Sulfinic acids 17,[4] **20**,[73] **40**,[35] **45**,[74] **51**,[75] **57**,[74] and **81**[76,77] were prepared as previously described. The sodium or magnesium salts of the sulfinic acids were carefully acidified with 60% sulfuric acid in water at 0 °C, extracted three times with ether, and dried ($MgSO_4$). The combined ether extracts were concentrated to give the sulfinic acids.

Reaction of S-Butyl Butanethiosulfinate (36) and Butanesulfinic Acid (57). A solution of **57** (0.126 g, 1.03 mmol) in 1.5 mL of $CDCl_3$ was added to an equimolar amount of **36** (0.200 g, 1.03 mmol) in 1.5 mL of $CDCl_3$ in a 10-mm NMR tube at 0 °C. After 7 min, the reaction was followed by ^{13}C NMR at 0 °C. The reaction was essentially complete after 40 min at 0 °C. The disappearance of the resonances of the sulfur-bonded carbon atoms of **36** and **57** was used to monitor the reaction.

Oxidation of Alkanethiosulfinates with MCPBA. The oxidation was carried out using the previously described techniques.[4,6,12,41] The general procedure for the low-temperature ^1H NMR and ^{13}C NMR experiments is given below.

The apparatus used for these experiments is shown in Figure 4. It consists of a 10-mL cylinder surrounded by a vacuum jacketed Dewar flask with a medium glass frit at the bottom. A 25-mL three-neck flask with a ground-glass joint at the bottom of it was placed on top of the 10-mL cylinder. A nitrogen inlet, an overhead stirrer, and a 10-mL addition funnel were placed on the three-neck flask. The bottom delivery tube of the addition funnel was fitted with a small piece of $^1/_8$-in.-diameter Teflon tubing, which ended directly above the 10-mL cylinder. Below the glass frit, the tube ended in a male ground-glass joint (Figure 4), which was connected to one neck of a two-neck 10-mL pear-shaped flask. A septum with a $^1/_{16}$-in. Teflon tube through it was placed on the other neck of the pear-shaped flask. The Teflon tube was inserted about 1 cm through the septum and the outside of the Teflon tube was clamped.

In a typical experiment, after the apparatus was thoroughly dried in an oven and cooled while nitrogen was bled into the 10-mL cylinder, 1.7 mmol of thiosulfinate dissolved in 0.5 mL of $CDCl_3$ was placed inside the 10-mL cylinder. The Dewar was charged with 2-propanol and cooled to the desired temperature with dry ice while a positive pressure of nitrogen was applied from the top, and the stirrer was started. Three minutes after the desired temperature in the Dewar was achieved, a solution of 1.7 mmol of 81% MCPBA dissolved in 4.5 mL of $CDCl_3$ was added dropwise within a 5-min period. The addition funnel was then removed and replaced with a ground-glass stopper. After 45–60 min, the stirrer was stopped and the temperature of the bath brought to −45 °C. Another dry ice/2-propanol bath at −40 °C was placed around the 10-mL pear-shaped flask.

A nitrogen pressure of 5 lb was applied to the apparatus while the stopper and the stirrer fitting on the other two necks of the three-neck flask were kept in place by hand. After filtration of the solution into the pear-shaped flask (5–10 min), a 10-mm NMR tube in which the air was replaced with nitrogen was placed in a dry ice/2-propanol bath at −40 °C. The outside end of the Teflon tube was unclamped and placed inside the NMR tube, and the end of the Teflon tube inside the septum was pushed to the bottom of the pear-shaped flask. Nitrogen pressure through a needle that pierced the septum forced the solution into the NMR tube within 10–15 s. The NMR tube was immediately capped and a narrow strip of parafilm was placed along the lower edge of the cap. The NMR tube, which was still immersed in the dry ice/2-propanol bath, was taken immediately to the NMR spectrometer.

The WM-250 NMR spectrometer was fitted with the multinuclear probe and the synthesizer was tuned to the frequency of the ^{13}C nucleus. In addition to ^{13}C NMR spectra, ^1H NMR spectra were obtained with this probe by using the broad-band decoupler as the receiving coil and the ^1H NMR preamplifier instead of the multinuclear synthesizer. Nucleus changeover, including change of acquisition parameters in the computer, required 2–3 min. Owing to the presence of sidebands, the ^1H NMR spectra obtained in this manner were not as well resolved as those obtained with the ^1H probe.

Preliminary experiments showed that when 5-mm instead of 10-mm NMR tubes were used to contain the cold solutions, the temperatures of the solutions rose during the 30–60-s interval required for the transfer of the NMR tube from the dry ice/2-propanol bath to the probe of the spectrometer. Since the available ^1H NMR probe only accepted 5-mm NMR tubes, it was not used for these experiments.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research and to the National Science Foundation for assistance in the purchase of the NMR spectrometers. We also express our thanks to Professor John L. Kice (Texas Tech University) for helpful discussions.

Registry No. 12, 2949-92-0; (±)-**26**, 67501-06-8; **27**, 85085-04-7; **28**, 85085-05-8; (±)-**30**, 85085-12-7; **31a**, 82871-76-9; **31b**, 82871-77-0; (±)-**33**, 85085-08-1; (±)-**34**, 85085-09-2; (±)-**35**, 85085-10-5; (±)-**36**, 85085-11-6; (±)-**37**, 85097-11-6; **38**, 85084-97-5; **39**, 85084-98-6; **40**, 17696-73-0; **41**, 85084-99-7; **43**, 85085-13-8; **44**, 85085-14-9; **45**, 55109-28-9; **46**, 1113-13-9; **47**, 70565-74-1; **49**, 85085-00-3; **50**, 85085-01-4; **55**, 85085-02-5; **56**, 85085-03-6; **61**, 85085-06-9; **62**, 85085-07-0; MCPBA, 937-14-4.

Supplementary Material Available: Tables and figures of product distributions from MCPBA oxidation and NMR chemical shifts of products (11 pages). Ordering information is given on any current masthead page.

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Enantioselective Synthesis of the Carbocyclic Nucleosides (−)-Aristeromycin and (−)-Neplanocin A by a Chemicoenzymatic Approach

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Abstract: An efficient synthesis of the carbocyclic nucleosides (−)-aristeromycin and (−)-neplanocin A has been developed in an enantioselective and stereocontrolled manner starting from the Diels–Alder adduct of cyclopentadiene and dimethyl acetylenedicarboxylate. The symmetric unsaturated dimethyl ester, dimethyl (3aα,4β,7β,7aα)-3a,4,7,7a-tetrahydro-2,2-dimethyl-4,7-methano-1,3-benzodioxole-5,6-dicarboxylate, was quantitatively hydrolyzed with pig liver esterase to yield a half-ester with reasonably high optical yield. Decarboxylative ozonolysis followed by chemical transformation afforded versatile chiral intermediates of cyclopentylamine and cyclopentenylamine that were converted to (−)-aristeromycin and (−)-neplanocin A, respectively.

Since the pioneering synthesis of the racemic carbocyclic analogue of adenosine[1] by Shealy and Clayton and subsequent isolation of aristeromycin (**1**) as the (−) enantiomer from *S. citricolor* n.sp.,[2] the interest in this class of compounds has grown

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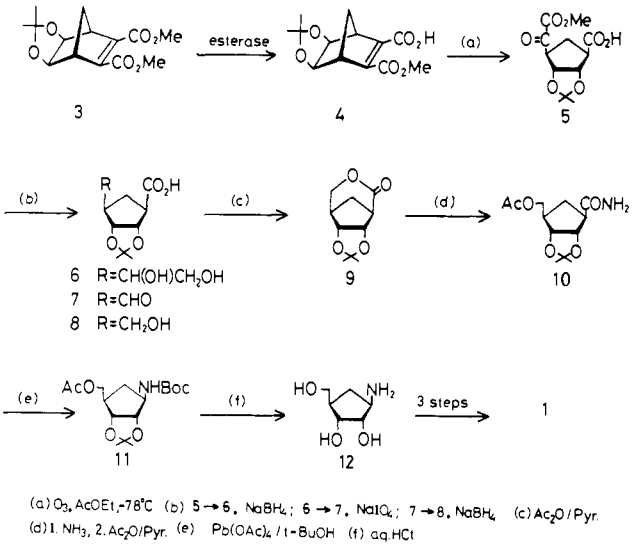
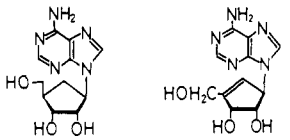
Scheme I



rapidly, and other carbocyclic analogues of purine and pyrimidine nucleosides have attracted a great deal of synthetic[3] and biological study.[4] Furthermore, a new antibiotic named neplanocin A (**2**) was isolated from *Actinoplanacea ampullariella* sp., and it has been shown that **2** is a novel carbocyclic analogue of adenosine with a cyclopentene moiety and exhibits remarkable antitumor activity against L1210 leukemia in mice and low toxicity.[5] These naturally occurring carbocyclic nucleosides are all obtained in optically active forms, and the absolute structures were established by X-ray analysis[6] (**1** and **2**). However, all of the cyclopentane



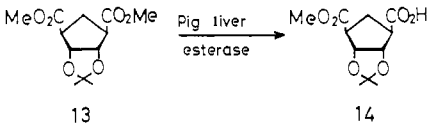
nucleosides previously synthesized were obtained in racemic forms, and the chiral carbocyclic moiety seems to be not easily accesible by conventional synthetic means or partial degradation of **1** and **2**. We wish to report here the first and enantioselective synthesis of (−)-aristeromycin (**1**) and (−)-neplanocin A (**2**) through the optically active half-ester **4**, enzymatically generated starting from the symmetric unsaturated diester **3** as shown in Schemes I, II, and III.

(−)-Aristeromycin (1)

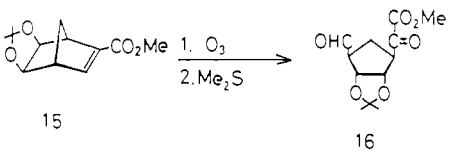
The control of absolute stereochemistry is indeed a central problem in the synthesis of biologically significant enantiomers of natural products. However, the key intermediate, 4β-amino-2α,3α-dihydroxy-1β-cyclopentanemethanol, for the synthesis of carbocyclic ribonucleosides was always obtained in racemic form by previous synthetic efforts of a number of groups.[3] An efficient access to chirality is the enantioselective generation of an asymmetric compound from a prochiral[7a] or a meso starting material[7b] by introduction of an enzymatic step in the synthetic strategy (Scheme I).

Thus, an unsaturated half-ester **4** and a δ-lactone **9** were considered to be versatile intermediates for the enantioselective synthesis of the sugar moiety of **1** and **2**, if **4** and **9** are formed in optically active forms from a readily available diester **3**[9] in meso form. The diester **3** was efficiently prepared by Danishefsky's procedure[9] from cyclopentadiene and dimethyl acetylenedicarboxylate, and it was treated with pig liver esterase[10] in aqueous acetone (3 g of **3**, 30 mL of acetone, 300 mL of 0.1 M phosphate buffer solution, 4140 units of the esterase,[10] pH 8.0, 30–32 °C, 5 h) to afford the half-ester **4** in optically active form and in quantitative yield. The absolute configuration of **4** was assumed to be the same as in the case of ribose system[7b] and indeed confirmed to be **4** by synthetic transformation to **1** and **2**. The optical purity of the half-ester **4** directly obtained by the enzyme-catalyzed reaction was found to be about 80% ee, but the optically pure material was most easily and preferably obtained by recrystallization of the δ-lactone **9**. The crude half-ester **4** was without further purification subjected to ozonolysis in ethyl acetate at −78 °C for 3 h, and the decarboxylative cleavage took place completely by bringing the solution to room temperature to afford the α-keto ester acid **5** in nearly quantitative yield. In the present chemicoenzymatic strategy, this decarboxylative ozonolysis step is very important as well the enzymatic process, because it is necessary to generate the carbocyclic skeleton with two chemically differentiated functional groups located at the 1,4-positions for further transformation.

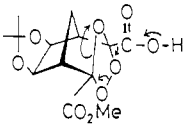
It should be mentioned here that another potential substrate or a meso diester **13**[1] could be used for the synthesis of carbocyclic



nucleosides, but the optical purity of the half-ester **14** enzymatically produced was found not enough for our synthetic purpose (about 60% ee). Just and co-workers[8] showed that the racemic ester **15** was cleaved with ozone to afford aldehydo keto ester **16**,



which was further oxidized to give racemic δ-lactone **9** in 49% overall yields from **15**. The aldehydo keto ester **16** was used for the synthesis of carbocyclic C-nucleosides without resolution. The decarboxylative ozonolysis can be reasonably explained by regiospecific decomposition of the ozonide intermediate **17** without losing optical purity.



Three successive treatments of **5** (reduction with $NaBH_4$, **5** → **6**; cleavage of the vicinal glycol with $NaIO_4$ and 2 N HCl, **6** → **7**; and reduction with $NaBH_4$, **7** → **8**) afforded the alcohol **8**.

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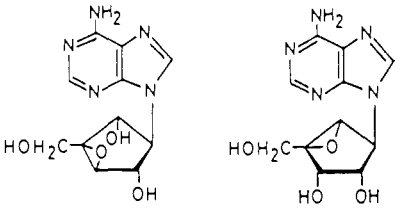
(10) This was purchased from Sigma Co. and corresponds to 30 mg of the protein.

Treatment of **8** with Ac_2O–Py at room temperature for 12 h afforded crystalline δ-lactone **9** in 60% overall yields from **5** after workup and chromatography on silica gel. The product showed $[\alpha]^{25}_D$ +35.9° (*c* 0.8, $CHCl_3$) and mp 127–137 °C, and it was confirmed that recrystallization from a mixed solvent of methylene chloride, *n*-hexane, and ether (1:5:5) easily afforded optically pure δ-lactone **9** in 80% yield with $[\alpha]^{25}_D$ +44.4° (*c* 1.0, $CHCl_3$), mp 140–141.5 °C, and R_f 0.61 (ether). Treatment of the purified lactone **9** with NH_3 in methanol followed by acetylation with Ac_2O–Py gave the carbamoyl derivative **10** as a colorless oil [$[\alpha]^{20}_D$ −32.6° (*c* 1.55, $CHCl_3$)] in 98% yield after workup and chromatography on silica gel. Hofmann degradation of **10** with $Pb(OAc)_4$ in *tert*-butyl alcohol proceeded smoothly by adding Et_3N drop by drop under reflux, affording **11** as a colorless oil [$[\alpha]^{25}_D$ −4.7° (*c* 0.62, $CHCl_3$)] in 78% yield after removal of the solvent and chromatography on silica gel. The protective groups were removed with 2 N HCl and the free cyclopentylamine **12** was obtained by purification with Amberlite CG-120 (H^+ form) in 97% yield, showing $[\alpha]^{20}_D$ −10.3° (*c* 1.52, H_2O).[11] The remainder of the synthesis of **1** from **12** was carried out according to the known three-step sequence[1,12] (successive treatment with 5-amino-4,6-dichloropyrimidine, triethyl orthoformate, and NH_3). (−)-Aristeromycin was obtained in 46% overall yields from **12** after purification with Amberlite CG-120 (H^+ form), showing $[\alpha]^{20}_D$ −53.0° (*c* 0.53, DMF) and mp 214–215 °C dec. The synthetic sample was confirmed to be identical in all respects with natural aristeromycin[13] (14 steps in about 17% overall yields from **3** to **1**).

(−)-Neplanocin A (2)

Among neplanocins, A (**2**), B (**18**), C (**19**), D (**20**), and F (**21**),



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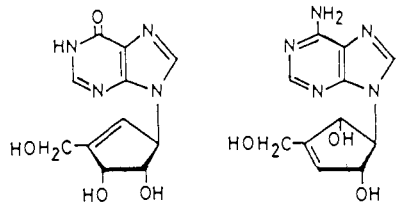

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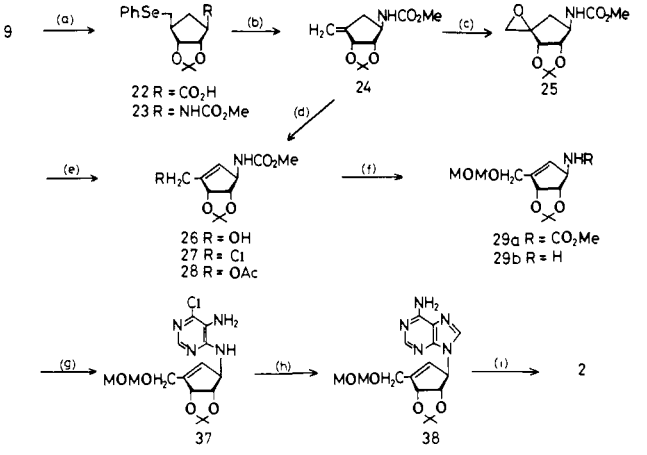
neplanocin A (**2**) has the most remarkable effect on the life prolongation in mice bearing L1210 leukemia (the increased life span was found to be 120% against L1210 leukemia at a dose of 5 mg/kg, per day).[14] Therefore, neplanocin A was selected as our next synthetic target.

Thus, the δ-lactone **9** was treated with PhSeNa generated in situ from diphenyl diselenide and $NaBH_4$ in DMF to afford the selenide **22** in 93% yield [$[\alpha]^{25}_D$ +9.5° (*c* 1.93, $CHCl_3$)].[15] It was converted to the methyl carbamate **23**, $[\alpha]^{20}_D$ +18.8° (*c* 1.05, $CHCl_3$), in 91% yield by a one-pot reaction of four-step sequence

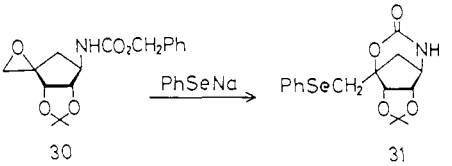
Scheme II



(a) 9→22, PhSeNa ; 22→23, 1 $ClCO_2Et$ / NEt_3 , 2 NaN_3 , 3 Δ in C_6H_6 , 4 MeOH (b) 1 O_3 , 2 catalytic Pyr (c) MCPBA (d) 24→27, t-BuOCl / HCO_2Me , 27→28, NaOAc / KI , 28→26, Na_2CO_3 (e) 25→26, 1 Me_3SiOTf / 2,6-Lutidine , 2 DBU , 3 K_2CO_3 (f) 26→29a, $MeOCH_2Cl$ / i-Pr_2NEt ; 29a→29b, aq KOH (g) 5-Amino-4,6-dichloropyrimidine / NEt_3 (h) 1 $HC(OEt)_3$ / Ac_2O 2 NH_3 (i) 2N HCl / MeOH

(treatment with ethyl chloroformate and then NaN_3, Curtius rearrangement at 80 °C in benzene, and addition of methanol to the isocyanate intermediate). The exo methylene of **24** was easily introduced by treatment of **23** with ozone at −78 °C for 15 min followed by removal of the selenoxide with a trace amount of pyridine[15] (95% yield with $[\alpha]^{20}_D$ +138.8° (*c* 1.01, $CHCl_3$)). Formation of the allyl alcohol **26** from **24** was the most crucial step in the present approach (Scheme II).

Three routes were extensively investigated. The first route was based on the isomerization of the oxirane **25** to the allylic alcohol **26**. The epoxide **25**, chromatographically homogeneous, was obtained in 91% yield with *m*-chloroperbenzoic acid, and only Noyori's procedure[16] (Me_3SiOTf, 2,6-lutidine, and DBU) was successfully applied to yield regiospecifically the required cyclopentane alcohol **26** in 28% yield with 34% recovery of **25**. The second route was based on an ene-type reaction.[17] Treatment of **24** with *tert*-butyl hypochlorite at −78 °C in methyl formate gave regiospecifically the allyl chloride **27** in good yield, and the allyl acetate **28** was obtained from **27** with sodium acetate in the presence of potassium iodide in DMF (48% yield form **24**). Then the allyl acetate was hydrolyzed with sodium carbonate to yield **26** in quantitative yield. The latter procedure seems to be more practical for a larger scale synthesis, because it is operationally very easy. The stereochemistry of the epoxide **25** was unambiguously determined to be β by the reaction in which the cyclic carbamate **31** was formed in excellent yield by treatment of the benzyl carbamate **30**, similarly prepared as in the case of the methyl carbamate **23**, with PhSeNa. The formation of the cyclic



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carbamate is only possible between β-epoxide and β-benzyl carbamate groups in cis relation.

The primary alcohol of **26** was quantitatively protected with $MeOCH_2Cl$ (MOM-Cl) to afford stable **29a**. The third route to the cyclopentene moiety is summarized in Scheme III. Thus, the methyl ester of **7** was once isolated (71.2% overall yields from **4**) and converted to the enol acetate **32** with Ac_2O in the presence of *p*-(dimethylamino)pyridine in 73% yield. The enol acetate **32**

(11) Racemic **12** was obtained by Shealy and Clayton[1] and Cermak and Vince (Cermak, R. C.; Vince, R. *Tetrahedron Lett.* **1981**, *22*, 2331).
(12) Montgomery, J. A.; Temple, C. *J. Am. Chem. Soc.* **1957**, *79*, 5238.
(13) Natural aristeromycin, $[\alpha]^{25}_D$ −52.5° (*c* 1.0, DMF) and mp 213–215 °C (dec), was kindly supplied by Takeda Chemical Industries, Ltd.
(14) Hayashi, M.; Yaginuma, S.; Muto, N.; Tsujino, M. *Nucleic Acid Res. Symp. Ser.* **1980**, *8*, 65.
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(16) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 2738.
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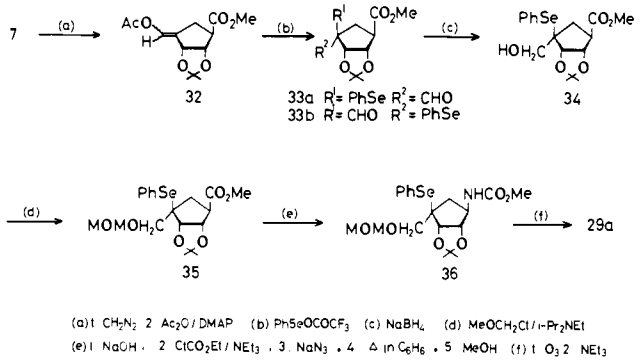
Scheme III



was considered to be a mixture of *E* and *Z* isomers in about a 1:5 ratio from ^{1}H NMR of the vinyl proton, but the mixture was used for the next step without separation. Treatment of **32** with phenylselenenyl trifluoroacetate[18] at 0–10 °C afforded a mixture of the phenylselenenyl derivatives **33a** and **33b** in almost equal amount (91.8% yield), which were easily separated by column chromatography on silica gel. The same reaction at −78 °C afforded **33a** predominantly (73% yield) along with some **33b** (12% yield). The stereochemistry of **33a** and **33b** was assigned reasonably by ^{1}H NMR (see Experimental Section). The formyl group of **33a** was first reduced to the alcohol **34** with $NaBH_4$ in 95% yield. Protection of the primary alcohol of **34** (**34** → **35**, 87% yield) followed by quantitative hydrolysis with NaOH and Curtius rearrangement (74% yield) afforded the methyl carbamate **36** in excellent yield. Introduction of the endo double bond took place again regiospecifically by oxidative removal of the phenylseleno group of **36** with ozone and then with triethylamine to afford **29a** in 98% yield. The other isomer, **33b**, gave also the same unsaturated methyl carbamate **29a** by the same series of reactions. The unsaturated methyl carbamate **29a** was hydrolyzed with KOH in aqueous methanol under reflux for 12 h to afford the cyclopentenaneamine **29b** in quantitative yield. The free amine **29b** was found to be rather stable at room temperature and was without further purification subjected to the three-step sequence of reactions (successive treatment with 5-amino-4,6-dichloropyrimidine, **29b** → **37**, triethyl orthoformate, and NH_3, **37** → **38**), and finally the protective group was removed with 2 N HCl in methanol at room temperature for 16 h. After removal of the solvent, the product was purified by an ion exchange resin on Amberlite CG-120 (H^+ form), affording **2** in 42% overall yield from **26**. The synthetic neplanocin A showed $[\alpha]^{20}_D$ −152° (*c* 0.3, H_2O) and mp 220–222 °C after recrystallization from MeOH–H_2O (9:1). The synthetic sample was confirmed to be identical in all respects with natural neplanocin A.[19]

The key features of the present methodolgy include the following: (1) pig liver esterase efficiently hydrolyzed the meso bicyclic diester compound **3** with reasonably high optical purity; (2) decarboxylative ozonolysis of the unsaturated half-ester **4** directly afforded the desired carbocyclic skeleton **5** with two differentiated functional groups at the 1,4-positions; (3) the key intermediates **12** and **29b** with desired absolute configuration have become available for synthesis of various carbocyclic nucleosides not accessible from natural sources. Further investigation of the present chemicoenzymatic approach to other potential carbocyclic nucleosides is in progress in our laboratory, and the results will be reported in due course.

Experimental Section

Melting points were measured on a Yamato MP-21 apparatus and were uncorrected. Nuclear magnetic reasonance (^{1}H NMR and ^{13}C NMR) spectra were obtained on a JEOL FX-100 spectrometer and chemical shifts are expressed in ppm downfield from Me_4Si. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded on a JASCO A-102 spectrometer. Mass spectra (MS) were measured with a JEOL JMS-01 SG-2 mass spectrometer. Optical rotations were measured with a JASCO DIP-140 digital polarimeter. Silica gel (Wakogel C-200) was used for column chromatography and silica gel (Kiesel gel 60 F254, Merck) for thin-layer chromatography (TLC).

(3a*S*,4*S*,7*R*,)-3a,4,7,7a-Tetrahydro-2,2-dimethyl-6-(methoxycarbonyl)-4,7-methano-1,3-benzodioxole-5-carboxylic Acid (4). To a solution of 3 g (10.6 mmol) of the diester **3** in 30 mL of acetone and 300 mL of 0.1 M phosphate buffer (pH 8) was added 3 mL (4140 units) of pig liver esterase.[10] The mixture was incubated for 5 h at 30–32 °C and then acidified to pH 2 with 2 M hydrochloric acid and extracted with CH_2Cl_2 (3 × 300 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo to afford 2.84 g (99.6%) of half-ester **4** as a white solid: mp 115–118 °C; $[\alpha]^{25}_D$ −23.8° (*c* 1.17, $CHCl_3$); IR (KBr) 3425, 2990, 2925, 2670, 1725, 1640, 1440, 1385, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$/Me_4Si) δ 1.35 and 1.49 (2 s, 6 H, $C(CH_3)_2$), 1.97 (m, 2 H, CH_2), 3.40 (m, 2 H, 2 CH), 3.94 (s, 3 H, CO_2CH_3), 4.38 (d, *J* = 1 Hz, 2 H, 2 OCH). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.22; H, 6.01.

(1*R*,5*R*,6*R*,7*S*)-6,7-[(Dimethylmethylene)dioxy]-3-oxabicyclo[3.2.1]octan-2-one (9). To a solution of the half ester **4** (2.184 g, 8.14 mmol) in 20 mL of ethyl acetate was bubbled through ozone for 3 h at −78 °C and then nitrogen for 30 min. Then, the solution was allowed to stand at room temperature and the solvent was concentrated in vacuo to afford the keto ester **5** as a colorless syrup. To a solution of the keto ester **5** in 20 mL of methanol was added portionwise 2 g (53 mmol) of sodium borohydride at 40–50 °C. The mixture was refluxed for 3 h and then cooled with ice water. Hydrochloric acid (2 M) was added carefully until the pH became 7. To a solution of the diol **6** was added 2 g (9.35 mmol) of sodium periodate and the mixture was stirred for 30 min at room temperature. The white precipitate thus produced was removed by filtration and washed with methanol. To the combined filtrate containing the aldehyde **7** was added portionwise 1.1 g (29 mmol) of sodium borohydride, and the mixture was stirred for 1 h at room temperature and neutralized with 2 M hydrochloric acid. The solvent was concentrated in vacuo to afford the crude alcohol **8**. It was lactonized with acetic anhydride (6 mL) in pyridine (10 mL) overnight at room temperature. Workup as usual afforded the crude lactone **9**, which was purified by silica gel column chromatography using AcOEt–*n*-hexane (1:2) as eluant. The lactone **9** (968 mg) was obtained in 60% yield as white needles: mp 127–137 °C; $[\alpha]^{25}_D$ +35.9° (*c* 0.8, $CHCl_3$). It was recrystallized from CH_2Cl_2–Et_2O–*n*-hexane (1:5:5): mp 140–141.5 °C; $[\alpha]^{25}_D$ +44.4° (*c* 1.0, $CHCl_3$); R_f 0.61 (Et_2O); IR (KBr) 3450, 3000, 2925, 1740, 1480, 1410, 1385, 1375, 1345 cm^{-1}; ^{13}C NMR ($CDCl_3$/Me_4Si) δ 23.88 (t), 25.49 (2 q), 39.43 (d), 48.35 (d), 72.03 (d), 81.39 (d), 82.70 (d), 111.24 (s), 170.24 (s); ^{1}H NMR ($CDCl_3$/Me_4Si) δ 1.33 and 1.48 (2 s, 6 H, $C(CH_3)_2$), 2.01 (m, 2 H, CH_2), 2.43 (m, 1 H, OCH_2CH), 2.98 (m, 1 H, COCH), 4.28 (m, 2 H, CH_2O), 4.62 (br s, 2 H, 2 CH); MS (*m*/*e*) 198 (M^+), 183 ($M^+ - CH_3$), 141. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.32; H, 7.02.

(1*R*,2*S*,3*R*,4*R*)-4-(Acetoxymethyl)-2,3-[(dimethylmethylene)dioxy]cyclopentane-1-carboxamide (10). To a solution of 286.2 mg (1.44 mmol) of the lactone **9** in 3 mL of methanol was bubbled NH_3 gas at 0 °C, and it stood overnight at room temperature. The solvent was evaporated to dryness, and the alcohol was acetylated with acetic anhydride (2 mL) in pyridine (3 mL) overnight at room temperature. Workup as usual afforded the crude amide **10**, which was purified by a silica gel column chromatography using AcOEt–*n*-hexane (1:1) as eluant. The amide **10** (363.4 mg) was obtained in 98% yield as a colorless syrup: $[\alpha]^{20}_D$ −32.6° (*c* 1.55, $CHCl_3$); IR (neat) 3425, 3325, 3200, 2975, 2925, 1735, 1660, 1615, 1450, 1420, 1380, 1340 cm^{-1}; ^{1}H NMR ($CDCl_3$/Me_4Si) δ 1.31 and 1.50 (2 s, 6 H, $C(CH_3)_2$), 2.07 (s, 3 H, OAc), 1.68–2.52 (m, 3 H, $AcOCH_2CHCH_2$), 2.76 (m, 1 H, H_2NCOCH), 4.10 (d, *J* = 6 Hz, 2 H, $AcOCH_2$), 4.41 (m, 1 H, OCH), 4.47 (m, 1 H, OCH), 6.12 and 6.40 (2 br s, 2 H, $CONH_2$); MS (*m*/*e*) 257 (M^+).

(1*R*,2*S*,3*R*,4*R*)-4-(Acetoxymethyl)-1-[(*tert*-butoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]cyclopentane (11). To a solution of 257.3 mg (1.0 mmol) of the amide **10** in 5 mL of *tert*-butyl alcohol was added 6.6 mg (1.23 mmol) of lead tetraacetate under an atmosphere of argon. To the deep solution was added 0.4 mL of triethyamine dropwise (1 drop/3 s) at 70 °C. The initial reddish color of the solution faded to pale pink. At this point, conversion to the isocyanate was essentially complete and the remainder of the triethylamine was added more quickly. The reaction mixture was heated under reflux for 5 h and the solvent was evaporated to dryness. Purification by silica gel column chromatography using ether–*n*-hexane (1:2) as eluant gave the carbamate **11** (289 mg) in 78% yield as a colorless syrup: $[\alpha]^{25}_D$ −4.7° (*c* 0.62, $CHCl_3$); IR (neat) 3350, 2950, 2925, 1740, 1710, 1515, 1450, 1365 cm^{-1}; ^{1}H NMR ($CDCl_3$/Me_4Si) δ 1.29 and 1.48 (2 s, 6 H, $C(CH_3)_2$), 1.44 (s, 9 H, $CO_2C(CH_3)_3$), 2.09 (s, 3 H, OAc), 1.50–2.58 (m, 3 H, CH_2,

(18) (a) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434. (b) Clive, D. L. J. *Aldrichimica Acta* **1978**, 43.

(19) Natural neplanocin A, $[\alpha]^{23}_D$ −157° (*c* 0.5, H_2O) and mp 220–222 °C, was kindly supplied by Toyo Jozo Co., Ltd.

$AcOCH_2CH$), 3.80–4.22 (m, 3 H, $AcOCH_2$, NCH), 4.42 (br s, 2 H, 2 OCH), 5.00 (br s, 1 H, N*H*Boc); MS (*m/e*) 258 ($M^+ - CH_3 - C(CH_3)_3$), 216, 198.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-cyclopentaneamine (12). The carbamate **11** (174.8 mg, 0.53 mmol) was dissolved in methanol (2 mL) containing 2 M hydrochloric acid (2 mL), the solution was heated under reflux for 1 h, and the solvent was evaporated to dryness. Purification on a cation exchange resin (Amberlite CG-120 H^+ form) using 0.07 M NH_4OH as eluant gave the cyclopentaneamine **11** (75.0 mg) in 97% yield as a colorless syrup: $[\alpha]^{20}_D$ −10.3° (*c* 1.52, H_2O). The unstable free amine was directly used for the next step.

Aristeromycin (1). To a solution of **12** (75.7 mg, 0.52 mmol) and 5-amino-4,6-dichloropyrimidine (200 mg, 1.22 mmol) in 6 mL of 1-butanol was added 0.35 mL (4.77 mmol) of triethylamine, and the mixture was heated under reflux for 50 h. The solvent was evaporated in vacuo and the residue was dissolved in 15 mL of water and washed with CH_2Cl_2 (2 × 10 mL). The solvent was evaporated to dryness and the residue was purified with a cation exchange resin (Amberlite CG-120 H^+ form) eluting with 0.07 M NH_4OH. After removal of the solvent, the residue was dissolved in 5 mL of triethyl orthoformate containing 5 drops of concentrated HCl and the mixture was stirred for 24 h at room temperature. The solvent was evaporated to dryness under a reduced pressure and the residue was purified with a cation exchange resin (Amberlite CG-120 H^+ form) using 0.07 M NH_4OH as eluant. Aristeromycin **1** (62.8mg) was obtained in 46.4% yield as white crystals, showing mp 214–215 °C dec (50% aqueous EtOH); $[\alpha]^{20}_D$ −53.0° (*c* 0.528, DMF); IR (KBr) 3400, 3210, 3110, 2950, 2850, 1660, 1610, 1580, 1460, 1340, 1300 cm^{-1}; ^1H NMR (Me_2SO-d_6, D_2O/TSP) δ 1.5–2.5 (m, 3 H, CH_2, $CHCH_2OH$), 3.50 (d, *J* = 5 Hz, 2 H, CH_2OH), 3.84 (dd, *J* = 2.5, 5 Hz, 1 H, OCH), 4.29 (dd, *J* = 2.5, 5 Hz, 1 H, OCH), 4.73 (dt, *J* = 9, 9 Hz, 1 H, NCH), 7.17 (s, 2 H, NH_2), 8.12 and 8.20 (2 s, 2 H, aromatic protons); MS (*m/e*) 248, 136, 135.

(1*R*,2*S*,3*R*,4*S*)-2,3-[(Dimethylmethylene)dioxy]-4-[(phenylseleno)methyl]cyclopentane-1-carboxylic Acid (22). A solution of 173 mg (0.56 mmol) of diphenyl diselenide in 3 mL of dry DMF was deoxygenated by bubbling nitrogen for 20 min. Sodium borohydride (45 mg, 1.21 mmol) was added portionwise, and the temperature was slowly raised to 100 °C under an atmosphere of argon. A solution of 201 mg (1.01 mmol) of the lactone **9** ($[\alpha]^{25}_D$ +42.5°) in 2 mL of dry DMF was added to the solution and the oil-bath temperature was raised to 120 °C. The mixture was stirred at 120 °C for 2 h. After cooling with ice, the reaction mixture was poured into a cold 1.7 M hydrochloric acid solution and extracted with ethyl acetate. The organic layer was washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated to dryness. Purification by silica gel column chromatography using CH_2Cl_2–AcOEt (2:1) as eluant gave **22** (335 mg) in 93% yield as a colorless oil; $[\alpha]^{23}_D$ +9.5° (*c* 1.93, $CHCl_3$); R_f 0.61 (AcOEt); IR (neat) 1740, 1710, 1580, 1480, 1380, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si) δ 1.28 and 1.44 (2 s, 6 H, $C(CH_3)_2$), 1.80 and 2.38 (m, 3 H, CH_2, $CHCH_2SePh$), 2.92 (m, 3 H, CH_2SePh, COCH), 4.34 (dd, *J* = 3.3, 6.5 Hz, 1 H, OCH), 4.82 (dd, *J* = 4.5, 6.5 Hz, 1 H, OCH), 7.17 and 7.42 (m, 5 H, aromatic protons); MS (*m/e*) 356 ($M^+ + 2$), 354 (M^+), 340 ($M^+ - CH_3$).

(1*R*,2*S*,3*R*,4*S*)-1-[(Methoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]-4-[(phenylseleno)methyl]cyclopentane (23). To a solution of 920 mg (2.79 mmol) of **22** in 16 mL of acetone was added triethylamine (0.43 mL, 3.35 mmol) and then ethyl chloroformate (0.3 mL, 3.35 mmol) at −78 °C with stirring. The temperature of the solution was brought to −40 °C. The mixture was stirred at −40 °C for an additional 30 min and then treated with saturated aqueous sodium azide (254 mg, 4.19 mmol) at −10 °C for 30 min. The reaction mixture was poured into a cold saturated NaCl solution and extracted with methylene chloride. The organic layer was washed with water, dried (Na_2SO_4), and evaporated to dryness. The oily residue was dissolved in dry benzene (10 mL), and the solution was heated at 90 °C for 30 min. Then, dry methanol (10 mL) was added to the solution and the mixture was heated at 90 °C for 2 h. After removal of the solvent, purification by silica gel column chromatography using CH_2Cl_2 as eluant gave the methyl carbamate **23** (906 mg) in 91% yield: $[\alpha]^{24}_D$ +16.1° (*c* 1.44, $CHCl_3$). The carbamate **23** was recrystallized from a mixed solvent of ether–*n*-hexane (1:1): mp 81–83 °C; $[\alpha]^{20}_D$ +18.8° (*c* 1.05, $CHCl_3$); R_f 0.28 (*n*-hexane/AcOEt = 2/1); IR (KBr) 3350, 1730, 1710, 1385, 1375, 1580, 1480, 740, 695 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si δ 1.28 and 1.47 (2 s, 6 H, $C(CH_3)_2$), 1.64 and 2.34 (m, 3 H, CH_2, $CHCH_2SePh$), 3.00 (m, 2 H, CH_2SePh), 3.67 (s, 3 H, CO_2CH_3), 3.90 (m, 1 H, NCH), 4.40 (m, 2 H, 2 OCH), 4.77 (d, *J* = 6 Hz, 1 H, NH), 7.24 and 7.48 (m, 5 H, aromatic protons); MS (*m/e*) 385 ($M^+ + 2$), 383 (M^+), 370, 369, 228. Anal. Calcd for $C_{17}H_{23}NO_4Se$: C, 53.13; H, 6.03; N, 3.65. Found: C, 53.05; H, 6.07; N, 3.87.

(1*R*,2*S*,3*R*)-1-[(Methoxycarbonyl)amino]-4-methylene-2,3-[(dimethylmethylene)dioxy]cyclopentane (24). A solution of 167 mg (0.435 mmol) of the carbamate **23** in 5 mL of dry CH_2Cl_2 was treated with ozone at −78 °C for 15 min. The temperature of the solution was allowed to remain at room temperature and to this solution was added a trace of pyridine. The reaction mixture was refluxed for 2 h. After the solution was cooled with ice water, purification by silica gel column chromatography using CH_2Cl_2 as eluant gave the exo methylene derivative **24** (94 mg) in 95% yield as a colorless oil: $[\alpha]^{20}_D$ +138.3° (*c* 1.01, $CHCl_3$); R_f 0.47 (AcOEt/*n*-hexane = 1/1); IR (neat) 3350, 1730, 1710, 1385, 1375, 910 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si) δ 1.32 and 1.47 (2 s, 6 H, $C(CH_3)_2$), 2.06 and 2.91 (d, *J* = 14 Hz, 1 H, m, 1 H, CH_2), 3.68 (s, 3 H, CO_2CH_3), 4.00 (t of dd, *J* = 7 Hz, 1 H, NCH), 4.44 (m, 1 H, NH), 4.50 (d, *J* = 5.5 Hz, 1 H, OCH), 4.74 (d, *J* = 5.5 Hz, 1 H, OCH), 5.18 and 5.28 (2 d, *J* = 2 Hz, 2 H, H_2C=C); MS (*m/e*) 228 ($M^+ + 1$), 212 ($M^+ - CH_3$), 170.

(3*R*,4*R*,5*S*,6*R*)-4,5-[(Dimethylmethylene)dioxy]-6-[(methoxycarbonyl)amino]-1-oxospiro[2.4]heptane (25). To an ice-cooled solution of 46 mg (0.21 mmol) of **24** in dry CH_2Cl_2 (5 mL) was added *m*-chloroperbenzoic acid (57 mg, 0.32 mmol) portionwise. The mixture was stirred for 16 h at room temperature and poured into a saturated sodium bicarbonate solution. The organic layer was washed with water, dried over Na_2SO_4, and evaporated to dryness. Purification by silica gel column chromatography using CH_2Cl_2 as eluant gave the epoxide **25** (45 mg) in 91% yield: mp 102–104 °C; $[\alpha]^{20}_D$ +111.3° (*c* 1.0, $CHCl_3$); R_f 0.36 (AcOEt/*n*-hexane = 1/1); IR ($CHCl_3$) 3450, 1720, 1385, 1375, 1260, 870 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si) δ 1.27 and 1.46 (2 s, 6 H, $C(CH_3)_2$), 1.30 and 2.68 (d, *J* = 14 Hz, 1 H, dd, *J* = 7, 14 Hz, 1 H, CH_2), 2.93 and 2.97 (2 d, *J* = 10 Hz, 2 H, OCH_2), 3.68 (s, 3 H, CO_2CH_3), 4.10 (m, 1 H, NCH), 4.18 (dd, *J* = 2, 5 Hz, 1 H, OCH), 4.66 (d, *J* = 5 Hz, 1 H, OCH), 5.10 (m, 1 H, NH). Anal. Calcd for $C_{11}H_{17}NO_5$: C, 54.31; H, 7.04; N, 5.76. Found: C, 54.22; H, 7.00; N, 5.64.

(1*R*,2*S*,3*R*)-4-(Hydroxymethyl)-1-[(methoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (26). To a solution of trimethylsilyl triflate 0.54 mL (2.1 mmol) in 3 mL of dry toluene was added 2,6-lutidine (0.2 mL, 2.1 mmol) at −78 °C under an atmosphere of argon. After the mixture was stirred of 30 min at −78 °C, a solution of **25** (103 mg, 0.42 mmol) in 2 mL of dry toluene was added to the solution dropwise. The reaction mixture was stirred at −78 °C for 30 min and the temperature was brought to −20 °C. After the solution was stirred at −20 °C for 3 h, DBU (0.3 mL) was added dropwise. The reaction mixture was stirred at room temperature for 16 h, poured into a saturated sodium bicarbonate solution, and extracted with ethyl acetate. Workup as usual afforded the crude silylated allyl alcohol. The oily residue was dissolved in 2 mL of methanol, and the reaction mixture was treated, portionwise, with potassium carbonate (270 mg) and stirred at room temperature for 2 h. After removal of the solvent, the residue was extracted with CH_2Cl_2. Workup as usual afforded the crude allyl alcohol **26**, which was purified by silical gel column chromatography using AcOEt–*n*-hexane (1:1) following AcOEt as eluant. The allyl alcohol **26** (29mg) was obtained in 27% yield with recovery of 34% **25** and recrystallized from Et_2O–AcOEt (2:1) mp 139–140 °C; $[\alpha]^{20}_D$ −67.2° (*c* 0.5, $CHCl_3$); R_f 0.32 (AcOEt/*n*-hexane = 4/1); IR (KBr) 3400, 3350, 1695, 1380, 1370, 1040 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si) δ 1.35 and 1.42 (2 s, 6 H, $C(CH_3)_2$), 1.62 (s, 1 H, OH), 3.69 (s, 3 H, CO_2CH_3), 4.33 (s, 2 H, CH_2OH), 4.54 (m, 2 H, NCH, OCH), 4.60 (s, 1 H, NH), 5.18 (d, *J* = 5.5 Hz, 1 H, OCH), 5.60 (s, 1 H, CH=). Anal. Calcd for $C_{11}H_{17}NO_5$: C, 54.31; H, 7.04; N, 5.76. Found: C, 54.13; H, 7.05; N, 5.95.

(1*R*,2*S*,3*R*)-4-(Chloromethyl)-1-[(methoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (27). To a solution of 340 mg (1.496 mmol) of the exo methylene product **24** in 10 mL of methyl formate was added dropwise 264 μL (2.21 mmol) of freshly distilled *tert*-butyl hypochlorite at −78 °C under an atomosphere of argon. After stirring for 3 h at −78 °C, the reaction mixture was poured into a cold saturated sodium bicarbonate solution and extracted with CH_2Cl_2 several times. Workup as usual afforded the crude allyl chloride, which was purified by silica gel column chromatography using CH_2Cl_2 as eluant to give **27** (305 mg). This product contained some impurity but was used without further purification for the next step. The pure sample **27** was obtained as white crystals by further purification by silica gel column chromatography using *n*-hexane–AcOEt (4:1): R_f 0.54 (*n*-hexane/AcOEt = 1/1); mp 87.5–88.5 °C; IR (neat) 3330, 1710, 1525, 1370, 1041. 865 cm^{-1}; ^1H NMR ($CDCl_3$/Me_4Si) δ 1.35 and 1.39 (2 s, 6 H, $C(CH_3)_2$), 3.68 (s, 3 H, CO_2CH_3), 4.17 (s, 2 H, CH_2Cl), 4.54 (d, *J* = 5.5 Hz, 1 H, OCH), 4.62 (m, 1 H, NCH), 4.88 (br d, *J* = 8 Hz, 1 H, NH), 5.23 (d, *J* = 5.5 Hz, 1 H, OCH), 5.70 (d, *J* = 1.4 Hz, 1 H, =CH); MS (*m/e*) 246 ($M^+ - CH_3$), 204, 188, 168, 167, 129. Anal. Calcd for $C_{11}H_{16}NO_4Cl$: C, 50.48; H, 6.16; N, 5.35. Found: C, 50.26; H, 6.11; N, 5.45.

(1*R*,2*S*,3*R*)-4-(Acetoxymethyl)-1-[(methoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (28). A solution of the crude allyl chloride **27** (305 mg, 1.16 mmol), 289 mg (1.74 mmol) of potassium iodide, and 285 mg (3.48 mmol) of anhydrous sodium acetate in 6 mL of dry DMF was stirred at 50–60 °C for 5 h. After cooling, the reaction mixture was poured into a cold saturated NaCl solution and extracted with AcOEt several times. Workup as usual afforded the crude allyl acetate **28**, which was purified by silica gel column chromatography using *n*-hexane–AcOEt (4:1) as eluant to give the pure **28** (203 mg) (48% yield from **15**) as a colorless oil: R_f 0.36 (*n*-hexane/AcOEt = 1/1); IR (neat) 3340, 1745, 1730, 1704, 1530, 1375 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.34 and 1.39 (2 s, 6 H, $C(CH_3)_2$), 2.10 (s, 3 H, OAc), 3.67 (s, 3 H, CO_2CH_3), 4.52 (d, J = 5.5 Hz, 1 H, OCH), 4.61 (br s, 1 H, NCH), 4.71 (s, 2 H, CH_2OAc), 4.92 (br d, J = 8 Hz, 1 H, NH), 5.15 (d, J = 5.5 Hz, 1 H, OCH), 5.60 (d, J = 1.4 Hz, 1 H, =CH); MS (*m/e*) 270 ($M^+ - CH_3$), 228 ($M^+ - CH_3 - Ac$), 210 ($M^+ - CH_3 - AcOH$), 185, 168, 167, 153.

(1*R*,2*S*,3*R*)-4-(Hydroxymethyl)-1-[(methoxycarbonyl)amino]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (26) from 28. To a solution of 203 mg (0.71 mmol) of the acetate **28** in 5 mL of methanol was added 75 mg (0.71 mmol) of sodium carbonate. The reaction mixture was stirred at room temperature for 2 h, and then neutralized with dilute hydrochloric acid. The solvent was evaporated and the residue was extracted with CH_2Cl_2. Workup as usual afforded 173 mg of the crude allyl alcohol **26**, which was purifed by recrystallization with ether–AcOEt (2:1). The pure **29a** (152 mg) was obtained in 88% yield: $[\alpha]^{20}_D$ −67.1° (*c* 1.05, $CHCl_3$). This sample was confirmed to be identical in all respects with the sample obtained from the epoxide **25** as described above.

(1*S*,5*R*,6*S*,7*S*)-6,7-[(Dimethylmethylene)dioxy]-1-[(phenylseleno)methyl)]-4-aza-2-oxa-3-oxobicyclo[3.2.1]octane (31). A solution of 52 mg (0.17 mmol) of diphenyl diselenide in 1 mL of dry DMF was deoxygenated by bubbling nitrogen through for 20 min. Sodium borohydride (13 mg, 0.36 mmol) was added and the temperature was slowly raised by using an oil bath to 100 °C under an atmosphere of argon. A solution of 90 mg (0.28 mmol) of the epoxide of benzyl carbamate **30** in 1 mL of dry DMF was added and the oil bath temperature was raised to 120 °C. The reaction mixture was stirred for 2 h at 120 °C, cooled, poured into a saturated NaCl solution, and extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4, and evaporated to dryness. Purification by silica gel column chromatography using AcOEt–*n*-hexane (1:1) as eluant gave the cyclic carbamate **31** (73 mg) in 70% yield: mp 170–172.5 °C; R_f 0.18 (AcOEt/*n*-hexane = 1/1); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.27 and 1.39 (2 s, 6 H, $C(CH_3)_2$), 1.91 and 2.09 (d, J = 14 Hz, 1 H, dd, J = 4, 14 Hz, 1 H, CH_2), 3.33 (d, J = 1 Hz, 2 H, CH_2SePh), 3.59 (br s, 1 H, NCH), 4.47 (dd, J = 1.1, 5.5 Hz, 1 H, OCH), 4.62 (d, J = 5.5 Hz, 1 H, OCH), 6.99 (d, J = 5.5 Hz, 1 H, NH), 7.24 and 7.54 (m, 5 H, aromatic protons); IR (KBr) 3260, 1709, 1664, 1580, 1380, 1390, 1215 cm^{-1}; MS (*m/e*) 369 (M^+ + 2), 367 (M^+), 171, 169, 154. The benzyl carbamate **30** was prepared in 76% overall yield from **22** in a similar manner as described in the case of **25**.

Methyl (1*R*,2*S*,3*R*,4*S*)-2,3-[(Dimethylmethlene)dioxy]-4-formylcyclopentane-1-carboxylate (Methyl Ester of 7). To a solution of the half-ester **4** (4 g, 14.9 mmol) in 25 mL of ethyl acetate was bubbled through ozone for 3 h at −78 °C and then nitrogen for 30 min. The temperature of the solution was allowed to remain at room temperature and the solvent was concentrated in vacuo to afford the keto ester **5** as a colorless syrup. To the solution of the keto ester **5** in 30 mL of methanol was added portionwise 5.6 g (151 mmol) of sodium borohydride at 40–50 °C. The mixture was refluxed for 30 min and cooled with ice water. Hydrochloric acid (2 M) was added carefully until the pH became 5. To the solution containing the diol **6** was added 3.8 g (17.9 mmol) of sodium periodate and the mixture was stirred for 30 min at room temperature. The white precipitate formed was removed by filteration and the filtrate was extracted with ethyl acetate (3 × 50 mL). To the organic solution was added diazomethane in ether until the yellow color characteristic of diazomethane persisted. The solvent was evaporated to dryness. Purification by silica gel column chromatography using *n*-hexane–AcOEt (4:1) as eluant afforded the methylester of the aldehyde **7** (2.42 g) in 71.2% yield as a colorless syrup: R_f = 0.59 (*n*-hexane/AcOEt = 1/1); IR (neat) 2830, 2730, 1725, 1440, 1380, 1375 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.36 and 1.50 (2 s, 6 H, $C(CH_3)_2$), 2.40 (m, 2 H, CH_2), 2.95 (m, 2 H, $CHCHO$, $CHCO_2CH_3$), 3.69 (s, 3 H, CO_2CH_3), 4.92 (m, 2 H, 2 OCH), 9.71 (s, 1 H, CHO); MS (*m/e*) 227 ($M^+ - 1$), 213 ($M^+ - CH_3$), 125.

Methyl (1*R*,2*S*,3*R*)-4-(Acetoxymethylene)-2,3-[(dimethylmethylene)dioxy]cyclopentane-1-carboxylate (32). To a solution the methyl ester of **7** (1.33 g, 5.83 mmol), *p*-(dimethylamino)pyridine (356 mg, 2.92 mmol), and triethylamine (1.62 mL, 11.66 mmol) in 15 mL of dry THF was added dropwise anhydrous acetic acid (1.38 mL, 14.58 mmol) at 0–10 °C under an atomosphere of argon. The reaction mixture was stirred for 16 h at room temperature, poured into ice water, and extracted with ethyl acetate. The organic layer was washed with a saturated sodium bicarbonate solution and water. Workup as usual afforded the crude enol acetate **32**, which was purified by silica gel column chromatography using *n*-hexane–AcOEt (1:1) as eluant to give the enol acetate **32** (1.15 g) in 73% yield as a colorless syrup: R_f 0.74 (*n*-hexane/AcOEt = 1/1); IR (neat) 1760, 1730, 1439, 1370 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.47 (2 s, 6 H, $C(CH_3)_2$), 2.15 (s, 3 H, OAc), 2.81 (m, 2 H, CH_2), 3.05 (m, 1 H, $CHCO_2CH_3$), 3.69 (s, 3 H, CO_2CH_3), 4.86 (dd, J = 2, 6 Hz, 1 H, OCH), 4.97 (d, J = 6 Hz, 1 H, OCH), 7.18 (br s, 0.17 H, =CHOAc), 7.36 (t of dd, J = 2 Hz, 0.83 H, =CHOAc); MS (*m/e*) 271 (M^+ + 1), 255 ($M^+ - CH_3$), 243, 227, 213.

Methyl (1*R*,2*S*,3*S*,4*S*)-2,3-[(Dimethylmethylene)dioxy]-4-formyl-4-(phenylseleno)cyclopentane-1-carboxylate and Methyl (1*R*,2*S*,3*S*,4*R*)-2,3-[(Dimethylmethylene)dioxy]-4-formyl-4-(phenylseleno)cyclopentane-1-carboxylate (33a and 33b). (A) To an emulsion of silver trifluoroacetate 537 mg (2.43 mmol) in 12 mL of dry CH_2Cl_2 was added dropwise 430 mg (2.24 mmol) of phenylselenenyl chloride in 2 mL of dry CH_2Cl_2 at 0–10 °C. After stirring for 30 min at 0–10 °C, to the solution was added dropwise the enol acetate **32** (506 mg, 1.87 mmol) in 6 mL of dry CH_2Cl_2 and the reaction mixture was stirred for 2 h at room temperature, poured into an ice water, and washed with sodium bicarbonate solution. The organic layer was dried over Na_2SO_4 and the solvent was evaporated in vacuo. The residual brown syrup was purifed by silca gel column chromatography using *n*-hexane–AcOEt (4:1) as eluant to give the α-phenylseleno product **33b** (321 mg) in 44.7% yield as white crystals and the β-phenylseleno product **33a** (338mg) in 47.1% yield as a colorless syrup.

(B) To a solution of the enol acetate **32** (60 mg, 0.22 mmol) in 1 mL of dry CH_2Cl_2 was added dropwise phenylselenenyl trifluoroacetate, which was prepared from silver trifluoroacetate (72.9 mg, 0.33 mmol) and phenylselenenyl chloride (63.2 mg, 0.33 mmol) in 2 mL of CH_2Cl_2. The reaction mixture was stirred for 8 h at −78 to −30 °C. Workup as usual afforded the mixture (72.3 mg) **33a**/**33b** in a 7:1 ratio in 85% yield.

33a: R_f 0.29 (*n*-hexane/AcOEt = 4/1); $[\alpha]^{20}_D$ −31.6° (*c* 1.0, $CHCl_3$); IR (neat) 2850, 2730, 1730, 1707, 1440, 1385, 1375 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.36 and 1.62 (2 s, 6 H, $C(CH_3)_2$), 2.50 and 2.51 (d, J = 7 Hz, 1 H, d, J = 5 Hz, 1 H, CH_2), 3.17 (dd, J = 5, 7 Hz, 1 H, $CHCO_2CH_3$), 3.58 (s, 3 H, CO_2CH_3), 4.89 (s, 2 H, 2 OCH), 7.24–7.38 and 7.40–7.56 (m, 5 H, aromatic protons), 9.22 (s, 1 H, CHO); MS (*m/e*) 384 (M^+ + 2), 382 (M^+), 326, 3248 243, 169, 157.

33b: R_f 0.36 (*n*-hexane/AcOEt = 4/1); $[\alpha]^{20}_D$ +284° (*c* 1.07, $CHCl_3$); mp 115–116 °C; IR (KBr) 1710, 1690. 1438, 1382, 1370 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.29 and 1.38 (2 s, 6 H, $C(CH_3)_2$), 2.22 and 2.72 (d, J = 15 Hz, 1 H, dd, J = 8, 15 Hz, 1 H, CH_2), 3.08 (d, J = 8 Hz, 1 H, $CHCO_2CH_3$), 3.78 (s, 3 H, CO_2CH_3), 4.65 (d, J = 6 Hz, 1 H, OCH), 5.31 (d, J = 6 Hz, 1 H, OCH), 7.28–7.56 (m, 5 H, aromatic protons), 9.40 (s, 1 H, CHO); MS (*m/e*) 384 (M^+ + 2), 382 (M^+), 326, 324, 314, 312, 297, 295. Anal. Calcd for $C_{17}H_{20}O_5Se$: C, 53.27; H, 5.26. Found: C, 53.01; H, 5.17.

Methyl (1*R*,2*S*,3*S*,4*R*)-2,3-[(Dimethylmethylene)dioxy]-4-(hydroxymethyl)-4-(phenylseleno)cyclopentane-1-carboxylate (34). To a solution of the aldehyde **33a** (40 mg, 0.104 mmol) in 3 mL of CH_2Cl_2 and 1.5 mL of methanol was added portionwise 1.8 mg (0.208 mmol) of sodium borohydride at −78 °C. After stirring for 15 min at −78 °C, to the solution was added acetic acid until the pH became 6. The reaction mixture was poured into a sodium bicarbonate solution and extracted with CH_2Cl_2 (3 × 5 mL). Workup as usual afforded the crude alcohol **34**, which was purified by silica gel column chromatography using CH_2Cl_2 as eluant to give the alcohol **34** (38 mg) in 95% yield as a colorless oil: R_f 0.30 (*n*-hexane/AcOEt = 2/1); IR (neat) 3490, 1725, 1580, 1440, 1380 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.62 (2 s, 6 H, $C(CH_3)_2$), 1.92 and 2.14 (d, J = 15 Hz, 1 H, dd, J = 8, 15 Hz, 1 H, CH_2), 2.68 (br s, 1 H, OH), 3.21 and 3.53 (m, 2 H, CH_2OH, $CHCO_2CH_3$), 3.43 (m, 1 H, CH_2OH), 3.71 (s, 3 H, CO_2CH_3), 4.65 (d, J = 7.5 Hz, 1 H, OCH), 4.92 (dd, J = 6, 7.5 Hz, 1 H, OCH), 7.33 and 7.58 (m, 5 H, aromatic protons); MS (*m/e*) 386 (M^+ + 2), 384 (M^+), 354, 352, 229 (M^+ − SePh), 171, 153.

Methyl (1*R*,2*S*,3*S*,4*R*)-2,3-[(Dimethylmethylene)dioxy]-4-[((methoxymethyl)oxy)methyl]-4-(phenylseleno)cyclopentane-1-carboxylate (35). To an ice-cooled solution of the alcohol **34** (170 mg, 0.441 mmol) in 2 mL of dry CH_2Cl_2 was added dropwise 110 mg (0.851 mmol) of diisopropylethylamine and 68 mg (0.851 mmol) of methoxymethyl chloride under an atmosphere of argon. The reaction mixture was stirred at room temperature for 16 h, poured into ice water, and extracted with CH_2Cl_2 (3 × 5 mL). Workup as usual afforded the crude **35**, which was purified by silica gel column chromatography using *n*-hexane–AcOEt (4:1) as eluant. The methoxymethyl product **35** (165 mg) was obtained in 87% yield as a colorless oil: R_f 0.49 (*n*-hexane/AcOEt = 2/1); IR (neat)

1735, 1579, 1440, 1380, 1370 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.62 (2 s, 6 H, $C(CH_3)_2$), 2.13 (d, J = 8.5 Hz, 2 H, CH_2), 3.22 (s, 3 H, OCH_3), 3.24 (d, 1 H, $CHCO_2CH_3$), 3.55 and 3.74 (m, 1 H, d, J = 10 Hz, 1 H, CH_2O), 3.72 (s, 3 H, CO_2CH_3), 4.56 (s, 2 H, OCH_2O), 4.72 (d, J = 8 Hz, 1 H, OCH), 4.91 (dd, J = 5, 8 Hz, 1 H, OCH), 7.28 and 7.56 (m, 5 H, aromatic protons); MS (m/e) 430 (M^+ + 2), 428 (M^+), 311, 309, 273 (M^+ - SePh), 211, 183, 169.

(1*R*,2*S*,3*S*,4*R*)-2,3-[(Dimethylmethylene)dioxy]-4-[((methoxymethyl)oxy)methyl]-1-[(methoxycarbonyl)amino]-4-(phenylseleno)cyclopentane (36). To a solution of 112 mg (0.261 mmol) of the ester **35** in 8 mL of acetone was added dropwise 8 mL of 0.13 M NaOH with cooling by an ice bath. After stirring for 2 h with cooling by an ice bath, 1 M HCl was added to the solution until the pH became 5. The reaction mixture was extracted with CH_2Cl_2 several times and the organic layer was washed with a saturated NaCl solution and dried over Na_2SO_4. Workup as usual afforded the corresponding carboxylic acid, which was purified by short silica gel column chromatography using *n*-hexane–AcOEt (1:1) as eluant to give the pure carboxylic acid (108 mg) in quantitative yield. To a solution of 108 mg (0.26 mmol) of the free acid and 55 μL (0.39 mmol) of triethylamine in 3 mL of acetone was added dropwise 33 μL (0.31 mmol) of ethyl chloroformate at −78 °C. After stirring for 30 min at −78 °C, 34 mg (0.52 mmol) of sodium azide in 0.3 mL of H_2O was added to the solution at −78 °C. After stirring for 30 min at −78 °C, the temperature was allowed to rise to −10 °C gradually and the mixture was stirred at −10 °C for 30 min, poured into ice water, and extracted with benzene several times. Workup as usual afforded the carbonyl azide, which was dissolved in 10 mL of dry benzene; the mixture was refluxed for 1 h, and then 10 mL of dry methanol was added to the solution. After refluxing for 3 h, the solvent was evaporated to give the crude carbamate **36**. Purification by silica gel column chromatography using *n*-hexane–AcOEt (3:1) as eluant gave the pure carbamate **36** (85.5 mg) in 74% yield as a colorless oil: R_f 0.21 (*n*-hexane/AcOEt = 2/1); IR (neat) 3345, 1710, 1520, 1370, 863 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.33 and 1.62 (2 s, 6 H, $C(CH_3)_2$), 1.60 and 1.86 (d, J = 14 Hz, 1 H, dd, J = 6, 14 Hz, 1 H, CH_2), 3.32 (s, 3 H, OCH_3), 3.38 and 3.80 (2d, J = 10 Hz, 2 H, CH_2O), 3.65 (s, 3 H, CO_2CH_3), 4.47 (d, J = 7 Hz, 2 H, NC*H*, OC*H*), 4.58 (s, 2 H, OCH_2O), 4.67 (d, J = 7 Hz, 1 H, OCH), 5.43 (br d, J = 8 Hz, 1 H, N*H*), 7.31 and 7.65 (m, 5 H, aromatic protons); MS (m/e) 445 (M^+ + 2), 443 (M^+), 413, 411, 352, 350, 288, 230, 198.

(1*R*,2*S*,3*R*)-1-[(Methoxycarbonyl)amino]-4-[((methoxymethyl)oxy)methyl]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (29a from 36). A solution of 33 mg (0.074 mmol) of the phenylseleno product **36** in 3 mL of dry CH_2Cl_2 was treated with ozone in oxygen at −78 °C for 15 min and then nitrogen was bubbled through the solution for 10 min. The temperature of the solution was allowed to rise to room temperature and 10 mg of triethylamine was added to the solution. After refluxing for 2 h, purification by silica gel column chromatography using CH_2Cl_2 as eluant gave the allyl alcohol **29a** (21 mg) in 98.6% yield. The sample was confirmed to be identical in all respects with the authentic sample obtained from **26**.

(1*R*,2*S*,3*R*)-1-[(Methoxycarbonyl)amino]-4-[((methoxymethyl)oxy)methyl]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (29a). To an ice-cooled solution of 84 mg (0.35 mmol) of the allyl alcohol **26** in 6 mL of dry CH_2Cl_2 was added 89 mg (0.69 mmol) of diisopropylethylamine and 56 mg (0.69 mmol) of methoxymethyl chloride under an atmosphere of argon. The reaction mixture was stirred at room temperature for 16 h and poured into ice water. Workup as usual afforded the crude **29a**, which was purified by silica gel column chromatography using AcOEt–*n*-hexane (1:1) as eluant. The methoxymethyl derivative **29a** (99 mg) was obtained quantitative yield: mp 51–52 °C; $[\alpha]^{20}_D$ −43.7° (*c* 2.19, $CHCl_3$); R_f 0.56 (AcOEt/*n*-hexane = 4/1); IR (neat) 3300, 1710, 1380, 1370, 1040 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.41 (2 s, 6 H, $C(CH_3)_2$), 3.40 (s, 3 H, OCH_3), 3.69 (s, 3 H, CO_2CH_3), 4.21 (s, 2 H, CH_2O), 4.52 (d, J = 6 Hz, 1 H, OCH), 4.67 (s, 2 H, OCH_2O), 4.71 (m, 2 H, NCH, NH), 5.15 (d, J = 5 Hz, 1 H, OCH), 5.63 (s, 1 H, CH=C); MS (m/e) 288 (M^+ + 1), 272 (M^+ - CH_3), 256 (M^+ - OCH_3), 241, 229, 226, 198. Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.29; H, 7.34; N, 4.83.

(1*R*,2*S*,3*R*)-4-[(Methoxymethyl)oxymethyl]-2,3-[(dimethylmethylene)dioxy]-4-cyclopenten-1-amine (29b). To a solution of 127 mg (0.442 mmol) of **29a** in 14 mL of methanol was added 2.5 N KOH (14 mL) under an atmosphere of argon. The reaction mixture was stirred and refluxed for 12 h. After the solution was cooled with ice water, the solvent was evaporated and the residue was extracted with ethyl acetate. Workup as usual afforded the crude amine **29b** (101 mg) in quantitative yield. The cyclopentenamine **29b** was used without further purification for the next step. The pure sample **29b** was obtained by purification by silica gel column chromatography using CH_2Cl_2–MeOH (19:1) as eluant: $[\alpha]^{20}_D$ −37.1° (*c* 1.0, $CHCl_3$); R_f 0.24 (CH_2Cl_2/MeOH = 9/1); IR ($CHCl_3$) 3380, 1450, 1380, 1370, 1235, 1145, 1050 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.39 (2 s, 6 H, $C(CH_3)_2$), 1.46 (s, 2 H, NH_2), 3.39 (s, 3 H, OCH_3), 3.94 (br s, 1 H, NCH), 4.18 (br s, 2 H, CH_2O), 4.39 (d, J = 5.5 Hz, 1 H, OCH), 4.68 (s, 2 H, OCH_2O), 5.18 (br d, J = 5.5 Hz, 1 H, OCH), 5.71 (br s, 1 H, CH=C).

(1*R*,2*S*,3*R*)-1-(5-Amino-6-chloro-4-pyrimidinylamino)-4-[((methoxymethyl)oxy)methyl]-2,3-[(dimethylmethylene)dioxy]-4-cyclopentene (37). To a solution of 101 mg (0.44 mmol) of **29b** and 181 mg (1.1 mmol) of 5-amino-4,6-dichloropyrimidine in 14 mL of *n*-butyl alcohol was added 0.6 mL of triethylamine and the solution was heated under reflux for 40 h. After removal of the solvent, the residue was extracted with CH_2Cl_2. Workup as usual afforded the crude condensed product **37**, which was purified by silica gel column chromatography using AcOEt–*n*-hexane (1:1 in the beginning and then 4:1) as eluant. The condensed compound **37** (116 mg) was obtained in 87% yield based on the recovered **29b** (16%) as a colorless oil: $[\alpha]^{20}_D$ −77.5° (*c* 1.06, $CHCl_3$); R_f 0.38 (AcOEt/*n*-hexane = 4/1); IR (neat) 3350, 3250, 1640, 1570, 1380, 1370 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.35 and 1.43 (2 s, 6 H, $C(CH_3)_2$), 3.39 (s, 3 H, OCH_3), 3.65 (br s, 2 H, NH_2), 4.21 (s, 2 H, CH_2O), 4.51 (d, J = 6 Hz, 1 H, OCH), 4.67 (s, 2 H, OCH_2O), 5.13 (m, 3 H, NCH, OCH, NH), 5.73 (s, 1 H, CH=C), 8.10 (s, 1 H, aromatic protons).

9-[(1*R*,2*S*,3*R*)-4-[((Methoxymethyl)oxy)methyl]-2,3-[(dimethylmethylene)dioxy]-4-cyclopenten-1-yl]adenine (38). A mixture of **37** (116 mg, 0.325 mmol), triethyl orthoformate (1.8 mL), and acetic anhydride (1 mL) was stirred at room temperature for 2 h. After removal of the solvent, the residue was poured into a cold saturated sodium bicarbonate solution and extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, and evaporated to dryness. The residue was dissolved in 2 mL of dry methanol and ammonia gas was bubbled through the solution at −78 °C for 1 h. The reaction mixture was then heated at 45 °C for 16 h in a sealed tube. After removal of the solvent, the residue was extracted with CH_2Cl_2. Workup as usual afforded the crude **38**, which was purified by silica gel column chromatography using AcOEt–*n*-hexane (1:1) at the beginning, then (4:1), and finally CH_2Cl_2–MeOH (19:1) as eluant. The protected compound **38** (66 mg) was obtained in 60% yield as white crystals: mp 134–136 °C; $[\alpha]^{20}_D$ −69.8° (*c* 1.10, $CHCl_3$); R_f 0.47 (CH_2Cl_2/MeOH = 9/1); IR (KBr) 3425, 3250, 1680, 1625, 1575 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.37 and 1.48 (2 s, 6 H, $C(CH_3)_2$), 3.42 (s, 3 H, OCH_3), 4.35 (s, 2 H, CH_2O), 4.72 (d, J = 5.5 Hz, 1 H, OCH), 4.73 (s, 2 H, OCH_2O), 5.38 (d, J = 5.5 Hz, 1 H, OCH), 5.58 (br s, 1 H, NCH), 5.81 (s, 1 H, CH=C), 6.15 (s, 2 H, NH_2), 7.69 and 8.35 (2 s, 2 H, aromatic protons); UV 262 nm (MeOH).

Neplanocin A (2). To a solution of 22 mg (0.063 mmol) of **38** in 1 mL of methanol was added mL of 2 M hydrochloric acid. The reaction mixture was stirred at room temperature for 16 h. After removal of the solvent, the residue was dissolved in water. Purification with a cation exchange resin (Amberlite CG-120, H^+ form) using 0.07 M NH_4OH as eluant gave synthetic neplanocin A (**2**) (13.3 mg) in 80% yield. The pure **2** was obtained by recrystallization from MeOH–H_2O (9:1): mp 220–222 °C (dec); $[\alpha]^{20}_D$ −152° (*c* 0.3, H_2O); R_f 0.49 (AcOEt/EtOH/H_2O = 3/1/1); IR (KBr) 3400, 1660, 1615, 1580, 1300, 1125 cm^{-1}; ^1H NMR (Me_2So-d_6/TSP) δ 4.16 (s, 2 H, CH_2OH), 4.35 (dd, J = 5, 5.5 Hz, 1 H, OCH), 4.48 (d, J = 5 Hz, 1 H, OCH), 5.06 (br s, 3 H, 3 OH), 5.37 (s, 1 H, NCH), 5.73 (d, J = 1.5 Hz, 1 H, CH=C), 7.21 (s, 2 H, NH_2), 8.07 and 8.14 (2 s, 2 H, aromatic protons); MS (m/e) 263 (M^+), 234, 216, 204, 135 (B + 1), 136 (B + 2), 119, 108. Anal. Calcd for $C_{11}H_{13}N_5O_3 \cdot 0.5H_2O$: C, 48.53; H, 5.18; N, 25.72. Found: C, 48.95; H, 4.98; N, 25.25.

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Registry No. 1, 19186-33-5; **2**, 72877-50-0; **3**, 72627-49-7; **4**, 85440-76-2; **5**, 85026-57-9; **6**, 84955-42-0; **7**, 84955-43-1; **7** methyl ester, 85390-36-9; **8**, 84955-44-2; **9**, 85026-58-0; **10**, 84955-45-3; **11**, 84955-46-4; **12**, 85026-59-1; **22**, 84955-47-5; **23**, 84955-52-2; **24**, 84955-48-6; **25**, 84955-49-7; **26**, 84955-50-0; **27**, 85390-32-5; **28**, 85390-33-6; **29a**, 85390-42-7; **29b**, 84955-51-1; **30**, 85390-35-8; **31**, 85390-34-7; **32**, 85390-37-0; **33a**, 85390-38-1; **3b**, 85440-77-3; **34**, 85390-39-2; **35**, 85390-40-5; **36**, 85390-41-6; **37**, 85390-43-8; **38**, 85390-44-9; esterase, 9013-79-0; 5-amino-4,6-dichloropyrimidine, 5413-85-4.