perature, the mixture was heated to reflux in an oil bath. The mixture was then evaporated to dryness in vacuo (water pump) at 70 °C, with anhydrous acetonitrile (5 mL) and iodotrimethylsilane (0.5 mL) then being added to the residue. The mixture was heated to reflux in an oil bath, and after 1 h, a complete conversion into guanosine had been effected as determined by comparing the reaction mixture with authentic guanosine by TLC.

Acknowledgment. This investigation was supported by Grant No. CA-28381 awarded by the National Cancer Institute, by DHEW, and in part by the UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases and the Scientific Working Group on Filariasis (I.D. 840398). We also thank Deanna VanSickle for assistance in the preparation of this paper and acknowledge the NIH Biomedical Research Support (Grant RR01437) for funds toward the purchase of an IBMWP-270SY NMR spectrometer.

Registry No. 1, 2627-69-2; **6**, 99268-01-6; **8**, 23192-64-5; **9**, 99268-02-7; **10**, 99268-03-8; **11a**, 99268-04-9; **11b**, 99268-05-0; **12a**, 99268-22-1; **12b**, 99268-23-2; **13**, 56086-84-1; **14**, 99268-06-1; **15**, 118-00-3; $^{18}O_2$, 32767-18-3.

Highly Selective Total Synthesis of Enantiomerically Pure (–)-Anisomycin

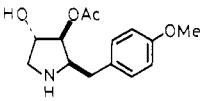
Hideo Iida, Naoki Yamazaki, and Chihiro Kibayashi*

Tokyo College of Pharmacy, Horinouchi, Hachioji, Tokyo 192-03, Japan

Received October 2, 1985

A chiral total synthesis of optically pure (–)-anisomycin (**1**) has been achieved. The method consists of the virtually complete regio- and stereocontrolled reactions involving no separation of isomers through the entire sequence. The scheme starts with the readily available 4-*O*-benzyl-2,3-*O*-bis(methoxymethyl)-L-threose (**5**) from diethyl L-tartrate as the chiral building block and involves highly selective α-chelation-controlled addition of hydride using $Zn(BH_4)_2$ to (3*R*,4*S*)-5-(benzyloxy)-3,4-bis[(methoxymethyl)oxy]-1-(4-methoxyphenyl)pentan-2-one (**9**) yielding the *lyxo* alcohol **8b** and stereospecific cyclization of (2*S*,3*R*,4*S*)-1-azido-2,3-bis[(methoxymethyl)-oxy]-5-(4-methoxyphenyl)-4-[(methylsulfonyl)oxy]pentane (**11**) to the (2*R*,3*S*,4*S*)-anisylpyrrolidine **12** via intramolecular S_N2 displacement. At the final critical stage, the selective introduction of the acetyl group into *N*-(benzyloxycarbonyl)deacetylanisomycin (**14**) is achieved with complete regiochemical control via the reaction sequence involving protection by the *tert*-butyldimethylsilyl group followed by acetylation–deprotection.

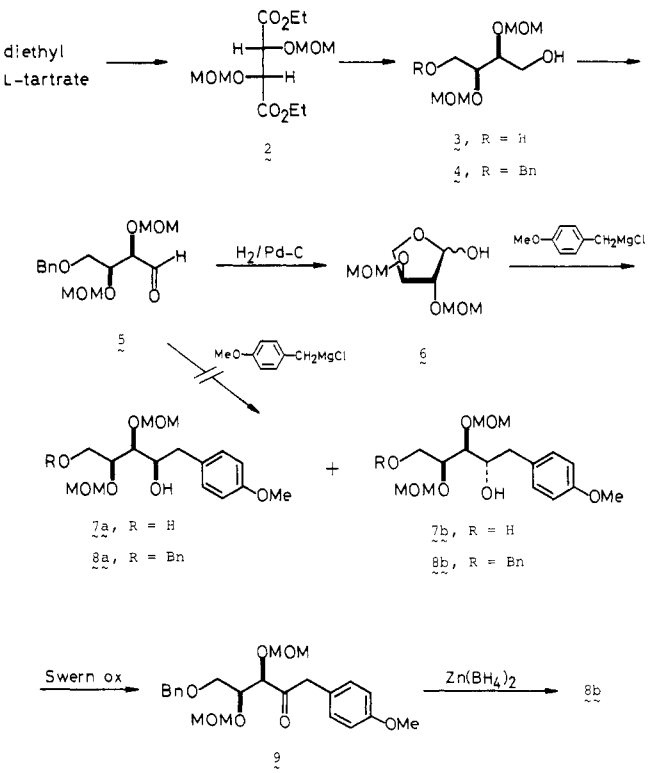
Anisomycin (**1**) is an antibiotic that has been isolated from fermentation broth filtrates of various species of *Streptomyces*.[1] The structure and relative stereochem-



istry of anisomycin were first studied chemically[2] and then determined by X-ray crystallographic analysis[3] to be **1**. The absolute stereochemistry was established as 2*R*,3*S*,4*S* by chemical correlation studies.[4] Anisomycin possesses strong and selective activities against pathogenic protozoa and fungi and has been used successfully clinically in the treatment of amebic dysentery and trichomonas vaginitis.[5] It has been shown to block ribosomal peptide synthesis.[5]

Anisomycin has attracted considerable synthetic interest, and two total syntheses of the racemic form[6] and four chiral syntheses[7] have been reported. Of the chiral syntheses two early ones starting from tartaric acid[7a] and diethyl tartrate[7b] were nonstereoselective and resulted in very low overall yields. Alternative elegant approaches by Moffatt et al.[7c] and Buchanan et al.[7d] have used carbohydrates as chiral templates. A problem encountered in the synthesis of anisomycin has been the chemo-, regio-, and stereoselective introduction of the acetyl group in the 3-position of the pyrrolidine ring. To resolve this problem,

Scheme I



(1) Sobin, B. A.; Tanner, F. W., Jr. *J. Am. Chem. Soc.* **1954**, *76*, 4053.
(2) Beereboom, J. J.; Butler, K.; Pennington, F. C.; Solomons, I. A. *J. Org. Chem.* **1965**, *30*, 2334.
(3) Schaefer, J. P.; Wheatley, P. J. *J. Org. Chem.* **1968**, *33*, 166.
(4) Wong, C. M. *Can. J. Chem.* **1968**, *46*, 1101.
(5) Korzybski, T.; Kowszyk-Gindifer, Z.; Kurytowicz, W. "Antibiotics"; American Society of Microbiology: Washington, DC, 1978; Vol. 1, pp 343–346.
(6) (a) Oida, S.; Ohki, E. *Chem. Pharm. Bull.* **1969**, *17*, 1405. (b) Schumacher, D. P.; Hall, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 6076.
(7) (a) Wong, C. M.; Buccini, J.; Chang, I.; Te Raa, J.; Schwenk, R. *Can. J. Chem.* **1969**, *47*, 2421. (b) Felner, I.; Schenker, K. *Helv. Chim. Acta* **1970**, *53*, 754. (c) Verheyden, J. P. H.; Richardson, A. C.; Bhatt, R. S.; Grant, B. D.; Fitch, W. L.; Moffatt, J. G. *Pure Appl. Chem.* **1978**, *50*, 1363. (d) Buchanan, J. G.; MacLean, K. A.; Paulsen, H.; Wightman, R. H. *J. Chem. Soc., Chem. Commun.* **1983**, *486*.

0022-3263/86/1951-1069$01.50/0

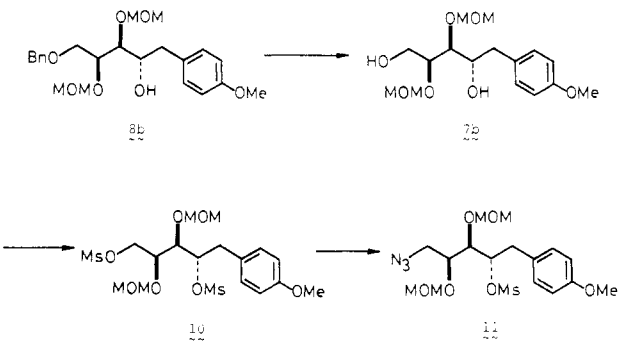
with two exceptions,[7a,c] the nucleophilic epoxide ring opening has been employed in the reported synthetic approaches.[6,7b,d]

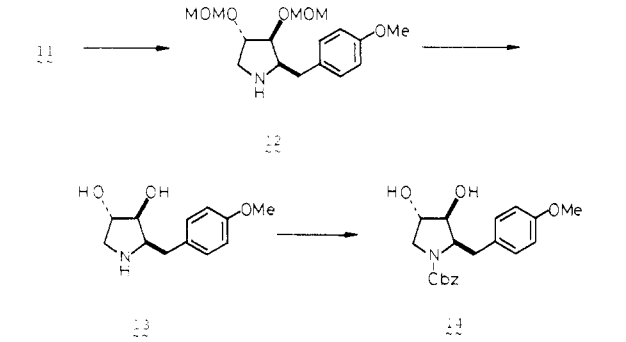
We envisaged an efficient route to natural levorotatory anisomycin (1) starting with diethyl tartrate by means of a stereoselective chelation-controlled process, thus involving no separation problem in this process and the following entire sequence. In addition, more efficient direct techniques for the selective introduction of the acetyl group into the 3-hydroxy group of the pyrrolidine ring seemed possible via protection by the bulky group such as *tert*-butyldimethylsilyl group followed by acetylation–deprotection reaction sequence. In this paper, we describe the development of successful approach to (−)-anisomycin (1) in an enatiomerically pure state based on these two central ideas.

Our initial study was designed to utilize 4-*O*-benzyl-2,3-*O*-bis(methoxymethyl)-L-threose (**5**)[8] as a chiral building block which was synthesized as shown in Scheme I. Thus the L-threitol derivative **3** was prepared from L-diethyl tartrate by methoxymethylation (MOMCl, $(i\text{-Pr})_2NEt$, $CHCl_3$) to give **2** followed by $LiAlH_4$ reduction in 74% overall yield. Monobenzylation of **3** was effected by treatment with 1 equiv of benzyl chloride (4 N NaOH, CH_2Cl_2) in the presence of a phase-transfer catalyst ($(n\text{-Bu})_4NBr$) to form **4** in 74% yield, which was then subjected to Swern oxidation[9] ($(COCl)_2$, Me_2SO, Et_3N) to give **5** in 82% yield. Treatment of the aldehyde **5** with (*p*-methoxybenzyl)magnesium chloride resulted in the formation of a complex mixture, along with an appropriate amount of bibenzyl. Desired Grignard addition successfully occurred when (*p*-methoxybenzyl)magnesium chloride was allowed to react with the lactol **6**, obtained from **5** by hydrogenation over Pd/C in methanol (91% yield), and produced a chromatographically separable mixture of two diastereomers, *xylo*-**7a** and *lyxo*-**7b**, in a ratio of 79:21.

Since the desired *lyxo* alcohol **7b** accessible in this way was a minor product, the additional vexing procedure for the configurational inversion of the 4-hydroxy group in the major **7a** is needed to convert *xylo*-**7a** to *lyxo*-**7b**.[10] In addition, the requirement for diastereoisomeric separation appeared to impair the synthetic value of this method. In order to circumvent these problems, we envisaged to obtain a high degree of diastereofacial selectivity in the formation of the *lyxo*-**8b** via metal hydride reduction of the alkoxy ketone.[11] Accordingly, a diastereoisomeric mixture of the alcohols **8a** and **8b**, prepared by selective benzylation (BnCl, 4 N NaOH, $(n\text{-Bu})_4NBr$, CH_2Cl_2) of a mixture of the diols **7a** and **7b**, was subjected to Swern oxidation to generate the ketone **9** in 64% overall yield from **7a** + **7b**. The ketone **9** was converted to the *lyxo*-**8b** in 91% yield by treatment with zinc borohydride (Et_2O, 0 °C → room temperature) with virtually complete diastereofacial control (>99:1, determined by 400-MHz ^1H NMR).[12] The anti selectivity of hydride addition observed in this case with the α,β-alkoxy carbonyl system are consistent with the formation of the five-membered α-chelate model[13] rather than the six-membered β-chelate model.[11,14]

The synthesis of the alcohol **8b** having the requisite three contiguous asymmetric centers, C-2, C-3, and C-4, for the natural product was now established. With this alcohol in hand, the stereospecific construction of the pyrrolidine ring system was then investigated. Accordingly, **8b** was debenzylated by catalytic hydrogenolysis to give the diol **7b**, dimesylation of which afforded **10**. Selective displacement of the dimesylate **10** by azide ion (NaN_3) in DMF (80 °C, 30 min) introduced the nitrogen function to provide the monoazide **11** in 39% overall yield from **8b**. When **11** was catalytically hydrogenated (Pd/C, MeOH, 1 h), the resulting amine spontaneously cyclyzed via intramolecular displacement with inversion of configuration to stereospecifically produce **12** in 94% yield.



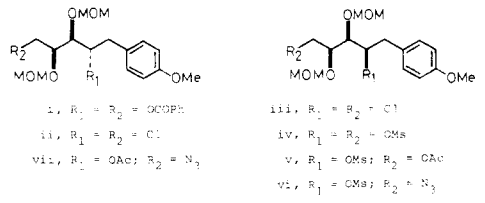


Removal of the protecting methoxymethyl groups in **12** by acid treatment (aqueous HCl/MeOH, reflux) provided

(8) The synthesis of **5** has been previously reported by us in the following communication: Iida, H.; Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1985**, *26*, 3255.

(9) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(10) For the inversion of the absolute configuration at C-4 in **7a**, Mitsunobu reaction ($PhCO_2H$, Ph_3P, DEAD) of the diol **7a** was carried out in anticipation of obtaining i; however, it resulted in affording an intractable mixture of products. Treatment of **7a** with $SOCl_2$/pyridine generated a diastereomeric mixture of the dichlorides ii and iii along with an intractable mixture of reaction products. In another way, treatment of the dimesylate iv, prepared from **7a**, with Et_4NOAc gave only the monoaetate v, $[\alpha]^{20}_D$ +4.5° (*c* 3.58, MeOH). When the monoazide vi, derived from the dimesylate iv, was treated with Et_4NOAc a trace amount of the C-4 inverted product vii, $[\alpha]^{20}_D$ −48.6° (*c* 0.41, MeOH), was formed.



(11) For a recent review, see: Ohishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 388.

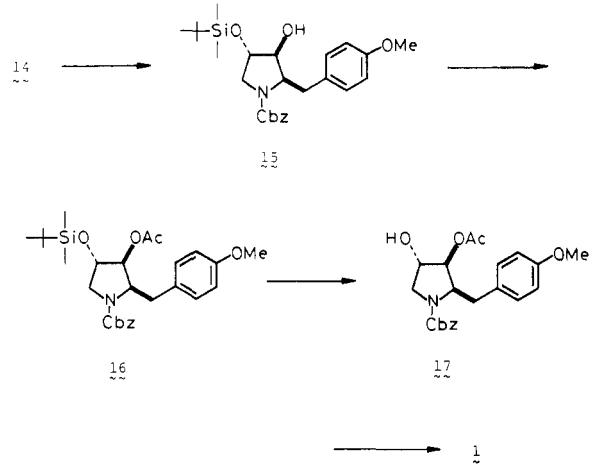
(12) Upon reduction of the ketone **9** using $NaBH_4$, Vitride, and $LiAlH_4$ the desired *lyxo* selectivity was also observed in each case in *lyxo*/*xylo* ratios of 72:28; 95:5, and 64:36, respectively. Reduction with L-Selectride, on the other hand, provided the undesired *xylo* isomer **8a** in 95:5 selectivity. These results and related hydride reductions will be reported in detail elsewhere.

(13) Still, W. C.; McDonald J. H., III *Tetrahedron Lett.* **1980**, *21*, 1031.

(14) If the hydride addition proceeded via β-chelation-controlled process the syn alcohol **8a** would be the predominant product. For example of β-chelation-controlled hydride addition, see: (a) Nakata, T.; Ohishi, T. *Tetrahedron Lett.* **1980**, *21*, 1641. (b) DeShong, P.; Ramesh, S.; Perez, J. J. *J. Org. Chem.* **1983**, *48*, 2117. (c) Nakata, T.; Tani, Y.; Hatozaki, M.; Ohishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 1411. (d) Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4241. (e) Burke, S. D.; Armistead, D. M.; Schoenen, F. *Ibid.* **1984**, *49*, 4322.

deacetylanisomycin (**13**) in 81% yield, which was treated with benzyl chloroformate under the alkaline conditions to give *N*-(benzyloxycarbonyl)deacetylanisomycin (**14**) in 72% yield. In practice, the transformation **12** → **14** can conveniently be performed in tandem as one-pot reaction; thus the acidic solution of **13** generated by deprotection of **12** was consequently treated with Na_2CO_3 and benzyl chloroformate to lead to **14**.

The final critical step involving selective protection of the 4-hydroxy group proceeded as planned when **14** was treated with 1.2 equiv of *tert*-butyldimethylsilyl chloride and 2.4 equiv of imidazole in DMF at room temperature for 1 h, thus affording the silyl ether **15** as a single isomer in 80% yield. This result is consistent with the concept that the bulky *tert*-butyldimethylsilyl group approaches from the less sterically hindered α-side opposite to the bulky *p*-methoxybenzyl group at the C-2 position. Acetylation of **15** with acetic anhydride and pyridine followed by removal of the protecting silyl group with tetra-*n*-butylammonium fluoride provided **17** in overall yield of 82%. Conversion of **17** to (−)-anisomycin (**1**) was accomplished by hydrogenation in 95% yield. Comparison of the



melting point, specific optical rotation, ^1H and ^{13}C NMR, and mass spectra of synthetic (−)-**1** with those of the literature[15] completely confirmed the identity of (−)-anisomycin, thus proving 100% enantiomeric purity of our synthetic material. Antiprotozoal and antifungal activities of synthetic (−)-anisomycin are under investigation.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were measured at 90, 200, or 400 MHz. ^{13}C NMR spectra were recorded at 50.1 or 100.6 MHz. Mass spectra were obtained at an ionizing potential of 70 eV. Optical rotations were measured at the sodium D line in a 0.05-dm cell at the designated concentration in g per 100 mL. TLC was run on Wako precoating silica gel 70 FM plates. Column chromatography refers to flash chromatography on Merck silica gel 60 (230–400 mesh).

Diethyl 2,3-*O*-Bis(methoxymethyl)-L-tartrate (2). To a stirred, cooled (0 °C) mixture of diethyl L-tartrate (100 g, 0.485 mol) and *N,N*-diisopropylethylamine (157 g, 1.21 mol) in $CHCl_3$ (200 mL) was added a solution of chloromethyl methyl ether (98 g, 1.21 mol) in $CHCl_3$ (100 mL). The mixture was heated at 60 °C with stirring. After 36 h, ether (1 L) was added to the cooled (to room temperature) reaction mixture to separate the hydrochloride of the base which was removed by filtration. The filtrate was evaporated to leave an oil which was purified by distillation to give **2** (112.7 g, 79.0%) as a pale yellow oil: bp 152–154 °C (0.6 mmHg); $[\alpha]^{20}_D$ +142.7° (*c* 1.57, MeOH): IR (neat) 1760, 1735 cm^{-1}; ^1H NMR (90 MHz) ($CDCl_3$) δ Me_4Si 1.31 (6 H, t, *J* = 7 Hz), 3.34 (6 H, s), 4.24 (4 H, q, *J* = 7 Hz), 4.64 (2 H, 1/2 AB q, *J* = 7.5 Hz), 4.68 (2 H, s), 4.78 (2 H, 1/2 AB q, *J* = 7.5 Hz); mass spectrum, *m/e* 263 (M^+ − 31, 1.2), 217 (54), 192 (45), 117 (100).

Anal. Calcd for $C_{12}H_{22}O_8$: C, 48.97; H, 7.53. Found: C, 48.72; H, 7.37.

2,3-*O*-Bis(methoxymethyl)-L-threitol (3). To a stirred, cooled (0 °C) suspension of $LiAlH_4$ (20.1 g, 0.53 mol) in ether (400 mL)/THF (500 mL) was added dropwise a solution of **2** (100 g, 0.340 mol) in THF (100 mL). The mixture was stirred at room temperature for 14 h and quenched by addition of 4 N KOH (30 mL) and then water under ice cooling. The mixture was filtered through a Celite pad and washed with THF (1 L), and after drying ($MgSO_4$) the solvent was evaporated. The residue was recrystallized from $CHCl_3$/diisopropyl ether/hexane to give **3** (67.1 g, 94%) as colorless needles: mp 62–63 °C; $[\alpha]^{23}_D$ −7.7° (*c* 3.37, MeOH); IR (neat) 3420 cm^{-1}; ^1H NMR (90 MHz) ($CDCl_3$) δ Me_4Si 2.93 (2 H, br t), 3.41 (6 H, s), 3.71 (4 H, br s), 3.74 (2 H, s), 4.66 (2 H, d, *J* = 7.5 Hz), 4.74 (2 H, d, *J* = 7.5 Hz); mass spectrum, *m/e* 191 (M^+ − 1 − H_2O, 0.8), 189 (0.8), 179 (1.2), 147 (44), 117 (74), 105 (51), 103 (47), 88 (100), 73 (82).

Anal. Calcd for $C_8H_{18}O_6$: C, 45.71; H, 8.63. Found: C, 45.43; H, 8.57.

1-*O*-Benzyl-2,3-*O*-bis(methoxymethyl)-L-threitol (4). A mixture of **3** (10.0 g, 47.6 mmol), benzylchloride (6.0 g, 47.6 mmol), 4 N NaOH (35 mL), and tetrabutylammonium bromide (750 mg) in CH_2Cl_2 (30 mL) was heated at 50 °C for 14 h with stirring. After water (20 mL) was added to the reaction mixture the organic phase was extracted with CH_2Cl_2 (3 × 100 mL) and the combined extracts were dried ($MgSO_4$). Evaporation of the solvent followed by chromatography on a silica gel column with hexane/ethyl acetate (2:1) gave **4** (10.6 g, 74%) as a colorless oil: $[\alpha]^{24}_D$ −2.9° (*c* 2.66, MeOH); IR (neat) 3450, 740, 700 cm^{-1}; ^1H NMR (90 MHz) ($CDCl_3$) δ Me_4Si 3.03 (1 H, br t), 3.37 (6 H, s), 3.57–4.07 (6 H, m), 4.52 (2 H, s), 4.60–4.86 4 H, m), 7.30 (5 H, s); mass spectrum, *m/e* 301 (M^+ + 1, 1.3), 283 (0.7), 269 (3.0), 255 (5.0), 237 (11), 223 (38), 91 (100).

Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.82; H, 8.05.

4-*O*-Benzyl-2,3-*O*-bis(methoxymethyl)-L-threose (5). To a stirred and cooled (−78 °C) solution of oxalyl chloride (8.45 g, 67 mmol) in CH_2Cl_2 (40 mL) was added a solution of Me_2SO (10.4 g, 133 mmol) in CH_2Cl_2 (30 mL) over a period of 5 min. After 15 min with stirring at −78 °C, a solution of **4** (10.0 g, 33 mmol) in CH_2Cl_2 (30 mL) was added to the mixture over a period of 5 min. After 1 h of stirring at −78 °C, triethylamine (20.2 g, 200 mmol) was added to the reaction mixture over a period of 5 min, and the mixture was stirred for further 5 min. The reaction was allowed to warm to ambient temperature and water (50 mL) was added to the mixture. The organic phase was separated, the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL), and the combined extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent left an oil which was chromatographed on silica gel with hexane/ethyl acetate (4:1) to give **5** (8.1 g, 82%) as a colorless oil: $[\alpha]^{24}_D$ +13.3° (*c* 4.85, MeOH); IR (neat) 1730, 740, 700 cm^{-1}; ^1H NMR (90 MHz) ($CDCl_3$) δ Me_4Si 3.28 (3 H, s), 3.40 (3 H, s), 3.63 (1 H, apparent s), 3.70 (1 H, apparent s), 4.02–4.32 (2 H, m), 4.52 (2 H, apparent s), 4.60–4.83 (4 H, m), 7.32 (5 H, s), 9.75 (1 H, s); ^{13}C NMR (50.1 MHz) ($CDCl_3$) δ $CDCl_3$ 55.96 (q), 56.25 (q), 68.31 (t), 73.57 (t), 76.08 (d), 81.63 (d), 96.90 (t), 97.54 (t), 127.82 (d), 128.49 (d), 137.78 (s), 201.58 (d); mass spectrum, *m/e* 299 (M^+ + 1, 0.08), 267 (0.4), 253 (1.6), 237 (2.9), 221 (2.5), 205 (1.5), 191 (3.0), 181 (2.8), 91 (100).

Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.02; H, 7.51.

2,3-*O*-Bis(methoxymethyl)-L-*threo*-furanose (6). The aldehyde **5** (10.1 g, 33.86 mmol) was hydrogenated over 10% Pd/C (5.1 g) at 1 atm of H_2 in methanol (150 mL) for 1 h. The catalyst was removed by filtration and replaced with fresh catalyst (5.1 g) and hydrogenation was continued for another 1 h. The mixture was filtered and the catalyst was rinsed with methanol. The filtrate was evaporated in vacuo. The oil residue was purified by chromatography on silica gel (hexane/ethyl acetate, 2:1 then 1:1) to give 6.4 g (91%) of **6** as a colorless oil: $[\alpha]^{20}_D$ −20.8° (*c* 5.19, MeOH); ^1H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 3.31, 3.33, 3.36 (total 6 H, with 1:3:1 ratio, each s), 3.69 (0.6 H, dd, *J* = 9.8, 3.0 Hz), 4.00–4.25 (4.4 H, m), 4.60–4.75 (4 H, m), 5.23 (0.6 H, s), 5.35 (0.4 H, d, *J* = 4.1 Hz); mass spectrum, *m/e* 209 (2.5), 207

(15) See Experimental Section.

(2), 191 (20), 161 (20), 148 (20), 147 (45), 146 (80), 145 (25), 132 (25), 129 (40).

Reaction of 2,3-*O*-Bis(methoxymethyl)-L-*threo*-furanose (6) with (4-Methoxybenzyl)magnesium Chloride. To a stirred, refluxed mixture of Mg turnings (6.19 g, 0.255 mol) and dry THF (100 mL) under N_2 was added dropwise an approximately half amount of 19.94 g (0.127 mol) of *p*-methoxybenzyl chloride over a period of 2–3 min. The heating bath was removed and the half remainder of *p*-methoxybenzyl chloride was further added dropwise to this mixture with stirring at the rate to maintain reflux. The resulting mixture was stirred at room temperature for an additional 5 min and then cooled to −10 °C. To this mixture was added a solution of **6** (5.3 g, 25.5 mmol) in THF (40 mL), and the reaction was allowed to warm to ambient temperature. After being stirred for 14 h, the reaction mixture was quenched with cold water (10 mL) and extracted with ether (400 mL). The ether extracts were dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel with hexane/ethyl acetate (1:1) followed by ethyl acetate to give 5.8 g (69%) of a mixture of the *xylo* and *lyxo* isomers **7a** and **7b** in a 79:21 ratio (by ^1H NMR spectrum). A part of this mixture was separated by silica gel chromatography (hexane/ethyl acetate, 1:1, then 1:2, then ethyl acetate) to afford the pure *xylo* and *lyxo* isomers **7a** and **7b**. For (2*S*,3*S*,4*R*)-2,3-bis[(methoxymethyl)oxy]-5-(4-methoxyphenyl)-1,4-pentanediol (**7a**): $[\alpha]^{20}_D$ −3.5° (*c* 11.56, MeOH); ^1H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 2.60–2.80 (1 H, br s), 2.82 (2 H, d, *J* = 6.8 Hz), 3.08–3.26 (1 H, br s), 3.35 (3 H, s), 3.46 (3 H, s), 3.64 (1 H, t, *J* = 3.6 Hz), 3.72–3.88 (3 H, m; containing 3 H, s at 3.79), 4.01–4.11 (1 H, unresolved), 4.63 (1 H, 1/2 AB q, *J* = 6.9 Hz), 4.72 (1 H, 1/2 AB q, *J* = 6.9 Hz), 4.76 (1 H, 1/2 AB q, *J* = 6.8 Hz), 4.80 (1 H, 1/2 AB q, *J* = 6.8 Hz), 6.85 (2 H, 1/2 AB q, *J* = 8.6 Hz), 7.17 (2 H, 1/2 AB q, *J* = 8.6 Hz). For (2*S*,3*S*,4*S*)-2,3-bis[(methoxymethyl)oxy]-5-(4-methoxyphenyl)-1,4-pentanediol (**7b**): $[\alpha]^{20}_D$ −22.7° (*c* 16.21, MeOH); ^1H NMR (200 MHz) ($CDCl_3$) δ $CHCl_3$ 2.62 (1 H, dd, *J* = 13.7, 9.7 Hz), 2.82 (1 H, br s), 2.99 (1 H, dd, *J* = 14.0, 3.1 Hz), 3.13 (1 H, br s), 3.41 (3 H, s), 3.47 (3 H, s), 3.65 (1 H, dd, *J* = 6.8, 3.4 Hz), 3.77 (3 H, s; containing 2 H, unresolved), 3.85–4.00 (2 H, m), 4.67–4.83 (4 H, m), 6.85 (2 H, 1/2 AB q, *J* = 9.7 Hz), 7.18 (2 H, 1/2 AB q, *J* = 9.7 Hz).

(2*R*,3*S*,4*S*)- and (2*S*,3*S*,4*S*)-5-(Benzyloxy)-3,4-bis-[(methoxymethyl)oxy]-1-(4-methoxyphenyl)-2-propanol (8a and 8b). To a stirred mixture of the alcohols **7a** and **7b** (5.83 g, 17.7 mmol), prepared by the Grignard reaction of **6**, tetrabutylammonium bromide (326 mg, 1.01 mmol), and 6 N NaOH (8.8 mL) in CH_2Cl_2 (20 mL) was added dropwise a solution of benzyl chloride (2.79 g, 22.0 mmol) in CH_2Cl_2 (5 mL) at room temperature over a period of 5 min. The mixture was heated at 60 °C. After 24 h, water (10 mL) was added to the reaction mixture and the resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on a silica gel column with hexane/ethyl acetate (3:1 followed by 2:1) to give a 79:21 mixture (by ^1H NMR spectrum) of **8a** and **8b** (5.12 g, 69%) as a colorless oil. A part of this product mixture was separated by preparative TLC on silica gel (hexane/ethyl acetate, 1:1) to give the pure *xylo* and *lyxo* isomers **8a** and **8b**. For **8a**: $[\alpha]^{21}_D$ −2.1° (*c* 1.40, MeOH); ^1H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 2.72–2.90 (3 H, m), 3.31 (3 H, s), 3.44 (3 H, s), 3.63–3.72 (1 H, unresolved; containing 1 H, t, *J* = 4.2 Hz, at 3.65 and 1 H, dd, *J* = 5.0, 1.7 Hz, at 3.68), 3.78 (3 H, s), 3.93–4.03 (2 H, m), 4.51 (2 H, s), 4.62–4.81 (4 H, m), 6.83 (2 H, 1/2 AB q, *J* = 8.6 Hz), 7.17 (2 H, 1/2 AB q, *J* = 8.6 Hz), 7.17–7.40 (5 H, m); mass spectrum, *m/e* 299 (10), 237 (16), 207 (30), 191 (20), 163 (22), 150 (21), 135 (51), 121 (100), 91 (100). For **8b**: $[\alpha]^{20}_D$ −36.0° (*c* 7.00, MeOH); ^1H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 2.64 (1 H, dd, *J* = 14.0, 9.6 Hz), 2.97 (1 H, dd, *J* = 13.9, 3.1 Hz), 3.19 (1 H, d, *J* = 5.4 Hz), 3.38 (3 H, s), 3.43 (3 H, s), 3.64–3.71 (3 H, m), 3.79 (3 H, s), 3.89–3.98 (1 H, m), 4.09 (1 H, td, *J* = 5.6, 3.7 Hz), 4.54 (2 H, d, *J* = 2.4 Hz), 4.70–4.81 (4 H, m), 6.83 (2 H, 1/2 AB q, *J* = 6.6 Hz), 7.15 (2 H, 1/2 AB q, *J* = 6.6 Hz), 7.26–7.40 (5 H, m); mass spectrum, *m/e* 299 (2.2), 207 (24), 121 (8), 91 (100); exact mass calcd for $C_{23}H_{30}O_6$ ($M^+ - H_2O$) 402.2040, found 402.2041.

(3*S*,4*S*)-5-(Benzyloxy)-3,4-bis[(methoxymethyl)oxy]-1-(4-methoxyphenyl)pentan-2-one (9). To a stirred −78 °C solution of oxalyl chloride (2.71 g, 21.3 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of Me_2SO (3.33 g, 42.6 mmol) in CH_2Cl_2 (10 mL) over a period of 5 min, and the mixture was stirred for another 15 min at −78 °C. To this mixture was added dropwise a solution of a diastereomeric mixture of **8a** and **8b** (2.24 g, 5.33 mmol) in CH_2Cl_2 (10 mL) over a period of 5 min, and stirring was continued at −78 °C. After 1 h, triethylamine (6.47 g, 64.0 mmol) was added to the reaction mixture and the reaction was allowed to warm to ambient temperature. After addition water (20 mL) the mixture was stirred for 15 min, extracted with CH_2Cl_2 (3 × 100 mL), and washed with brine, and the extract was dried ($MgSO_4$). The solvent was evaporated to leave an oil which was purified by chromatography on silica gel (hexane/ethyl acetate, 3:1) to give **9** (2.08 g, 93%) as a colorless oil: $[\alpha]^{20}_D$ +5.6° (*c* 4.61, MeOH); ^1H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 3.30 (3 H, s), 3.36 (3 H, s), 3.65 (1 H, dd, *J* = 10.9, 9.7 Hz), 3.65 (1 H, dd, *J* = 23.3, 9.7 Hz), 3.78 (3 H, s), 3.86 (2 H, s), 4.20 (1 H, td, *J* = 6.1, 3.4 Hz), 4.38 (1 H, d, *J* = 3.4 Hz), 4.51 (2 H, s), 4.58, 4.59 (each 1 H, two sets of 1/2 AB q, *J* = 6.8 Hz each), 4.66, 4.71 (each 1 H, two sets of 1/2 AB q, *J* = 6.8 Hz each), 6.84 (2 H, 1/2 AB q, *J* = 6.6 Hz), 7.08 (2 H, 1/2 AB q, *J* = 6.6 Hz), 7.26–7.40 (5 H, m); mass spectrum, *m/e* 418 (3), 387 (4), 386 (16), 215 (40), 121 (100), 91 (91), 83 (39); exact mass calcd for $C_{23}H_{30}O_7$ (M^+) 418.1989, found 418.1961.

Reduction of (3*S*,4*S*)-5-(Benzyloxy)-3,4-bis[(methoxymethyl)oxy]-1-(4-methoxyphenyl)pentan-2-one (9) with Zinc Borohydride. To a stirred, cold (0 °C) solution of **9** (880 mg, 2.10 mmol) in ether (15 mL) was added 29.0 mL (4.21 mmol) of 0.145 M $Zn(BH_4)_2$[16] in ether. The reaction mixture was stirred at 0 °C for 10 min and at room temperature for 50 min. After addition of water (5 mL) and being stirred for 15 min, the mixture was extracted with ether (3 × 100 mL), dried ($MgSO_4$), and evaporated. The residue was chromatographed on silica gel with hexane/ethyl acetate (2:1) to give a colorless oil (801 mg, 91%) which was proved to be a mixture of **8a** and **8b** in a >99:1 ratio (determined by 400-MHz ^1H NMR) favoring **8b**.

(2*S*,3*S*,4*S*)-2,3-Bis[(methoxymethyl)oxy]-5-(4-methoxyphenyl)-1,4-pentanediol (7b). The benzyl ether **8b** (580 mg, 1.38 mmol) was dissolved in methanol (5 mL), and 580 mg of 10% Pd/C was added to the mixture. After 1 h of hydrogenation at 1 atm, the catalyst was filtered and the solvent was removed to give **7b** (456 mg, 100%) as a colorless oil, identical with a sample prepared via the Grignard reaction of the lactol **6**.

(2*R*,3*R*,4*S*)-2,3-Bis[(methoxymethyl)oxy]-5-(4-methoxyphenyl)-1,5-bis[(methylsulfonyl)oxy]pentane (10). To a stirred, ice-cooled solution of **7b** (420 mg, 1.27 mmol) and triethylamine (771 mg, 7.62 mmol) in CH_2Cl_2 (5 mL) was added mesyl chloride (436 mg, 3.81 mmol) in a dropwise manner using a syringe, and the mixture was stirred for 10 min. An equal volume of ether was added and the mixture was filtered to remove triethylamine hydrochloride. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (hexane/ethyl acetate, 2:1) to give **10** (540 mg, 87%) as a colorless oil: $[\alpha]^{20}_D$ −28.2° (*c* 15.02, MeOH); ^1H NMR (200 MHz) ($CDCl_3$) δ $CHCl_3$ 2.35 (3 H, s), 2.95–3.20 (2 H, m; including 3 H, s, at 3.09), 3.44 (3 H, s), 3.47 (3 H, s), 3.79 (3 H, s), 4.00–4.18 (2 H, m), 4.30–4.60 (2 H, unresolved), 4.65–4.85 (4 H, m), 4.85–5.05 (1 H, m), 6.87 (2 H, 1/2 AB q, *J* = 8.6 Hz), 7.19 (2 H, 1/2 AB q, *J* = 8.6 Hz); mass spectrum, *m/e* 423 (2.4), 346 (4), 271 (2.4), 207 (31), 121 (100).

(2*S*,3*R*,4*S*)-1-Azido-2,3-bis[(methoxymethyl)oxy]-5-(4-methoxyphenyl)-4-[(methylsulfonyl)oxy]pentane (11). A stirred mixture of **10** (700 mg, 1.44 mmol) and NaN_3 (112 mg, 1.73 mmol) in DMF (10 mL) was heated at 80 °C for 0.5 h. The mixture was cooled and ether (200 mL) was added. A white precipitate was formed which removed by filtration. The filtrate was evaporated, and the residue was treated with ether (50 mL). Further precipitation occurred and the precipitate was again removed by filtration. The solvent was removed under reduced pressure to leave an oil which was purified by column chromatography on silica gel (hexane/ethyl acetate, 5:1) to afford **11** (281 mg, 45%) as a colorless oil: $[\alpha]^{20}_D$ −34.4° (*c* 6.83, MeOH); ^1H NMR (90 MHz) ($CDCl_3$) δ Me_4Si 2.38–2.53 (1 H, m; containing 3 H, s, at 2.38), 3.00 (2 H, d, *J* = 6.6 Hz), 3.23–3.67 (1 H, m; containing two sets of 3 H, s, at 3.40), 3.68–4.13 (2 H, m; containing 3 H, s, at 3.73), 4.63–5.20 (1 H, m; containing 4 H, s, at 4.76), 6.83 (2 H,

(16) Gensler, W. J.; Johnson, F. A.; Sloan, D. B. *J. Am. Chem. Soc.* **1960**, *82*, 6074.

1/2 AB q, J = 8.4 Hz), 7.16 (2 H, 1/2 AB q, J = 8.4 Hz); mass spectrum, m/e 433 (1), 326 (2), 248 (17), 207 (22), 164 (23), 121 (100), 75 (21).

(2*R*,3*S*,4*S*)-2-(4-Methoxybenzyl)-3,4-*O*-bis(methoxymethyl)pyrrolidine (12). The azide **11** (60 mg, 0.138 mmol) was dissolved in methanol (2 mL), and 60 mg of 10% Pd/C was added to the mixture. After 1 h of hydrogenation at 1 atm, the catalyst was filtered and a saturated ammonia solution in $CHCl_3$ (0.5 mL) was added to the filtrate. The resulting mixture was stirred for 10 min at room temperature and concentrated in vacuo. Purification by a column chromatography on silica gel (ethyl acetate/chloroform saturated with NH_3, 1:1) gave **12** (41 mg, 95%) as a colorless oil: $[\alpha]^{20}_D$ -12.5° (c 1.52, MeOH); ^{1}H NMR (200 MHz) ($CDCl_3$) δ $CHCl_3$ 2.72–2.90 (3 H, m), 3.30 (3 H, s), 3.35–3.52 (2 H, m; containing 3 H, s, at 3.39), 3.78 (3 H, s), 3.86 (1 H, d, J = 3.9 Hz), 4.19 (1 H, dd, J = 6.3, 3.1 Hz), 4.53–4.82 (4 H, m), 6.83 (2 H, 1/2 AB q, J = 8.6 Hz), 7.17 (2 H, 1/2 AB q, J = 8.6 Hz); mass spectrum, m/e 312 (1.2), 280 (4.8), 260 (5), 204 (4.8), 190 (100), 128 (18), 121 (50), 96 (19).

(2*R*,3*S*,4*S*)-3,4-Dihydroxy-2-(4-methoxybenzyl)pyrrolidine (Deacetylanisomycin) (13). A solution of **12** (30 mg, 0.0963 mmol) in 2 mL of methanol/concentrated HCl/H_2O (2:1:1) was heated at reflux for 20 h. The reaction mixture was concentrated in vacuo and 0.5 mL of water was added to the residue. The mixture was made alkaline by addition of Na_2CO_3 and washed with $CHCl_3$ (2 × 20 mL). The aqueous layer was allowed to stand at room temperature overnight to separate **13** (17.4 mg, 81%) as colorless needles: mp 176–177 °C (lit.[2] mp 176–178 °C, lit.[7b] mp 172–174 °C); mass spectrum, m/e 224 (M + 1, 0.7), 122 (16), 121 (28), 102 (100).

(2*R*,3*S*,4*S*)-*N*-(Benzyloxycarbonyl)-3,4-dihydroxy-2-(4-methoxybenzyl)pyrrolidine (14). A. From 13. To a stirred 0 °C suspension of **13** (10 mg, 0.045 mmol) in CH_2Cl_2 (2 mL) was added at once an aqueous solution of Na_2CO_3 (5 mg, 0.047 mmol in 0.5 mL of H_2O), and then a solution of benzyl chloroformate (7.6 mg, 0.045 mmol) in CH_2Cl_2 (1 mL) was added dropwise via syringe. The stirred mixture was allowed to warm to room temperature. After 2.5 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 30 mL), dried ($MgSO_4$), and evaporated in vacuo. The residue was chromatographed on a silica gel column (hexane/ethyl acetate, 2:1 to ethyl acetate) to give **14** (11.5 mg, 72%) as a colorless oil which was solidified on standing: mp 127–129 °C (lit.[7b] mp 129–130 °C); $[\alpha]^{23}_D$ -8.2° (c 5.97, MeOH) [lit.[7b] $[\alpha]_D$ -8° (c 0.661)[17]]; ^{1}H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 1.90–2.18 (2 H, unresolved), 2.89 (1 H, dd, 13.7, 9.1 Hz), 2.98–3.46 (2 H, unresolved), 3.59 (1 H, dd, 11.7, 5.6 Hz), 3.77 (3 H, s), 3.93 (1 H, br s), 4.01 (1 H, br s), 4.22 (1 H, br s), 5.15 (2 H, br s), 6.78 (2 H, br s), 7.00–7.25 (2 H, unresolved), 7.27–7.42 (5 H, m); mass spectrum, m/e 357 (7), 236 (40), 192 (42), 121 (43), 91 (100), 65 (6); exact mass calcd for $C_{20}H_{23}NO_5$ (M^+) 357.1574, found 357.1544.

B. From 12. A solution of **12** (300 mg, 0.963 mmol) in 6 mL of methanol/concentrated HCl/H_2O (1:1:1) was refluxed for 20 h. After evaporation in vacuo, the residue was diluted with water (2 mL) and made alkaline by addition of excess Na_2CO_3 (ca. 150 mg). To this mixture was added a solution of benzyl chloroformate (164 mg, 0.967 mmol) in CH_2Cl_2 (1 mL) with stirring under cooling (0 °C). The mixture was warmed to room temperature and stirred for 2 h. Evaporation and chromatography on silica gel (hexane/ethyl acetate, 1:1) gave **14** (202 mg, 59% from **12**) as a colorless oil, identical in all respects with that derived from **13**.

(2*R*,3*S*,4*S*)-*N*-(Benzyloxycarbonyl)-3-hydroxy-2-(4-methoxybenzyl)-4-[(*tert*-butyldimethylsilyl)oxy]pyrrolidine (15). To a solution of **14** (164 mg, 0.459 mmol) in DMF (3 mL) was added imidazole (75 mg, 1.10 mmol) and *tert*-butyldimethylsilyl chloride (83 mg, 0.551 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was passed through a silica gel column using hexane/ethyl acetate (3:1). Most of DMF and impurities were removed by this operation. The resulting oily product was rechromatographed on silica gel (hexane/ethyl acetate, 5:1) to give **15** (172.7 mg, 80%) as a colorless oil: $[\alpha]^{24}_D$ -9.7° (c 15.51, MeOH); ^{1}H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ -0.02 (6 H, s), 0.81 (9 H, s), 1.73 (1 H, br s), 2.88 (1 H, br t, J = ca. 11.3 Hz), ca. 3.03, ca. 3.37 (total 1 H, each br s), 3.33 (1 H, dd, J = 11.3, 4.0 Hz), 3.48 (1 H, dd, J = 11.3, 5.3 Hz), 3.78 (3 H, s; containing 1 H), 3.92 (1 H, br s), 4.20 (1 H, br s), 5.17 (2 H, br s), 6.80 (2 H, br s), 7.00–7.25 (2 H, unresolved), 7.26–7.42 (5 H, m); mass spectrum, m/e 472 (M + 1, 0.5), 471 (M^+, 1), 415 (1.7), 414 (5), 412 (1.6), 370 (4), 351 (8), 350 (33), 308 (6), 307 (22), 306 (100), 211 (11), 121 (65); exact mass calcd for $C_{26}H_{37}NO_5Si$ (M^+) 471.2438, found 471.2428.

(2*R*,3*S*,4*S*)-3-Acetoxy-*N*-(benzyloxycarbonyl)-2-(4-methoxybenzyl)-4-[(*tert*-butyldimethylsilyl)oxy]pyrrolidine (16). A mixture of **15** (110 mg, 0.233 mmol) and acetic anhydride (71 mg, 0.697 mmol) in pyridine (1.5 g) was stirred at room temperature for 3 days. Concentration in vacuo followed by chromatography on a silica gel column (hexane/ethyl acetate 4:1) gave **16** (115 mg, 96%) as a colorless oil: $[\alpha]^{23}_D$ -10.6° (c 4.53, MeOH); ^{1}H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ -0.02 (6 H, s), 0.80 (9 H, s), 2.08 (3 H, s), ca. 2.83, ca. 3.20 (total 2 H, br s and br d, respectively), 3.33 (1 H, dd, J = 11.3, 4.5 Hz) 3.41 (1 H, br s), 3.77 (3 H, s), 3.90 (1 H, br s), 4.40 (1 H, br s), 4.82 (1 H, br d, J = ca. 13.7 Hz), 5.17 (2 H, br d, J = ca. 8.6 Hz), 6.77 (2 H, br s), 6.90–7.12 (2 H, unresolved), 7.26–7.42 (5 H, m); exact mass calcd for $C_{24}H_{30}NO_6Si$ ($M^+ - C_4H_9$) 456.1841, found 456.1844.

(2*R*,3*S*,4*S*)-3-Acetoxy-*N*-(benzyloxycarbonyl)-4-hydroxy-2-(4-methoxybenzyl)pyrrolidine (17). To a stirred 0 °C solution of **16** (110 mg, 0.214 mmol) in THF (4 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride (0.85 mL, 0.85 mmol). After 30 min, the solvent was evaporated below 30 °C and the residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 1:1) to give **17** (72.8 mg, 85%) as a colorless oil: $[\alpha]^{23}_D$ -3.0° (c 2.63, MeOH); ^{1}H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 2.11 (3 H, s), ca. 2.45, 2.87, 3.16 (total 3 H, each br s), 3.36–3.49 (1 H, m), 3.49–3.60 (1 H, m), 3.77 (3 H, s), 3.92–4.08 (1 H, br s), 4.45 (1 H, dd, J = 11.9, 7.1 Hz), 4.90 (1 H, t, J = 5.9 Hz), 5.14 (2 H, br s), 6.76 (2 H, 1/2 AB q, J = 8.3 Hz), 7.01 (2 H, 1/2 AB q, with broadening, $W_{1/4}$ = 66.1 Hz), 7.24–7.43 (5 H, m); mass spectrum, m/e 399 (3), 279 (6), 278 (36), 234 (10), 174 (35), 121 (24), 91 (100).

(-)-Anisomycin (1). A solution of **17** (23.2 mg, 0.0581 mmol) in ethanol (2 mL) was hydrogenated in the presence of 10% Pd/C (20 mg) at 1 atm for 15 min. The catalyst was removed by filtration and washed with ammoniac methanol. The filtrate was concentrated in vacuo and the residue was purified by chromatography on silica gel n$CHCl_3$/ammoniac MeOH, 10:1) followed by recrystallization from $CHCl_3$/hexane to yield **1** (14.7 mg, 95%) as white needles: mp 144–145 °C (lit.[2] mp 141.6–142.2 °C; lit.[7b] mp 140–141 °C); $[\alpha]^{23}_D$ -30.4° (c 1.32, MeOH) [lit.[2] $[\alpha]^{23}_D$ -30° (c 1, MeOH); lit.[7b] $[\alpha]^{20}_D$ -30° (c 0.15, MeOH); lit.[6b] $[\alpha]^{26}_D$ -26.0° (c 0.38 EtOH)]; ^{1}H NMR (400 MHz) ($CDCl_3$) δ $CHCl_3$ 1.98–2.25 (2 H, br s; containing 3 H, s, at 2.14), 2.69–2.85 (3 H, m), 3.42 (1 H, dd, J = 11.5, 6.6 Hz), 3.50 (1 H, ddd, J = 8.1, 6.3, 4.9 Hz), 3.78 (3 H, s), 4.17 (1 H, ddd, J = 6.6, 5.0, 1.6 Hz), 4.71 (1 H, dd, J = 4.9, 1.6 Hz), 6.83 (2 H, 1/2 AB q, J = 8.6 Hz), 7.10 (2 H, 1/2 AB q, J = 8.6 Hz); ^{13}C NMR (100.6 MHz) ($CDCl_3$) δ $CDCl_3$ 21.14 (q), 34.64 (t), 52.53 (t), 55.35 (q), 61.76 (d), 77.83 (d), 82.43 (d), 114.12 (d), 129.80 (d), 131.10 (s), 158.30 (s), 171.65 (s); IR ($CHCl_3$) 3620–3050 (br), 2930, 2830, 1720, 1605, 1500, 1370, 1240, 1170, 1025; mass spectrum, m/e 266 (1.6), 222 (0.6), 162 (2), 144 (59), 126 (16), 122 (12), 121 (26), 84 (100).

Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.37; H, 7.22; N, 5.26.

Registry No. 1, 22862-76-6; **2**, 100449-52-3; **3**, 99891-36-8; **4**, 99891-37-9; **5**, 99878-63-4; **6**, 100449-53-4; **7a**, 100449-54-5; **7b**, 100569-41-3; **8a**, 100449-55-6; **8b**, 100569-42-4; **9**, 100449-56-7; **10**, 100569-87-7; **11**, 100449-57-8; **12**, 100449-58-9; **13**, 27958-06-1; **14**, 27958-05-0; **15**, 100449-59-0; **16**, 100449-60-3; **17**, 27958-08-3; ii, 100449-61-4; iii, 100569-43-5; iv, 100449-62-5; v, 100449-63-6; vi, 100760-73-4; viii, 100449-64-7; diethyl L-tartrate, 87-91-2; 4-methoxybenzyl chloride, 824-94-2.

(17) No solvent has been reported.