Transformation of D-Erythrose to Some Pseudoaldopentofuranoses. Syntheses of (1*S*,2*R*,3*S*,4*S*)-, (1*R*,2*R*,3*S*,4*S*)-, and (1*R*,2*S*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentanes and (1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-cyclopentanamine[1]

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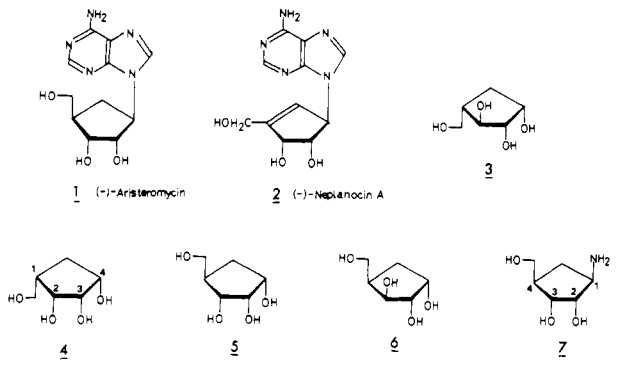
Received July 20, 1987

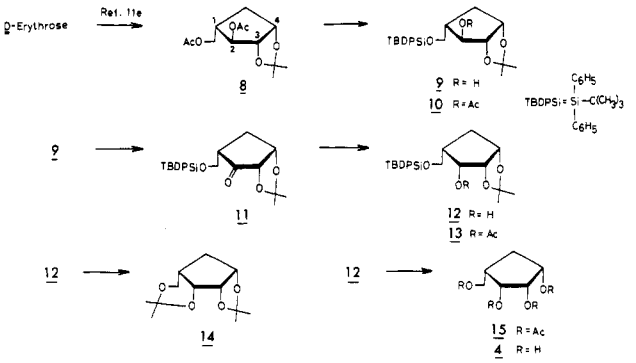
Sodium borohydride reduction of (1*S*,3*S*,4*S*)-1-[((*tert*-butyldiphenylsilyl)oxy)methyl]-3,4-(isopropylidenedioxy)-2-cyclopentanone (**11**), which was prepared from D-erythrose, proceeds exclusively from the β-face to provide 2*R*-hydroxyl derivative **12**. Compound **12** is a derivative of carbocyclic analogue of β-L-lyxofuranose. Silica gel promoted configurational inversion at the branched carbon in **11** followed by sodium borohydride reduction provides 1*R*,2*R* diastereomer **17** and **12** in a 2.8:1 ratio. The former is a protected form of carbocyclic α-D-ribofuranose. Replacement of the mesyloxy group in **23**, which was derived from **17**, by a hydroxyl group in a S_N2 fashion and deprotection of the product followed by acetylation gave a derivative of carbocyclic α-D-xylofuranose **24**. Compound **17** was also converted to compound **7**, a key intermediate for the synthesis of the carbocyclic nucleoside antibiotic (−)-aristeromycin (**1**), via a S_N2 replacement of the mesyloxy group in **26** by an azide group.

(−)-Aristeromycin (**1**) and (−)-neplanocin A (**2**) are representatives of carbocyclic nucleoside antibiotics.[2] In addition to their unique structures, by comparison with natural nucleosides such as adenosine, compounds **1**[3] and **2**[4] exhibit significant pharmacological activities such as antimicrobial (for **1**) and antitumor (for **2**) properties. Total syntheses of **1**[5] and **2**[6] have been achieved recently. Meanwhile, a great deal of efforts have been dedicated to synthesis and pharmacological evaluation of the modified carbocyclic nucleosides and related compounds in recent years.[7] As regards the synthesis of the carbocyclic nucleosides, the synthetic design deals primarily with access to the enatiomerically pure highly oxygenated cyclopentane skeleton.[8] For this purpose, a chemicoenzymatic approach,[5b] an asymmetric Diels–Alder cycloaddition approach,[9] and a strategy by an optical resolution of the intermediate[10] have been devised. In the course of our

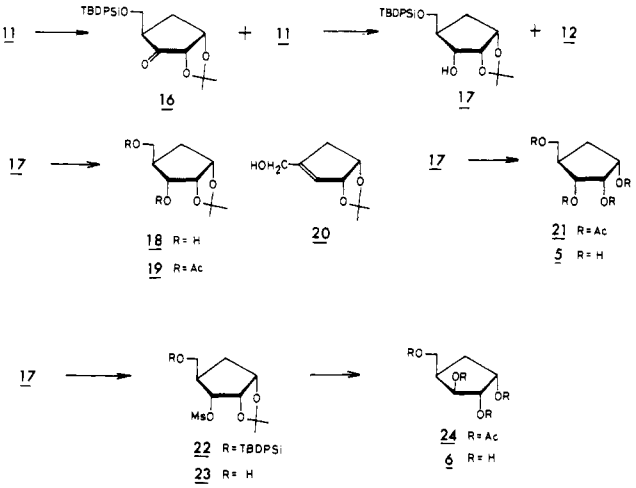


independent synthetic approaches directed toward enantiomerically pure highly oxygenated carbocycles using carbohydrates as starting materials,[11] we have developed interests in the synthesis of carbocyclic analogues of aldopentofuranoses.[12] In the previous papers,[11e] we have described a synthesis of (1*S*,2*S*,3*S*,4*S*)-2,3,4-trihydroxy-1-(hydroxymethyl)cyclopentane (**3**), which is considered as pseudo-β-L-arabinosufranose, from D-erythrose. The synthesis of **3** features (1) the newly developed intramolecular aldol cyclization of a D-erythrose derived intermediate and (2) the highly stereoselective hydroboration for introducing a hydroxyl group into a suitably protected

Scheme I



Scheme II



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(1) A part of the present work has been published in a previous paper: Tadano, K.; Hoshino, M.; Ogawa, S.; Suami, T. *Tetrahedron Lett.* **1987**, *28*, 2741.

(2) Suhadolnik, R. J. *Nucleoside Antibiotics*; Wiley: New York, 1970; pp 236–245 and the references cited therein.

(3) Isolation: Kusaka, T.; Yamamoto, H.; Shibata, M.; Muroi, M.; Kishi, T.; Mizuno, K. *J. Antibiot.* **1968**, *21*, 255. Structure determination including the absolute chemistry: Kishi, T.; Muroi, M.; Kusaka, T.; Nishikawa, M.; Kamiya, K.; Mizuno, K. *Chem. Pharm. Bull.* **1972**, *20*, 940.

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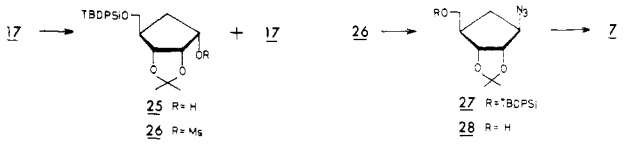
dihydroxylated 1-cyclopentene-1-methanol, providing a derivative of pseudo-β-L-arabinofuranose, **8**. In this article, we wish to report conversion of compound **8** to three pseudoaldopentofuranoses, namely, pseudo-β-L-lyxofuranose (**4**), pseudo-α-D-ribofuranose (**5**), and pseudo-α-D-xylofuranose (**6**), respectively. Furthermore, we have also synthesized a key intermediate, (1*R*,2*S*,3*R*,4*R*)-2,3-dihydroxy-4-(hydroxymethyl)-1-cyclopentanamine (**7**), for (−)-aristeromycin (**1**) synthesis.[13] Compounds **4**–**6** are possible precursors for the synthesis of novel carbocyclic nucleosides.

Results and Discussion

Synthesis of Pseudo-β-L-lyxofuranose (4) (Scheme I). Deacetylation of (1*S*,2*S*,3*S*,4*S*)-2-acetoxy-1-(acetoxymethyl)-3,4-(isopropylidenedioxy)cyclopentane (**8**)[11e] using sodium methoxide followed by preferential protection of the primary hydroxyl group with *tert*-butylchlorodiphenylsilane in the presence of imidazole provided a partially protected compound **9** in 91% yield. For the inversion of configuration at C-2 in **9**, hydride reduction of 2-cyclopentanone **11** was examined. Compound **11** was obtained by pyridinium chlorochromate (PCC)[14] oxidation of **9**. Sodium borohydride reduction of **11** in methanol at 0 °C gave a protected pseudo-β-L-lyxofuranose **12** in 80% yield. The hydride attack proceeds from the β-face of the cyclopentanone ring exclusively without formation of **9**.[15] The configurational inversion at C-2 was verified by the comparison of ^{1}H NMR spectrum of the acetate **13** obtained from **12** with that of the acetate **10** of **9**. Furthermore, the cis relationship of the side chain at C-1 and the hydroxyl group at C-2 in **12** was confirmed by a facile isopropylidenation of the desilylated derivative of **12**, which gave di-*O*-isopropylidene derivative **14** in 80% yield. Thus, the 1*S*,2*R*,3*S*,4*S* configuration was established. Deprotection of **12** by (1) tetrabutylammonium fluoride, (2) hydrolysis with aqueous acetic acid, and then acetylation provided a fully acetylated pseudo-β-L-lyxofuranose (**15**) in 92% yield. Deacetylation of **15** with sodium methoxide in methanol gave **4** in 95% yield.

Scheme III



Syntheses of Pseudo-α-D-ribofuranose (5) and Pseudo-α-D-xylofuranose (6) (Scheme II). We examined next the configurational inversion at the branched carbon (C-1) for preparation of the D-series of pseudoaldopentofuranoses. Toward that end, an epimerization at C-1 of cyclopentanone **11** was investigated under several conditions.[16] We found that silica gel worked efficiently as a promoter for the desired epimerization without occurence of undesirable side reactions such as β-elimination.[17] In fact, by storing a dichloromethane solution of **11** in the presence of silica gel at room temperature for several hours, a mixture of the epimerized compound **16** and the unreacted **11** was obtained. After filtration of the silica gel and concentration of the filtrate, the residue was directly reduced with sodium borohydride. A derivative of pseudo-α-D-ribofuranose **17** was obtained in 58% yield, and the pseudo-β-L-lyxofuranose derivative **12** was obtained in 21% yield. The fact that no other diastereomers were detected in the reaction mixture indicates that the attack of hydride to the carbonyl group in **16** proceeds from the β-face exclusively.[18] The structure of **17** was confirmed

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(5) (a) Total synthesis of **1** in a racemic form: Shealy, Y. F.; Clayton, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 3885; *J. Am. Chem. Soc.* **1969**, *91*, 3075. Saksena, A. K. *Tetrahedron Lett.* **1980**, *21*, 133. (b) Total synthesis of natural (−)-**1**: Arita, M.; Adachi, K.; Ito, Y.; Sawai, H.; Ohno, M. *J. Am. Chem. Soc.* **1983**, *105*, 4049.

(6) (a) Total synthesis of **2** in a racemic form: Jung, M.; Offenbacher, G.; Retey, J. *Helv. Chim. Acta* **1983**, *66*, 1915. (b) Total synthesis of natural (−)-**2**: Lim, M.-I.; Marquez, V. E. *Tetrahedron Lett.* **1983**, *24*, 4051 and 5559. See also ref 5b.

(7) (a) Daluge, S.; Vince, R. *J. Med. Chem.* **1972**, *15*, 171; *J. Med. Chem.* **1974**, *17*, 578; *J. Med. Chem.* **1977**, *20*, 612, 930; *J. Org. Chem.* **1978**, *43*, 2311. Vince, R.; Daluge, S.; Lee, H.; Shannon, W. H.; Arnett, G.; Schafer, T. W.; Nagabhushan, T.; Reichert, P.; Tsai, T. *Science* (Washington, D.C.) **1983**, *221*, 1405. (b) Suami, T.; Nishiyama, S.; Tadano, K.; Lichtenthaler, F. W. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2562. Tadano, K.; Emori, Y.; Ayabe, M.; Suami, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1572; *Bull. Chem. Soc. Jpn.* **1978**, *51*, 855. Tadano, K.; Horiuchi, S.; Suami, T. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 897. (c) Shealy, Y. F.; Clayton, J. D.; O'Dell, C. A. *J. Heterocycl. Chem.* **1973**, *10*, 601. Shealy, Y. F.; Frye, J. L.; Dubois, N. F.; Shaddix, S. C.; Brockman, R. W. *J. Med. Chem.* **1981**, *24*, 1083 and references cited therein. (d) Montgomery, J. A.; Clayton, S. J.; Thomas, H. J.; Shannon, W. M.; Arnett, G.; Bodner, A. J.; Kion, L. K.; Cantoni, G. L.; Chiang, P. K. *J. Med. Chem.* **1982**, *25*, 626. (e) Cookson, R. C.; Dudfield, P. J.; Scopes, D. I. C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 393. (f) Biggadike, K.; Borthwick, A. D.; Exall, A. M.; Kirk, B. E.; Roberts, S. M.; Youds, P.; Slawin, A. M. A.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 255.

(8) For some recent synthetic approaches to enantiomerically pure cyclopentanoids, see the following. From carbohydrates to prostanoids: Ferrier, R. J.; Prasit, P. *Pure Appl. Chem.* **1983**, *55*, 565 and references cited therein. Achab, S.; Das, B. C. *J. Chem. Soc., Chem. Commun.* **1983**, 391. From D-glucose to (−)-pentenomycin: 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. From (−)-quinic acid to (−)-pentenomycin: Elliot, J. D.; Hetmanski, M.; Palfreyman, M. N.; Purcell, N.; Stoodly, R. J. *Tetrahedron Lett.* **1983**, *24*, 965. From (+)-tartaric acid to dihydroxycyclopentanes: Barrière, F.; Barrière, J.-C.; Barton, D. H. R.; Cleophax, J.; Gateau-Olesker, A.; Gêro, S. D.; Tadj, F. *Tetrahedron Lett.* **1985**, *26*, 3119, 3121. Bestmann, H. J.; Moenius, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 994.

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(12) The compounds described in this article are considered to be carbocyclic analogues of carbohydrates, which are frequently designated as "pseudosugars". Throughout this article, compounds are named as derivatives of pseudoaldopentofuranoses for convenience.

(13) Racemic **7** was also synthesized by Shealy and Clayton[5a] and by Cermak and Vince: Cermak, R. C.; Vince, R. *Tetrahedron Lett.* **1981**, *22*, 2331.

(14) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(15) The same preferential attack of nucleophile from the less hindered β-face (exo direction) was observed when 5-deoxy-1,2-*o*-isopropylidene-β-L-*threo*-pentofuranos-3-ulose, a structurally similar compound to **11**, was treated with 2-lithio-1,3-dithiane: Paulsen, H.; Sinnwell, V.; Stadler, P. *Chem. Ber.* **1972**, *105*, 1978.

(16) The following reaction conditions were examined. (1) By treatment of **11** with *p*-toluenesulfonic acid (1.1 molar equiv) in CH_2Cl_2 at 0 °C for 6 h, an approximately 1:1 mixture of **11** and the deisopropylidene derivative was obtained. The structure of the latter was confirmed by isopropylidenation of the mixture, which regenerated **11** as a sole product. (2) By treatment of **11** with 0.1 molar equiv of DBU in benzene at room temperature for 17 h, a mixture of **16** (trace) and presumably the β-elimination products was obtained (^{1}H NMR spectrum of the mixture revealed signals at δ 5.4–5.6 and 6.1–6.3). The mixture was converted to a complex mixture by passage through a silica gel column; therefore, we could not purify each of the products for structure identification.

(17) For reviews on silica gel promoted organic synthesis: McKillop, A.; Young, D. W. *Synthesis*, **1979**, 401. Hojo, M.; Masuda, R. *Yuki Gosei Kagaku Kyokai Shi* **1979**, *37*, 557.

as follows. Compound **17** was converted to **19** by desilylation (tetrabutylammonium fluoride in THF, **17** to **18**) followed by acetylation in 92% yield. The acetate **19** was identical with an authentic sample, which was isolated as a minor product of the hydroboration of **20** after oxidation workup followed by acetylation (the ratio of the products, **8**:**19** was approximately 100:1)[11e] (TLC, mp, and ^{1}H NMR). Hence, pseudo-α-D-ribo form was established for compound **17**. Desilylation of **17** followed by acid hydrolysis and acetylation gave a fully acetylated pseudo-α-D-ribofuranose (**21**) in 91% yield. Deprotection of **21** gave compound **5** in 91% yield.

Pseudo-α-D-xylofuranose (**6**) was synthesized from compound **17** as follows. Sulfonylation of **17** with methanesulfonyl chloride in pyridine gave 2-*O*-mesyl derivative **22** in 96% yield. The silyl group was removed to give compound **23** in 97% yield. Refluxing a solution of **23** in aqueous DMF (H_2O:DMF = 1:10) in the presence of sodium acetate for 21 days and successive cleavage of the isopropylidene group (80% acetic acid) and acetylation provided a fully acetylated pseudo-α-D-xylofuranose (**24**) in 50% yield. The comparison of the ^{1}H NMR spectra of **24** with that of **21** comfirmed the configurational inversion at C-2 of **23**. The attack of water at C-2 of **23** in a S_N2 fashion proceeds quite slowly under these conditions.[19] Deacetylation of **24** using sodium methoxide gave pseudo-α-D-xylofuranose (**6**) in 95% yield.

Synthesis of (1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-cyclopentanamine (7) from Compound 17 (Scheme III). Finally, the synthetic intermediate (**7**) of (−)-aristeromycin (**1**) was synthesized from compound **17**. In order to liberate the hydroxyl group at C-4 in **17** for introduction of a leaving group, the 3,4-isopropylidene group was removed by using acetic acid, then reisopropylidenation was performed under stadard conditions. During the acid hydrolysis, however, partial desilylation occurred. Therefore, after reisopropylidenation, the desilylated products were selectively silylated with *tert*-butylchlorodiphenylsilane. The desired 2,3-isopropylidene derivative **25** was obtained in 25% yield, and compound **17** was recovered in 64% yield. Although compound **25** was a minor product, the recovered **17** can be recycled. Sulfonylation of compound **25** with methanesulfonyl chloride gave 4-*O*-mesyl derivative **26** in 95% yield. Treatment of **26** with sodium azide in hot DMF (120–140 °C) furnished a cyclopentyl azide **27** in a S_N2 fashion in 90% yield. Conversion of compound **27** to compound **7** was carried out as follows. The silyl group was removed to give **28** in 98% yield. Hydrolysis of **28** with 80% aqueous acetic acid followed by hydrogenation in the presence of Raney nickel provided **7** in 94% yield after purification through an Amberlite CG-120 column. The $[\alpha]_D$ value of the synthesized **7** [$[\alpha]^{23}_D$ − 10.7° (*c* 0.44, water)] matched well the reported one [$[\alpha]^{20}_D$ −10.3° (*c* 1.52, water)].[10] In addition, the 400-MHz ^{1}H NMR spectrum of the synthesized **7** is identical with that of the reported data.[10] The conversion of compound **7** to (−)-aristeromycin (**1**) by way of the condensation of **7** with 5-amino-4,6-dichloropyrimidine (three-step sequence) has been reported.[5b] Hence, our synthesis of **7** represents a formal total synthesis of **1**.

(18) The attack of several nucleophiles to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose, a similar bicyclic model to **16**, was examined. In general, the attack of nucleophiles to the carbonyl group at C-3 occurred from the less hindered β-face (exo direction) predominantly. The following examples were reported. (1) Hydride ($NaBH_4$) attack: Sowa, W.; Thomas, G. H. S. *Can. J. Chem.* **1966**, *44*, 836. (2) CH_3^- (CH_3Li or CH_3MgI) attack: Brimacombe, J. S.; Rollins, A. J.; Thompson, S. W. *Carbohydr. Res.* **1973**, *31*, 108. (3) $EtOCOCH_2^-$ ($EtOCOCH_2ZnBr$) attack: Yoshimura, J.; Kobayashi, K.; Sato, K.; Funabashi, M. *Bull. Chem. Soc. Jpn.* 1972, *45*, 1806.

(19) Under the same conditions employed for **23**, compound **22**, remained intact.

Experimental Section

General Procedures. Reactions were carried out at room temperature unless otherwise stated. The reaction mixtures and the combined extracts were concentrated in vacuo by an evaporator at 30–40 °C with a bath. Melting points were determined with a Mitamura Riken micro-melting point apparatus and are uncorrected. Specific rotations were measured by a Jasco DIP-4 polarimeter in a chloroform solution with a 10-mm cell. Column chromatography was performed with silica gel 60 (Katayama Chemicals, K070), and thin-layer chromatography (TLC) with a glass plate coated with Kieselgel 60 GF_{254} (Merck), followed by UV light detection and charring with sulfuric acid. Preparative TLC (PTLC) was performed on a glass plate (20 × 20 cm) coated with Kieselgel PF_{254} (Merck). IR spectra were recorded with a Hitachi 225 spectrometer. ^{1}H NMR spectra were recorded with a Varian EM-390 (90 MHz) or with a JEOL GNM-GX 400 FT NMR (400 MHz) spectrometer for $CDCl_3$ solutions with an internal standard of tetramethylsilane. High-resolution mass spectra were obtained by a Hitahi M-80 spectrometer.

Acetone was distilled over K_2CO_3. Dichloromethane (CH_2Cl_2) and *N*,*N*-dimethylformamide (DMF) were dried over CaH_2 and then distilled. Pyridine was distilled over NaOH. Tetrahydrofuran (THF) was distilled over $LiAlH_4$ and then over Na/benzophenone.

Standard Procedure for Deacetylation. To a stirred solution of the acetylated compound in methanol (4 mmol/20 mL) was added sodium methoxide in methanol (1 M solution, 1.5–3 molar equiv) at 0 °C. After completion of the reaction (TLC), the solution was neutralized with Amberlite IR-120 (H^+). Then the resin was removed by filtration and washed with methanol. The combined filtrate and washings were concentrated. The residue was chromatographed on a silica gel column.

Standard Procedure for Acetylation. Acetylation was performed with acetic anhydride in pyridine. The reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated. The residue was chromatographed on a silica gel column or purified by PTLC.

Standard Procedure for Silylation. To a stirred solution of the hydroxylated compound in DMF (4 mmol/30 mL) were added *tert*-butylchlorodiphenylsilane (1.5–3 molar equiv) and imidazole (3–6 molar equiv). The mixture was stirred and diluted with ethyl acetate after completion of the reaction (TLC). The solution was washed with water, and the aqueous layer was extracted with ethyl acetate. The combined extracts were dried over Na_2SO_4 and concentrated. The residue was chromatographed on a silica gel column.

Standard Procedure for Desilylation. To a stirred solution of the silylated compound in THF (0.5 mmol/6 mL) was added tetrabutylammonium fluoride (1 M in THF, 1.5–2 molar equiv). After completion of the reaction, the solution was concentrated. The residue was chromatographed on a silica gel column.

Standard Procedure for Isopropylidenation. To a stirred solution of the diol derivative in DMF (1 mmol/8 mL) were added 2,2-dimethoxypropane (2–3 molar equiv) and camphorsulfonic acid (0.1–0.3 molar equiv). After completion of the reaction (TLC), the mixture was neutralized with saturated aqueous $NaHCO_3$. To the mixture was added ethanol, and the resulting insoluble solids were removed by filtration through a Celite pad. The filtrate was concentrated, and the residue was chromatographed on a silica gel column.

(1*S*,2*S*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-2-hydroxy-3,4-(isopropylidenedioxy)cyclopentane (9). Compound **8**[11e] (1.17 g, 4.03 mmol) was deacetylated as described in the standard procedure. The reaction mixture was neutralized, and the resin was removed by filtration. After concentration of the filtrate, the residue (TLC R_f 0.37; ethanol–toluene, 1:5) was silylated with *tert*-butylchlorodiphenylsilane (1.61 mL) and imidazole (848 mg). After extractive workup and concentration of the extracts, the residue was chromatographed on silica gel (ethyl acetate–hexane, 1:10) to give **9** (1.67 g, 91%) as a colorless syrup. **9**: TLC R_f 0.20 (ethyl acetate–hexane, 1:4);

$[\alpha]^{26}_D$ +5.8° (*c* 1.00); IR $\nu_{max}^{CHCl_3}$ 3550, 2990, 2940, 2860, 1460, 1430, 1385, 1375, 1250, 1160 cm^{-1}; ^1H NMR δ 1.05 (9 H, s, $OSiC(CH_3)_3$), 1.27, 1.38 (3 H x 2, each s, $C(CH_3)_2$), 1.46–2.33 (3 H, m, H-1,5,5′), 2.40 (1 H, br s, OH), 3.73 (2 H, d, *J* = 6 Hz, CH_2OSi), 4.10 (1 H, dd, *J* = 3 and 6 Hz, H-2), 4.38 (1 H, dd, *J* = 3 and 7 Hz, H-3), 4.50–4.90 (1 H, m, H-4), 7.27–7.83 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.61; H, 8.00.

(1*S*,2*S*,3*S*,4*S*)-2-Acetoxy-1-[((*tert*-butyldiphenylsilyl)oxy)methyl]-3,4-(isopropylidenedioxy)cyclopentane (10). Compound **9** (11.4 mg, 0.03 mmol) was acetylated. After concentration of the reaction mixture, the residue was purified by PTLC (ethyl acetate–hexane, 1:5; $CHCl_3$ elution) to give **10** (12.5 mg, quantitative) as a colorless syrup. **10**: TLC R_f 0.51 (ethyl acetate–hexane, 1:4); $[\alpha]^{25}_D$ –6.2° (*c* 0.52); IR $\nu_{max}^{CHCl_3}$ 3080, 3000, 2940, 1735, 1460, 1430, 1390, 1380, 1245, 1160 cm^{-1}; ^1H NMR δ 1.06 (9 H, s, $OSiC(CH_3)_3$), 1.25, 1.33 (3 H x 2, each s, $C(CH_3)_2$), 1.46–2.40 (3 H, m, H-1,5,5′), 2.03 (3 H, s, $OCOCH_3$), 3.70 (2 H, dd, *J* = 5 and 6 Hz, CH_2OSi), 4.43 (1 H, dd, *J* = 1 and 7 Hz, H-3), 4.57–4.80 (1 H, m, H-4), 5.15 (1 H, dd, *J* = 1 and 3 Hz, H-2), 7.27–7.83 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{27}H_{36}O_5Si$: C, 69.19; H, 7.74. Found: C, 68.90; H, 7.70.

(1*S*,2*R*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-2-hydroxy-3,4-(isopropylidenedioxy)cyclopentane (12). To a stirred solution of **9** (128 mg, 0.30 mmol) in CH_2Cl_2 (7 mL) were added PCC (194.5 mg, 0.90 mmol) and molecular sieves (4A, powder, 50 mg). The mixture was stirred for 4 h and then charged on silica gel (12 g). The column was eluted with ether, and the etheral fraction corresponding to R_f 0.46 (ethyl acetate–hexane, 1:4) was concentrated to give **11**, which was directly reduced. To a solution of **11** in methanol (12 mL) was added sodium borohydride (28.5 mg, 0.75 mmol). The mixture was stirred at 0 °C for 1 h, and 1 M HCl was then added for neutralization. The solution was concentrated, and the residue was partitioned between ethyl acetate (50 mL) and water (50 mL). The aqueous layer was extracted with ethyl acetate (50 mL x 2). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by PTLC (ethyl acetate–hexane, 1:6; $CHCl_3$ elution) to give **12** (102 mg, 80%) as a colorless syrup. **12**: TLC R_f 0.55 (ethyl acetate–hexane, 1:4); $[\alpha]^{27}_D$ +10.6° (*c* 1.08); IR $\nu_{max}^{CHCl_3}$ 3500, 3060, 2990, 2930, 2860, 1460, 1385, 1375, 1300, 1260, 1155, 1105 cm^{-1}; ^1H NMR δ 1.05 (9 H, s, $OSiC(CH_3)_3$), 1.32, 1.43 (3 H x 2, each s, $C(CH_3)_2$), 1.47–2.37 (3 H, m, H-1,5,5′), 2.67 (1 H, br s, OH), 3.67 (1 H, dd, *J* = 6 and 10 Hz, H-2), 3.93–4.30 (2 H, m, CH_2OSi), 4.33–4.70 (2 H, m, H-3,4), 7.25–7.87 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.27; H, 8.01.

(1*S*,2*R*,3*S*,4*S*)-2-Acetoxy-1-[((*tert*-butyldiphenylsilyl)oxy)methyl]-3,4-(isopropylidenedioxy)cyclopentane (13). Compound **12** (17.2 mg, 0.04 mmol) was acetylated with acetic anhydride (0.8 mL) in pyridine (1 mL). The reaction mixture was diluted with ethyl acetate and washed with water. The extracts were dried over Na_2SO_4 and concentrated. The residue was purified by PTLC (ethyl acetate–hexane, 1:5; $CHCl_3$ elution) to give **13** (17.5 mg, 93%) as colorless needles, mp 112–113.5 °C. **13**: TLC R_f 0.40 (ethyl acetate–hexane, 1:4); $[\alpha]^{25}_D$ +34.8° (*c* 0.73); IR $\nu_{max}^{CHCl_3}$ 3070, 3050, 2990, 2860, 1735, 1455, 1430, 1380, 1260, 1240, 1210 cm^{-1}; ^1H NMR δ 1.03 (9 H, s, $OSiC(CH_3)_3$), 1.27, 1.37 (3 H x 2, each s, $C(CH_3)_2$), 1.50–2.20, 2.20–2.57 (2 H, 1 H, each m, H-1,5,5′), 2.00 (3 H, s, $OCOCH_3$), 3.77 (2 H, dd, *J* = 3 and 6 Hz, CH_2OSi), 4.47–4.73 (2 H, m, H-3,4), 5.12 (1 H, t, *J* = 5 Hz, H-2), 7.27–7.77 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{27}H_{36}O_5Si$: C, 69.19; H, 7.74. Found: C, 69.28; H, 7.78.

1,2:3,4-Di-*O*-isopropylidene Derivative 14 of (1*S*,2*R*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane. Compound **12** (27.4 mg, 0.06 mL) was desilylated with tetrabutylammonium fluoride (0.10 mL). After concentration of the mixture, the residue was chromatographed on silica gel (2 g, ethanol–toluene, 1:10). The fraction corresponding to R_f 0.47 (ethanol–toluene, 1:5) was concentrated to give the desilylated product. Isopropylidenation of this product in DMF (1.5 mL) with 2,2-dimethoxypropane (0.02 mL) in the presence of camphorsulfonic acid (2.2 mg) gave **14** (11.7 mg, 80%), after chromatography on a silica gel column (ethyl acetate–hexane, 1:6), as colorless crystals, mp 61–63 °C. **14**: TLC R_f 0.38 (ethyl acetate–hexane, 1:2); $[\alpha]^{27}_D$ +36.4° (*c* 0.45); IR ν_{max}^{KBr} 2980, 2920, 1380, 1270, 1260, 1225, 1210, 1195 cm^{-1}; ^1H NMR δ 1.33, 1.47, 1.56 (3 H, 6 H, 3 H, each s, 2 x $C(CH_3)_2$), 1.67–2.47 (3 H, m, H-1,5,5′), 3.63 (1 H, d, *J* = 12 Hz, H-4), 4.02–4.39 (2 H, m, $CH_2OC(CH_3)_2$), 4.42–4.83 (2 H, m, H-2,3); high-resolution mass spectrum, calcd for $C_{12}H_{20}O_4$ *m/z* 228.1360, M, found, 228.1344.

(1*S*,2*R*,3*S*,4*S*)-2,3,4-Triacetoxy-1-(acetoxymethyl)cyclopentane (15). Compound **12** (66.3 mg, 0.16 mmol) was desilylated as the preparation of **14**. A solution of the desilylated product in 80% aqueous acetic acid (4 mL) was heated at 60 °C for 2 h and then concentrated to give the deprotected product (TLC R_f 0.46; chloroform–methanol, 1:2). The residue was acetylated with acetic anhydride (2 mL) in pyridine (2 mL). After chromatography on a silica gel column (ethyl acetate–hexane, 1:5), compound **15** (45.3 mg, 92%) was obtained as colorless crystals, mp 103.5–104.5 °C. **15**: TLC R_f 0.38 (ethyl acetate–hexane, 2:3); $[\alpha]^{26}_D$ +11.8° (*c* 0.95); IR ν_{max}^{KBr} 3000, 2960, 1730, 1460, 1430, 1370, 1290, 1240, 1220, 1150, 1135 cm^{-1}; ^1H NMR δ 1.63–2.67 (3 H, m, H-1,5,5′), 2.03, 2.05, 2.08 (3 H, 6 H, 3 H, each s, 4 x $OCOCH_3$), 4.12 (1 H, d, *J* = 2 Hz, CH_2OAc), 4.20 (1 H, d, *J* = 3.5 Hz, CH_2OAc), 5.10–5.50 (3 H, m, H-2,3,4). Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.11; H, 6.37. Found: C, 53.41; H, 6.28.

(1*S*,2*R*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane, Pseudo-β-L-lyxofuranose (4). Compound **15** (38.3 mg, 0.12 mmol) was deacetylated with sodium methoxide (0.36 mL). After chromatographic purification on a silica gel (chloroform–methanol, 5:1), compound **4** (17.1 mg, 95%) was obtained as a colorless syrup. **4**: TLC R_f 0.46 (chloroform–methanol, 1:2); $[\alpha]^{24}_D$ +11.3° (*c* 0.84, methanol); ^1H NMR (CD_3OD) δ 1.27–1.83, 1.83–2.33 (1 H, 2 H, each m, H-1,5,5′), 3.47–4.40 (5 H, m, H-2,3,4, CH_2OH); high-resolution mass spectrum, calcd for $C_6H_{12}O_4$ *m/z* 148.0735, found, M, 148.0736.

(1*R*,2*R*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-2-hydroxy-3,4-(isopropylidenedioxy)cyclopentane (17). Compound **9** (476.8 mg, 1.12 mmol) was oxidized with PCC (722.8 mg) in the presence of molecular seives (200 mg) to give **11** (453 mg) after purification through a silica gel column (ether elution). To a solution of **11** in CH_2Cl_2 (7 mL) was added silica gel (8 g),[20] and the mixture was stored for 2.5 h. Then CH_2Cl_2 (10 mL) was added, and the silica gel was removed by filtration and washed with CH_2Cl_2. The combined filtrate and washings were concentrated to give a mixture of (1*R*,3*S*,4*S*)-1-[((*tert*-butyldiphenylsilyl)oxy)methyl]-3,4-(isopropylidenedioxy)-2-cyclopentanone (**16**) (TLC R_f 0.66; ethyl acetate–hexane, 1:4) and **11**. To a stirred solution of the mixture of **16** and **11** in methanol (14 mL) was added sodium borohydride (105.9 mg, 2.08 mmol). The mixture was stirred at 0 °C for 1 h, 1 M HCl was then added for neutralization, and the solution was concentrated. The residue was partitoned between ethyl acetate (80 mL) and water (80 mL). The aqueous layer was extracted with ethyl acetate (80 mL). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by repeated chromatography on a silica gel column (ethyl acetate–hexane, 1:40). Compound **17** (274.2 mg, 58%) was obtained from the fraction corresponding to R_f 0.51 (ethyl acetate–hexane, 1:4), and compound **12** (97.8 mg, 21%) was obtained from the fraction corresponding to R_f 0.55. **17**: colorless syrup: $[\alpha]^{26}_D$ +23.9° (*c* 1.01); IR $\nu_{max}^{CHCl_3}$ 3550, 2990, 2860, 1460, 1425, 1380, 1375, 1260, 1155, 1110 cm^{-1}; ^1H NMR δ 1.06 (9 H, s, $OSiC(CH_3)_3$), 1.32, 1.45 (3 H x 2, each s, $C(CH_3)_2$), 1.53–2.17 (3 H, m, H-1,5,5′), 2.17–2.40 (1 H, m, OH), 3.57–3.93 (1 H, m, H-2), 3.82 (2 H, d, *J* = 5 Hz, CH_2OSi), 4.37–4.68 (2 H, m, H-3,4), 7.30–7.90 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.45; H, 8.05.

Compound 17 from Compound 12. PCC oxidation of **12** (199.2 mg, 0.47 mmol), epimerization by means of silica gel, and successive sodium borohydride reduction as described above, resulted in the formation of **17** (108.9 mg, 55%) and a recovery of **12** (40.4 mg, 20%).

(1*R*,2*R*,3*S*,4*S*)-2-Acetoxy-1-(acetoxymethyl)-3,4-(isopropylidenedioxy)cyclopentane (19). Compound **17** (26.4 mg, 0.06 mmol) was desilylated with tetrabutylammonium fluoride (0.09 mL) to give **18** (12 mg; TLC R_f 0.45; ethanol–toluene, 1:5)

(20) We used silica gel purchased from Katayama Chemicals. For this epimerization, TLC-Kieselgel 60 GF_{254} (Merck) also worked effectively, and the same result as in the case of Katayama Chemicals' silica gel was obtained.

after a silica gel chromatography (ethanol–toluene, 1:10). Compound **18** was acetylated with acetic anhydride (1 mL) in pyridine (1 mL). Compound **19** (15.5 mg, 92%; TLC R_f 0.63; ethyl acetate–hexane, 2:3), which was identical with an authentic sample[11e] in respect of TLC behavior, mp, and ^{1}H NMR, was obtained after a silica gel chromatographic purification (ethyl acetate–hexane, 1:6).

(1*R*,2*R*,3*S*,4*S*)-2,3,4-Triacetoxy-1-(acetoxymethyl)cyclopentane (21). Compound **17** (58.6 mg, 0.14 mmol) was desilylated as described in the preparation of **19**. A solution of **18** in 80% aqueous acetic acid (4 mL) was heated at 60 °C for 4 h and concentrated. The residue was acetylated with acetic anhydride (2 mL) in pyridine (2 mL). Compound **21** (39.5 mg, 91%) was obtained after a silica gel chromatography (ethyl acetate–hexane, 1:4). **21**: colorless syrup: TLC R_f 0.41 (ethyl acetate–hexane, 2:3); $[\alpha]^{26}_D$ +38.5° (*c* 1.05); IR $\nu_{max}^{CHCl_3}$ 3020, 2950, 2890, 1730, 1440, 1365, 1235, 1215 cm^{-1}; ^{1}H NMR δ 1.70–2.33, 2.33–2.83 (2 H, 1 H, each m, H-1,5,5′), 2.04, 2.05, 2.07 (6 H, 3 H, 3 H, each s, 4 x OCOCH$_3$), 4.10 (2 H, d, J = 5.5 Hz, CH_2OAc), 4.95–5.43 (3 H, m, H-2,3,4). Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.11, H, 6.37. Found: C, 53.34; H, 6.41.

(1*R*,2*R*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane, Pseudo-α-D-ribofuranose (5). Compound **21** (43.5 mg, 0.14 mmol) was deacetylated with sodium methoxide (0.41 mL). After a silica gel chromatographic purification (chloroform–methanol, 1:5), compound **5** (18.5 mg, 91%) was obtained as a colorless syrup. **5**: TLC R_f 0.56 (chloroform–methanol, 1:2); $[\alpha]^{24}_D$ +33.0° (*c* 0.80, methanol); ^{1}H NMR (CD$_3$OD) δ 1.43–2.43 (3 H, m, H-1,5,5′), 3.57 (2 H, d, J = 6 Hz, CH_2OH), 3.66–4.30 (3 H, m, H-2,3,4); high-resolution mass spectrum, calcd for $C_6H_{13}O_4$ m/z 149.0812, found, M + H, 149.0786.

(1*R*,2*R*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-3,4-(isopropylidenedioxy)-2-[(methylsulfonyl)oxy]cyclopentane (22). To a stirred solution of **17** (246.0 mg, 0.58 mmol) in pyridine (8 mL) was added methanesulfonyl chloride (0.09 mL, 1.15 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C, and then diluted with ethyl acetate (100 mL). The solution was washed with water (50 mL x 2), saturated aqueous NaHCO$_3$ (50 mL), saturated brine (50 mL), and water (50 mL) successively. The organic layer was dried over Na$_2$SO$_4$ and concentrated. The residue was chromatographed on a silica gel column (ethyl acetate–hexane, 1:15), and the fraction corresponding to R_f 0.33 (ethyl acetate–hexane, 1:3) was concentrated to give **22** (264 mg, 96%) as a colorless syrup. **22**: $[\alpha]^{21}_D$ +45.7° (*c* 1.06); IR $\nu_{max}^{CHCl_3}$ 2990, 2930, 2860, 1460, 1425, 1385, 1360, 1260, 1170, 1105 cm^{-1}; ^{1}H NMR δ 1.07 (9 H, s, OSiC(CH$_3$)$_3$), 1.32, 1.45 (3 H x 2, each s, C(CH$_3$)$_2$), 1.60–2.57 (3 H, m, H-1,5,5′), 3.03 (3 H, s, OSO$_2$CH$_3$), 3.80–3.89 (2 H, m, CH_2OMs), 4.57–4.83 (3 H, m, H-2,3,4), 7.28–7.80 (10 H, m, OSi(C$_6$H$_5$)$_2$). Anal. Calcd for $C_{26}H_{36}O_6SSi$: C, 61.87; H, 7.19. Found: C, 61.75; H, 7.11.

(1*R*,2*R*,3*S*,4*S*)-1-(Hydroxymethyl)-3,4-(isopropylidenedioxy)-2-[(methylsulfonyl)oxy]cyclopentane (23). Desilylation of **22** (264 mg, 0.52 mmol) with tetrabutylammonium fluoride (0.79 mL) and purification on a silica gel column (ethyl acetate–hexane, 1:2) gave **23** (136 mg, 97%) as colorless needles, mp 80–81 °C. **23**: TLC R_f 0.40 (ethanol–toluene, 1:5); $[\alpha]^{19}_D$ +87.8° (*c* 1.02); IR ν_{max}^{KBr} 3580, 3010, 2990, 2890, 1380, 1370, 1345, 1295, 1270, 1205, 1185, 1175, 1165 cm^{-1}; ^{1}H NMR δ 1.32, 1.46 (3 H x 2, each s, C(CH$_3$)$_2$), 1.50–2.10, 2.10–2.66 (2 H, 2 H, each m, H-1,5,5′, OH), 3.12 (3 H, s, OSO$_2$CH$_3$), 3.75 (2 H, t, J = 2.5 Hz, CH_2OH), 4.47–4.73 (3 H, m, H-2,3,4). Anal. Calcd for $C_{10}H_{18}O_6S$: C, 45.10; H, 6.81. Found: C, 45.36; H, 6.71.

(1*R*,2*S*,3*S*,4*S*)-2,3,4-Triacetoxy-1-(acetoxymethyl)cyclopentane (24). A solution of **23** (86.6 mg, 0.33 mmol) in a mixture of DMF (7 mL) and water (0.7 mL) containing sodium acetate (80 mg, 0.98 mmol) was refluxed for 14 days, while sodium acetate was added after 7 (80 mg), 9 (160 mg) and 11 days (160 mg). The mixture was concentrated, and the residue was dissolved in water (15 mL). This aqueous solution was extracted with ethyl acetate (30 mL x 5). The combined extracts were dried over Na$_2$SO$_4$ and concentrated. The residue was dissolved in a mixture of DMF (5 mL) and water (0.5 mL), and the solution was refluxed in the presence of sodium acetate (240 mg) for 7 days and concentrated. The residue was dissolved in water (15 mL), and the aqueous solution was extracted with ethyl acetate (30 mL x 5). The combined extracts were dried over Na$_2$SO$_4$ and concentrated. The residue was dissolved in 80% aqueous acetic acid (4 mL), and the solution was heated at 60 °C for 6 h. The solution was then concentrated, and the residue was acetylated with acetic anhydride (2 mL) in pyridine (2 mL) for 2 h. The mixture was concentrated, and the residue was chromatographed on a silica gel column (ethyl acetate–hexane, 1:4). The fraction corresponding to R_f 0.46 (ethyl acetate–hexane, 2:3) was concentrated to give **24** (51.0 mg, 50%) as a colorless syrup. **24**: $[\alpha]^{21}_D$ +24.7° (*c* 1.02); IR $\nu_{max}^{CHCl_3}$ 3020, 2950, 1735, 1430, 1370, 1230, 1175 cm^{-1}; ^{1}H NMR δ 1.76–2.30, 2.52–3.02 (2 H, 1 H, each m, H-1,5,5′), 2.06 (12 H, s, 4 x OCOCH$_3$), 4.04 (2 H, dd, J = 2.5 and 3.5 Hz, CH_2OAc), 5.10–5.33 (3 H, m, H-2,3,4); high-resolution mass spectrum, calcd for $C_{14}H_{20}O_8$ m/z 316.1156 found, M, 316.1116.

(1*R*,2*S*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane, Pseudo-α-D-xylofuranose (6). Compound **24** (35.6 mg, 0.12 mmol) was deacetylated with sodium methoxide (0.34 mL). After chromatographic purification on a silica gel column (chloroform–methanol, 1:6), compound **6** (15.8 mg, 95%) was obtained as colorless crystals, mp 79.5–80.5 °C. **6**: TLC R_f 0.47 (chloroform–methanol, 1:4); $[\alpha]^{22}_D$ +13.4° (*c* 0.78, methanol); ^{1}H NMR (CD$_3$OD) δ 1.60–1.87, 2.17–2.60 (2 H, 1 H, each m, H-1,5,5′), 3.63 (2 H, dd, J = 2 and 7 Hz, CH_2OH), 3.67–4.27 (3 H, m, H-2,3,4). Anal. Calcd for $C_6H_{12}O_4$: C, 48.64; H, 8.17. Found: C, 48.69; H, 7.90.

(1*R*,2*R*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-4-hydroxy-2,3-(isopropylidenedioxy)cyclopentane (25). A solution of **17** (418 mg, 0.98 mmol) in a mixture of acetic acid–water–methanol (20:4:1, v/v; 15 mL) was stirred for 87 h and concentrated to give the deisopropylidene derivative (TLC R_f 0.36; ethanol–toluene, 1:5). The residue was isopropylidenated with 2,2-dimethoxypropane (0.36 mL) in the presence of camphorsulfonic acid (11 mg) for 3 h. After purification using a silica gel column chromatography (ethyl acetate–hexane, 1:35 to 1:2) and PTLC (ethyl acetate–hexane, 1:8; CHCl$_3$ elution), **17** (246 mg, 59%) and **25** (92 mg, 22%; TLC R_f 0.46, ethyl acetate–hexane, 1:4) were obtained. Additionally, the desilylated mixture was obtained from the fraction corresponding to R_f 0.34 (ethanol–toluene, 1:5). The mixture (28 mg) was silylated with *tert*-butylchlorodiphenylsilane (0.08 mL) and imidazole (44 mg), and **17** (23 mg, total 269 mg, 64%) and **25** (13.5 mg, total 105 mg, 25%) were obtained after a silica gel column chromatography. **25**: colorless syrup: $[\alpha]^{22}_D$ −16.8° (*c* 1.13); IR $\nu_{max}^{CHCl_3}$ 3540, 3070, 2990, 2860, 1455, 1435, 1380, 1375, 1270, 1160, 1110 cm^{-1}; ^{1}H NMR δ 1.07 (9 H, s, OSiC(CH$_3$)$_3$), 1.33, 1.48 (3 H x 2, each s, C(CH$_3$)$_2$), 1.60–2.00, 2.00–2.47 (2 H, 2 H, each m, H-1,5,5′,OH), 3.55 (2 H, dd, J = 2.5 and 5.5 Hz, CH$_2$OSi), 4.00–4.57 (3 H, H-2,3,4), 7.20–7.73 (10 H, m, OSi(C$_6$H$_5$)$_2$). Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.30; H, 8.00.

(1*R*,2*R*,3*S*,4*S*)-1-[((*tert*-Butyldiphenylsilyl)oxy)methyl]-2,3-(isopropylidenedioxy)-4-[(methylsulfonyl)oxy]cyclopentane (26). To a solution of **25** (102 mg, 0.24 mmol) in pyridine (5 mL) was added methanesulfonyl chloride (0.04 mL, 0.48 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h and then diluted with ethyl acetate (50 mL). The solution was washed with water (25 mL x 2), saturated aqueous NaHCO$_3$ (25 mL), saturated brine (25 mL), and water (25 mL) successively. The organic layer was dried over Na$_2$SO$_4$ and concentrated. The residue was purified by PTLC (ethyl acetate–hexane, 1:3) to give **26** (113.5 mg, 95%) as a colorless syrup. **26**: TLC R_f 0.44 (ethyl acetate–hexane, 1:3); $[\alpha]^{21}_D$ −22.6° (*c* 1.01); IR $\nu_{max}^{CHCl_3}$ 2990, 2930, 1450, 1425, 1380, 1355, 1260, 1170, 1110 cm^{-1}; ^{1}H NMR δ 1.08 (9 H, s OSiC(CH$_3$)$_3$), 1.31, 1.47 (3 H x 2, each s, C(CH$_3$)$_2$), 1.68–2.40 (3 H, m, H-1,5,5′), 3.02 (3 H, s, OSO$_2$CH$_3$), 3.43–3.67 (2 H, m, CH$_2$OSi), 4.46 (1 H, d, J = 5 Hz, H-2), 4.62 (1 H, t, J = 5 Hz, H-3), 5.13 (1 H, ddd, J = 3, 5, and 9 Hz, H-4), 7.21–7.77 (10 H, m, OSi(C$_6$H$_5$)$_2$). Anal. Calcd for $C_{26}H_{36}O_6SSi$: C, 61.87; H, 7.19. Found: C, 61.93; H, 7.24.

(1*R*,2*R*,3*S*,4*R*)-4-Azido-1-[((*tert*-butyldiphenylsilyl)oxy)methyl]-2,3-(isopropylidenedioxy)cyclopentane (27). A solution of **26** (102 mg, 0.20 mmol) in DMF (4 mL) in the presence of sodium azide (66 mg, 1.01 mmol) was heated at 120 °C for 2 h and then at 130 °C for 3 h with stirring. Then, sodium azide (78 mg) was added, and the mixture was heated at 140 °C for 4 h. The mixture was diluted with ethyl acetate (50 mL) and washed with water (25 mL x 2), ssaturated brine (25 mL × 2), and water (25 mL) successively. The organic layer was dried over Na$_2$SO$_4$

and concentrated. The residue was purified by PTLC (ethyl acetate–hexane, 1:10; $CHCl_3$ elution) to give **27** (82 mg, 90%) as a colorless syrup. **27**: TLC R_f 0.53 (ethyl acetate–hexane, 1:10); $[\alpha]^{21}_D$ -31.9° (*c* 1.19); IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 2860, 2100, 1460, 1430, 1380, 1260, 1170, 1160, 1110 cm^{-1}; ^1H NMR δ 1.07 (9 H, s, $OSiC(CH_3)_3$), 1.23, 1.43 (3 H × 2, each s, $C(CH_3)_2$), 1.53–2.57 (3 H, m, H-1,5,5'), 3.63 (2 H, d, J = 7 Hz, CH_2OSi), 3.95 (1 H, dt, J = 3 and 8 Hz, H-4), 4.28 (1 H, dd, J = 3 and 7 Hz, H-3), 4.45 (1 H, dd, J = 2 and 7 Hz, H-2), 7.20–7.80 (10 H, m, $OSi(C_6H_5)_2$). Anal. Calcd for $C_{25}H_{33}N_3O_3Si$: C, 66.48; H, 7.36; N, 9.30. Found: C, 66.38; H, 7.47; N, 9.03.

(1*R*,2*R*,3*S*,4*R*)-4-Azido-1-(hydroxymethyl)-2,3-(isopropylidenedioxy)cyclopentane (28). Compound **27** (80 mg, 0.18 mmol) was desilylated with tetrabutylammonium fluoride (0.27 mL), and compound **28** (37 mg, 98%) was obtained after a silica gel column chromatography (ethyl acetate–hexane, 1:6). **28** as a colorless syrup: TLC R_f 0.53 (ethyl acetate–hexane, 1:1); $[\alpha]^{19}_D$ -35.2° (*c* 1.05); IR $\nu_{max}^{CHCl_3}$ 3610, 3470, 2990, 2930, 2880, 2100, 1450, 1435, 1385, 1310, 1255, 1200, 1160 cm^{-1}; ^1H NMR δ 1.30, 1.45 (3 H × 2, each s, $C(CH_3)_2$), 1.50–1.83, 2.00–2.50 (1 H, 3 H, each m, H-1,5,5', OH), 3.63 (2 H, d, J = 6 Hz, CH_2OH), 3.97 (1 H, dt, J = 2 and 6 Hz, H-4), 4.43 (1 H, dd, J = 2 and 6 Hz, H-2 or -3), 4.58 (1 H, dd, J = 2 and 6 Hz, H-3 or -2). Anal. Calcd for $C_9H_{15}N_3O_3$: C, 50.69; H, 7.09; N, 19.71. Found: C, 51.01; H, 6.91; N, 19.69.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-cyclopentanamine (7). A solution of **28** (13.4 mg, 0.06 mmol) in 80% aqueous acetic acid (3 mL) was heated at 60 °C for 2 h and concentrated. The residue was dissolved in methanol (3 mL), and the solution was hydrogenated in the presence of Raney nickel T-4 under atmospheric hydrogen pressure for 30 min. The catalyst was passed through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated. The residue was charged on a coloumn of Amberlite CG-120 (H^+) (5 mL), and the column was eluted with 0.07 M aqueous ammonia. The ninhydrin positive fraction was concentrated to give **7** (8.7 mg, 94%) as a colorless syrup. **7**: TLC R_f 0.63 (methanol–water, 1:2); $[\alpha]^{23}_D$ -10.7° (*c* 0.44, water); ^1H NMR (400 MHz, CD_3OD) δ 1.07 (1 H, dt, $J_{1,5}$ = $J_{4,5}$ = 8.8 Hz, $J_{5,5'}$ = 12.7 Hz, H-5), 2.00–2.10 (1 H, m, H-4), 2.14 (1 H, ddd, $J_{1,5'}$ = 8.8 Hz, $J_{4,5'}$ = 7.3 Hz, $J_{5,5'}$ = 12.7 Hz, H-5'), 3.15 (1 H, dt, $J_{1,2}$ = 7.3 Hz, $J_{1,5}$ = $J_{1,5'}$ = 8.8 Hz, H-1), 3.51 (1 H, dd, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 5.4 Hz, H-2), 3.54 (2 H, dd, J = 1.5 and 5.9 Hz, CH_2OH), 3.83 (1 H, dd, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 4.4 Hz, H-3); ^{13}C NMR (CD_3OD) δ 31.86 (C-5), 46.74 (C-4), 56.79 (C-1), 64.59 (CH_2OH), 74.15 (C-3), 79.56 (C-2); high-resolution mass spectrum, calcd for $C_6H_{13}NO_3$ m/z 147.0894, found, M, 147.0886.

Acknowledgment. We thank to Mr. Akio Takahashi (Keio University) for performing elemental analyses.

An Approach to Pseudomonic Acids from D-Xylose[1]

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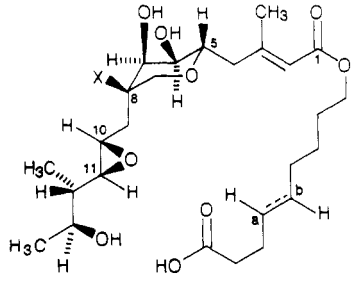
Received July 16, 1987

The four contiguous chiral centers present in pseudomonic acid C are constructed in an efficient way from D-xylose. The key steps involve a highly selective intermolecular radical reaction between benzyl 4-bromo-4-deoxy-2,3-di-*O*-benzoyl-β-L-lyxopyranoside (**9**) and phenyl vinyl sulfone for incorporating the lower appendage and a stereoselective intramolecular Michael addition to achieve the correct stereochemistry at the anomeric site.

Pseudomonic acids A (**1a**), B (**1b**), C (**1c**), and D (**1d**) are members of a small group of metabolites with antimicrobial and antimycoplasmal activity, produced by submerged fermentations of a strain of *Pseudomonas flourescens* NCIB 10586.[2] The detailed studies of structural and chemical characterizations of the major component pseudomonic acid A and the lesser components B, C, and D have been reported in a series of papers.[3] The pseudomonic acids display no cross resistance with other antibiotics due to their novel mechanism of action, namely, interference with bacterial protein synthesis by inhibition of isoleucyl-tRNA sythetase. The therapeutic value of these antibiotics has been clinically developed in the Beecham laboratories.[4]

In recent years, different strategies for the total synthesis of pseudomonic acid C and numerous approaches have been reported.[5] Herein, we detail our approach to (+)-pseudomonic acid C from D-xylose, the least expensive among all pentoses.



pseudomonic acids A–D

1a: X = H; C_a–C_b = C_2H_4
1b: X = OH; C_a–C_b = C_2H_4
1c: X = H; C_{10}–C_{11} no epoxide, double bond; C_a–C_b = C_2H_4
1d: X = H; C_a–C_b = (*E*)-CH=CH

A retrosynthetic analysis for the synthesis of pseudomonic acid C was arrived at as shown in Scheme I. It indicates that the most convenient locations for bond disconnections are at the two olefinic linkages leading to

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