.3, 68.5, 68.2, 67.9, 65.4, 64.8, 60.9, 60.5, 56.2, 56.1, 36.7, 35.8, 23.4, 23.3; HRMS (FAB) calcd for $C_{50}H_{54}N_2O_{14}SNa$ (M + H^+) 961.3194, found (M + H^+) 961.3175. Anal. Calcd for $C_{50}H_{53}N_2O_{14}SNa$: C, 62.49; H, 5.56; N, 2.92. Found: C, 61.70; H, 5.64; N, 2.83.

Bulgecin C (1c). To a stirred mixture of Pd black (33 mg) in 95% formic acid (500 μL) under nitrogen was added **49** (41 mg) in MeOH (500 μL). After 30 min, the mixture was filtered and the solvents were evaporated. The sticky residue was dissolved in H_2O (500 μL) and concentrated under a stream of nitrogen. The residue was further evaporated at 1 mmHg to give a foam (21 mg). Chromatography on 20 μ cellulose (1:4 H_2O–iPrOH) gave bulgecin C (**1c**) (14 mg, 70%) as a white foam: TLC R_f = 0.6 (1:3 H_2O–iPrOH); $[\alpha]_D$ = +6° (*c* = 0.51, 1 M AcOH in H_2O) [lit.[1] $[\alpha]_D$ = +2.9° (*c* = 0.6, 1 M AcOH)]; IR (KBr) 3420, 1640, 1570, 1255, 1045, 825 cm^{-1}; ^1H NMR (D_2O, sodium 3-(trimethylsilyl)-propionate-2,2,3,3-d_4 external standard) δ 4.65 (d, 1 H, *J* = 8.0 Hz), 4.43 (dd, 1 H, *J* = 5.2, 5.2 Hz), 4.22–4.14 (m, 2 H), 3.95 (dd, 1 H, *J* = 2.0, 10.4 Hz), 3.88–3.70 (m, 6 H), 3.64–3.56 (m, 1 H), 2.76–2.66 (m, 1 H), 2.40–2.30 (m, 1 H), 2.06 (s, 3 H); ^{13}C NMR (D_2O, 1,4-dioxane standard) δ 175.1, 173.8, 101.0, 79.2, 77.3, 74.8, 72.4, 65.4, 60.9, 59.9, 58.4, 55.7, 35.5, 22.6; HRMS (FAB) calcd for $C_{14}H_{23}N_2NaO_{12}S$ (M + Na^+) 489.0767, (M + H^+) 467.0948, found (M + Na^+) 489.0703, (M + H^+) 467.0974. The IR, ^1H, ^{13}C data were identical with that obtained in our laboratories for a sample of the authentic material.

(2*S*,4*S*,5*R*)-4-[(2-Acetamido-2-deoxy-β-D-glucopyranosyl)oxy]-5-(hydroxymethyl)-1,2-pyrrolidinedicarboxylic Acid (51). To a mixture of 95% formic acid (500 μL) and palladium black (61 mg, 0.57 mmol) under nitrogen was added **47** (60 mg, 0.078 mmol) in MeOH (600 μL). After 1 h of stirring, the mixture was filtered and the eluate was evaporated. The foam was dissolved in just enough 0.5 M $NaHCO_3$ to give a basic solution and chromatographed on AG 50W-X4 ion exchange resin. The column was eluted with H_2O until the eluate was neutral and then with 1.5 M aqueous ammonia. The product fractions were concentrated under a stream of nitrogen, and the residue was further evaporated at <0.5 mmHg to give **51** (25 mg, 89%) as a white foam. The foam was dissolved in a trace amount of H_2O and MeOH was added to form a precipitate. This mixture was sonicated, and the solid **51** was isolated by centrifugation: mp 228 °C dec (lit.[22] mp 235–238 °C dec); $[\alpha]_D$ = −4° (*c* = 0.7 H_2O) [lit.[22] −4.1° (*c* = 0.54, H_2O)]; IR (KBr) 3320, 1620, 1530, 1370, 1305, 1055 cm^{-1}; ^1H NMR (D_2O) δ 4.61 (d, 1 H, *J* = 8.2 Hz), 4.42 (app q, 1 H, *J* = 5.1 Hz), 4.20 (dd, 1 H, *J* = 6.9, 8.9 Hz), 3.95–3.40 (m, 9 H), 2.78–2.66 (m, 1 H), 2.43–2.32 (m, 1 H), 2.06 (s, 3 H); ^{13}C NMR (D_2O, first peak set to 23.1 (lit.[22] δ)) δ 175.6 (175.1), 174.4 (174.0), 101.7 (101.5), 79.8 (79.6), 76.9 (76.7), 74.5 (74.3), 70.7 (70.7), 66.0 (65.9), 61.6 (61.6), 60.5 (60.4), 58.9 (58.8), 56.5 (56.4), 36.0 (35.9), 23.1; HRMS (FAB) calcd for $C_{14}H_{24}N_2O_9$ (M + H^+) 365.1561, found (M + H^+) 365.1539. Anal. Calcd for $C_{14}H_{24}N_2O_9$: C, 46.14; H, 6.63; N, 7.68. Found: C, 45.44; H, 6.68; N, 7.40.

***N*-[(2*S*,4*S*,5*R*)-4-[(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)oxy]-5-(hydroxymethyl)-L-prolyl]-6-aminopenicillinic Acid Bis(phenylmethyl ester) (53a).** Carboxylic acid **47** (80 mg, 0.10 mmol) and amine **52** (69 mg, 0.13 mmol) in DMF (600 μL) were cooled in an ice bath, and $(EtO)_2P(O)CN$ (19 μL, 0.13 mmol) and Et_3N (35 μL, 0.25 mmol) were added. The cooling bath was removed and, after 2 h, the reaction mixture was diluted with EtOAc and extracted with 1 M $NaHSO_4$, H_2O, 10% $NaHCO_3$, and brine. After being dried, the organic phase was rotary evaporated, and the residue was chromatographed (2:3 EtOAc–benzene) to give **53a** (82 mg, 70%) as a foam: IR (KBr) 3380, 1770, 1705, 1680, 1120, 1070, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70–7.10 (m, 30 H), 6.98, 6.97 (2 d, 1 H, *J* = 6.4 Hz), 6.95 (s, 1 H), 5.63, 5.54 (2 d, 1 H, *J* = 4.0 Hz), 5.40–5.20 (m, 2 H), 5.05–4.85 (m, 2 H), 4.80–4.65 (m, 2 H), 4.60–4.10 (m, 10 H), 3.80–3.35 (m, 6 H), 2.80–2.60 (m, 2 H), 2.28–2.18 (m, 1 H), 1.74, 1.72 (2 s, 3 H), 1.57, 1.54 (2 s, 3 H), 1.20, 1.17 (2 s, 3 H). The crude product was used directly in the next step.

***N*-[(2*S*,4*S*,5*R*)-4-[(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-4-*O*-sulfo-β-D-glucopyranosyl)oxy]-5-(hydroxymethyl)-L-prolyl]-6-aminopenicillinic Acid Bis(phenylmethyl ester) (53b).** To **53a** (80 mg, 0.07 mmol) in DMF (600 μL) under nitrogen was added pyridine·SO_3 in DMF (1 M; 280 μL). After 1 h, additional pyridine·SO_3 in DMF (280 μL) was added. After 3 h, H_2O (10 mg, 0.56 mmol) and Et_3N (78 μL, 0.56 mmol) in Me_2CO (1 mL) were added. The mixture was applied to a column of AG 50W-X4 ion exchange resin (sodium form, 87 mequiv) and eluted with Me_2CO. The product fractions were reapplied to the column three times. Finally, the product fractions were evaporated, and the residue was chromatographed on silica (2 g; 1:49–1:10 iPrOH–EtOAc). Evaporation gave **53b** (70 mg, 80%) as a foam: IR (KBr) 3440, 1800, 1765, 1680, 1280, 1230, 1130, 1070, 820, 760, 720 cm^{-1}; ^1H NMR (CD_3OD) δ 7.60–7.15 (m, 30 H), 6.96 (s, 1 H), 5.54, 5.48 (2 d, 1 H, *J* = 4.4 Hz), 5.46, 5.35 (2 d, 1 H, *J* = 4.0 Hz), 5.20–4.95 (m, 2 H), 4.70–4.25 (m, 10 H), 4.20–4.05 (m, 2 H), 3.85–3.45 (m, 5 H), 2.75–2.60 (m, 1 H), 2.28 (d, 1 H, *J* = 15.2 Hz), 1.85, 1.79 (2 s, 3 H), 1.62, 1.59 (2 s, 3 H), 1.26, 1.22 (2 s, 3 H); HRMS (FAB) calcd for $C_{64}H_{67}N_4O_{16}S_2Na$ (M + Na^+) 1257.3789, found (M + Na^+) 1257.3792.

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