A Novel Transformation of Four Aldoses to Some Optically Pure Pseudohexopyranoses and a Pseudopentofuranose, Carbocyclic Analogues of Hexopyranoses and Pentofuranose. Synthesis of Derivatives of (1*S*,2*S*,3*R*,4*S*,5*S*)-, (1*S*,2*S*,3*R*,4*R*,5*S*)-, (1*R*,2*R*,3*R*,4*R*,5*S*)-, (1*S*,2*S*,3*R*,4*S*,5*R*)-2,3,4,5-Tetrahydroxy-1-(hydroxymethyl)cyclohexanes and (1*S*,2*S*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane

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Knoevenagel reactions with dimethyl malonate of the suitably protected acylic aldehydes **6**, **20**, **34**, and **46**, which were prepared from D-ribose, D-xylose, D-arabinose, and D-erythrose, respectively, proceeded smoothly to provide α,β-unsaturated diesters **7**, **21**, **35**, and **47** in acceptable yields. Hydrogenation or sodium borohydride reduction of **7**, **21**, **35**, and **47** and successive desilylation afforded methyl 4,5,6-tris(benzyloxy)-7-hydroxy-2-(methoxycarbonyl)heptanoates **9**, **23**, and **37** and methyl (4*S*,5*R*)-6-hydroxy-4,5-(isopropylidenedioxy)-2-(methoxycarbonyl)hexanoate (**49**). Treatment of **9**, **23**, **37**, and **49** with pyridinium chlorochromate furnished suitably protected 2,3,4,5-tetrahydroxycyclohexane-1,1-dicarboxylates **10**, **24** + **24'**, **38** + **38'**, and **51** + **51'** after acetylation of the cyclized products. By thermal demethoxycarbonylation accompanied by β-elimination of the acetyl groups and successive reduction by hydrides, the compounds **10**, **24** + **24'**, **38**, and **51** + **51'** were converted to compounds **12**, **26**, **40**, and **53**. Hydroboration of these 1-cyclohexene-1-methanols and 1-cyclopentene-1-methanol proceeded stereoselectively and after oxidative workup with hydrogen peroxide followed by acetylation, the four fully protected pseudohexopyranoses **13**, **27**, **27'**, and **41** and the fully protected pseudopentofuranose **54** were obtained. Debenzylation of **13**, **27**, **27'**, and **41** followed by acetylation gave rise to (1*S*,2*S*,3*R*,4*S*,5*S*)-, (1*S*,2*S*,3*R*,4*R*,5*S*)-, (1*R*,2*R*,3*R*,4*R*,5*S*)-, and (1*S*,2*S*,3*R*,4*S*,5*R*)-2,3,4,5-tetraacetoxy-1-(acetoxymethyl)cyclohexanes (**14**, **28**, **28'**, and **42**, respectively). Those are pentaacetates of pseudo-β-L-mannopyranose, pseudo-β-L-glucopyranose, pseudo-α-D-altropyranose, and pseudo-α-L-mannopyranose, respectively. Deprotection of **54** afforded pseudo-β-L-arabinofuranose, (1*S*,2*S*,3*S*,4*S*)-2,3,4-trihydroxy-1-(hydroxymethyl)cyclopentane (**56**).

2,3,4,5-Tetrahydroxy-1-(hydroxymethyl)cyclohexanes, designated as "pseudo-sugars", are carbocyclic analogues of carbohydrates. The ring oxygen atom in cyclic forms of carbohydrates is replaced by a methylene group to give pseudo sugars. This structural difference makes it of interest to compare the physiological effects of pseudo-sugars with those of "true sugars".[1] On the other hand, pseudo-sugars and related carbocyclic compounds are known to be components of some antibiotics (validamycins) and enzyme inhibitors (adiposins etc.).[2] New approaches to synthesis of pseudo-sugars and related compounds have been explored extensively by Ogawa and Suami recently.[2] Their synthesis of a number of pseudo-sugars which includes the total synthesis of validamycin A[3] commenced with 7-*endo*-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid, a Diels–Alder adduct of furan and acrylic acid. As the Diels–Alder adduct has been efficiently resolved recently,[4] a synthetic route to optically active pseudo-sugars is now available. Alternatively, Paulsen and Heiker reported the synthesis of optically active valienamine, a component of the validamycins family antibiotics, from quebrachitol (2-*O*-methyl-L-chiroinositol).[5] Paulsen and co-workers also synthesized (1*R*,2*S*,3*S*,4*S*,5*S*)- and (1*R*,2*R*,3*S*,4*R*,5*R*)-2,3,4,5-tetrahydroxy-1-(hydroxymethyl)cyclohexanes, namely, pseudo-α-D-galactopyranose and pseudo-β-D-mannopyranose, from the same starting material.[6] In connection with prostaglandin syntheses which utilize carbohydrates as chiral starting materials,[7] Ferrier and co-workers have studied the preparation of optically pure cyclopentanoids and cyclohexanoids; as a means to this end, they utilized the mercury(II) salt promoted intramolecular cyclization of 5,6-unsaturated hexopyranoses to optically pure polyhydroxylated cyclohexanones from which pseudo-sugars are eventually available.[8] Very recently, Wilcox and co-workers demonstrated an approach to optically pure carbocycles synthesis which featured "radical cyclization" of unsaturated halo sugars;[9] by extension of this strategy they realized the synthesis of pseudo-D-fructofuranose (a carboxyclic analogue of D-fructofuranose) and pseudo-D-fructofuranose 6-phosphate.[10]

In our independent efforts on the synthesis of optically pure carbocyclic compounds and pseudo-sugars employing carbohydrates as starting materials,[11] we describe herein a new transformation of carbohydrate-derived interme-

(1) Suami, T.; Ogawa, S.; Toyokuni, T. *Chem. Lett.* **1983**, 611. Suami, T.; Ogawa, S.; Takata, M.; Yasuda, K.; Suga, A.; Takei, K.; Uematsu, Y. *Chem. Lett.* **1985**, 719. Miwa, I.; Hara, H.; Okuda, J.; Suami, T.; Ogawa, S. *Biochem. Int.* **1985**, *11*, 809.

(2) Review in regard to the chemistry of the pseudo-sugars: Ogawa, S. *J. Synth. Org. Chem. Jpn.* **1985**, *43*, 26.

(3) Ogawa, S.; Ogawa, T.; Nose, T.; Toyokuni, T.; Iwasawa, Y.; Suami, T. *Chem. Lett.* **1983**, 921. Ogawa, S.; Nose, T.; Ogawa, T.; Toyokuni, T.; Iwasawa, Y.; Suami, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2369.

(4) Ogawa, S.; Iwasawa, Y.; Suami, T. *Chem. Lett.* **1984**, 355. Ogawa, S.; Iwasawa, Y.; Nose, T.; Suami, T.; Ohba, S.; Ito, M.; Saito, Y. *J. Chem. Soc. Perkin Trans. 1* **1985**, 903.

(5) Paulsen, H.; Heiker, F. R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 904.

(6) Paulsen, H., Deyn, W. v.; Roben, W. *Justus Liebigs Ann. Chem.* **1984**, 433.

(7) A representative example of prostaglandins synthesis from carbohydrates: Stork, G.; Takahashi, T.; Kawamoto, I.; Suzuki, T. *J. Am. Chem. Soc.* **1978**, *100*, 8272.

(8) Ferrier, R. J.; Prasit, P. *Pure Appl. Chem.* **1983**, *55*, 565 and the preceding reports from the Ferrier group cited therein.

(9) Wilcox, C. S.; Thomasco, L. M. *J. Org. Chem.* **1985**, *50*, 547.

(10) Wilcox, C. S.; Gaudino, J. *J. Am. Chem. Soc.* **1986**, *108*, 3102.

(11) (a) Suami, T.; Tadano, K.; Kameda, Y. Iimura, Y. *Chem. Lett.* **1984**, 1919. (b) Suami, T.; Tadano, K.; Ueno, Y.; Iimura, Y. *Chem. Lett.* **1985**, 37. (c) Suami, T.; Tadano, K.; Ueno, Y.; Fukabori, C. *Chem. Lett.* **1985**, 1557. (d) Tadano, K.; Suami, T. *J. Synth. Org. Chem. Jpn.* **1986**, *44*, 633. (e) Tadano, K.; Ueno, Y.; Fukabori, C.; Hotta, Y.; Suami, T., submitted for publication in *Bull. Chem. Soc. Jpn.*

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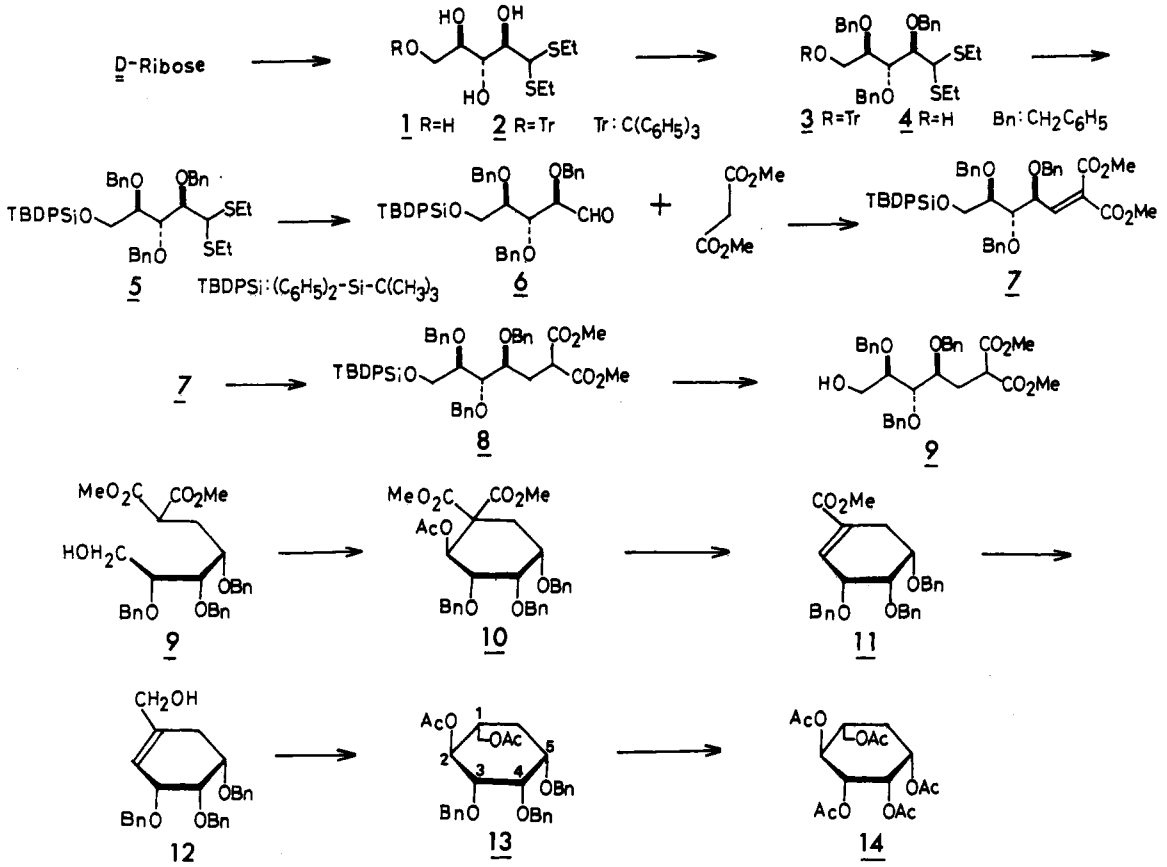
Scheme I



diates to some pseudo-sugars.[12] In our previous paper,[11a] we realized a one-step construction of a polyhydroxylated cyclohexane-1,1-dicarboxylate by base-catalyzed nucleophilic attack of the methylene of dimethyl malonate on both electrophilic termini (an aldehyde group and an iodomethylene group) of a L-arabinose derived intermediate. Although we achieved syntheses of pseudo-α-D-glucopyranose[13] and pseudo-β-L-altropyranose by using this one-step cyclization as a key reaction,[11a] competitive *C*-glycoside formation by C–O bond formation in place of C–C bond formation reduced the effectiveness of the method. To overcome this, we investigated stepwise C–C bond formation for construction of carbocyclic rings. Formation of the first C–C bond in preparation of the intermediates **9**, **23**, **37**, and **49** was achieved employing the Knoevenagel condensation of the aldose derived acyclic aldehydes **6**, **20**, **34**, and **46** with dimethyl malonate as the key step. The second C–C bond formation for cyclohexane or cyclopentane construction featured pyridinium chlorochromate oxidation of **9**, **23**, **37**, and **49**, which accompanied aldol cyclization without difficulty. In this manner, we have synthesized pentaacetyl derivatives of pseudo-β-L-mannopyranose (**14**), pseudo-β-L-glucopyranose (**28**), pseudo-α-D-altropyranose (**28′**), pseudo-α-L-mannopyranose (**42**), and pseudo-β-L-arabinofuranose (**56**) effectively.

Results and Discussion

Synthesis of (1*S*,2*S*,3*R*,4*S*,5*S*)-2,3,4,5-Tetraacetoxy-1-(acetoxymethyl)cyclohexane (14) from D-Ribose

(Scheme I). Initially, D-ribose was chosen as a starting aldose for synthesis of pseudo-sugars. The known D-ribose diethyl dithioacetal (**1**)[14] was selectively tritylated to afford compound **2** in 92% yield. Benzylation of the secondary hydroxyl groups in **2** with excess benzyl bromide in the presence of sodium hydride afforded the tri-*O*-benzyl derivative **3**. Deprotection of the trityl group with *p*-toluenesulfonic acid provided compound **4** in 61% from **2**. The primary hydroxyl group in **4** was then protected as silyl ether with *tert*-butyldiphenylchlorosilane, providing compound **5** in 98% yield. Dethioacetalization of **5** in aqueous acetonitrile in the presence of mercury(II) chloride gave an aldehyde **6**, which was used in the Knoevenagel condensation without purification.[15] By stirring a solution of **6** in a mixture of pyridine and acetic anhydride (2:1, v/v) in the presence of excess dimethyl malonate at ambient temperature for 42 h, Knoevenagel condensation proceeded smoothly to provide an α,β-unsaturated diester **7** in 85% yield. Hydrogenation of **7** in the presence of Raney nickel afforded a saturated diester **8** in 78% yield. Deprotection of the silyl ether in **8** with tetrabutylammonium fluoride furnished the intermediate **9** in 68% yield. The key cyclization of **9** to cyclohexane derivative was accomplished by treatment of **9** with pyridinium chlorochromate (PCC) followed by acetylation. As a result, an aldol cyclization product **10** was obtained in 69% yield as a single diastereomer. The stereochemistry of the newly introduced acetoxyl group, therefore the hydroxyl group in the cyclized

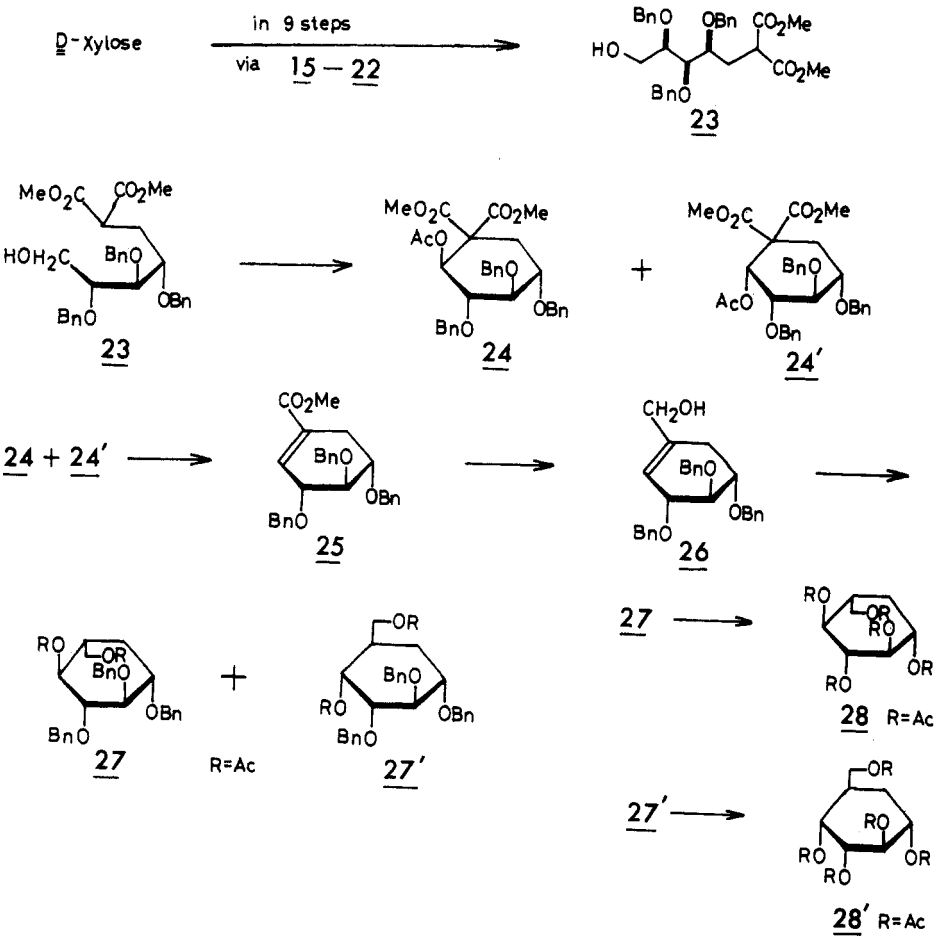
(12) A part of the present work has been published in a preliminary form: Tadano, K.; Maeda, H.; Hoshino, M.; Iimura, Y.; Suami, T. *Chem. Lett.* **1986**, 1081.

(13) A synthesis of pseudo-α-D-glucopyranose has been published very recently: Ogawa, S.; Nakamura, K.; Takagaki, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2956.

(14) Kenner, G. W.; Rodda, H. J.; Todd, R. *J. Chem. Soc.* **1949**, 1613.

(15) Dethioacetalization of compound **3** by the analogous conditions for preparation of **6** resulted a formation of O-detritylated product accompanied by dethioacetalization. On the other hand, 5-*O*-(*tert*-butyldiphenylsilyl)-D-ribose diethyl dithioacetal was prepared by silylation of **1** in a quantitative yield. Unfortunately, O-benzylation of the *O*-silyl derivative (benzyl bromide, sodium hydride in DMF) gave a complex mixture, and compound **5** could not be prepared in a practical yield.

Scheme II



product, was established on the basis of the ^{1}H NMR examination. In the ^{1}H NMR spectrum of **10**, a doublet with J = 12 Hz appeared at δ 5.77, which was attributable to proton on the carbon bearing the acetoxy group (H-2). This J value for H-2 is consistent with a trans diaxial relationship between H-2 and H-3 in the most stable 1*C* conformation. Therefore, the acetoxyl group in **10** oriented equatorially (2*S* configuration as depicted).

The transformation of compound **10** to pseudo-sugar **14** was achieved by the method described in our previous report.[11a] Thermal demthoxycarbonylation of **10** accompanied by β-elimination of the acetoxyl group furnished a cyclohexene-1-carboxylate **11** in 70% yield. Lithium aluminum hydride reduction of **11** gave a 1-cyclohexene-1-methanol **12** in 88% yield. For introduction of hydroxyl group at C-2 in **12**, hydroboration of allyl alcohol **12** was investigated. Treatment of **12** with a borane–THF complex in THF at 0 °C for 4 h, successive oxidation with hydrogen peroxide followed by acetylation, provided a fully protected pseudo-β-L-mannopyranose **13** in 66% yield. The other possible isomer, a derivative of pseudo-α-D-allopyranose, could not be detected. The hydroboration proceeded stereospecifically from the less hindered side opposite to the three benzyloxy groups to provide **13** exclusively. The structure of **13** was confirmed by conversion of **13** to the pentaacetate **14**. O-Debenzylation of **13** by hydrogenolysis in the presence of palladium–black followed by acetylation afforded **14** in 52% yield. The ^{1}H NMR spectrum of **14** was indistinguishable from that of pentaacetate of pseudo-β-DL-mannopyranose[16] and apparently different from that of the known pentaacetate of pseudo-α-DL-allopyranose.[17] The optical rotation value of **14** ($[\alpha]_D^{19.5}$ −1.1° (*c* 1.26, $CHCl_3$)) coincided with that of the reported pentaacetate of pesudo-β-D-mannopyranose[6] except for the sign.

Syntheses of (1*S*,2*S*,3*R*,4*R*,5*S*)- and (1*R*,2*R*,3*R*,4*R*,5*S*)-2,3,4,5-Tetraacetoxy-1-(acetoxymethyl)cyclohexane (28 and 28') from D-Xylose (Scheme II). The same reaction sequence used for the conversion of **1** to **9** was used for conversion of the known D-xylose diethyl dithioacetal (**15**)[18] to intermediate **23** via compounds **16**–**22**. The overall yield of **23** from **15** was 27% in eight steps. Oxidation of **23** by PCC and successive acetylation of the cyclized products furnished the two diastereomers **24** and **24'** in 34% and 21% yield, respectively. The stereochemistries of the newly introduced acetoxyl groups in **24** and **24'** were assigned on the basis of their ^{1}H NMR spectra.[19]

Thermal demethoxycarbonylation of **24** and **24'** accompanied by β-elimination of the acetoxyl groups gave **25** in 50% and 66% yield, respectively. Lithium aluminum hydride reduction of **25** gave compound **26** in 88% yield. Hydroboration of **26** followed by oxidative workup and

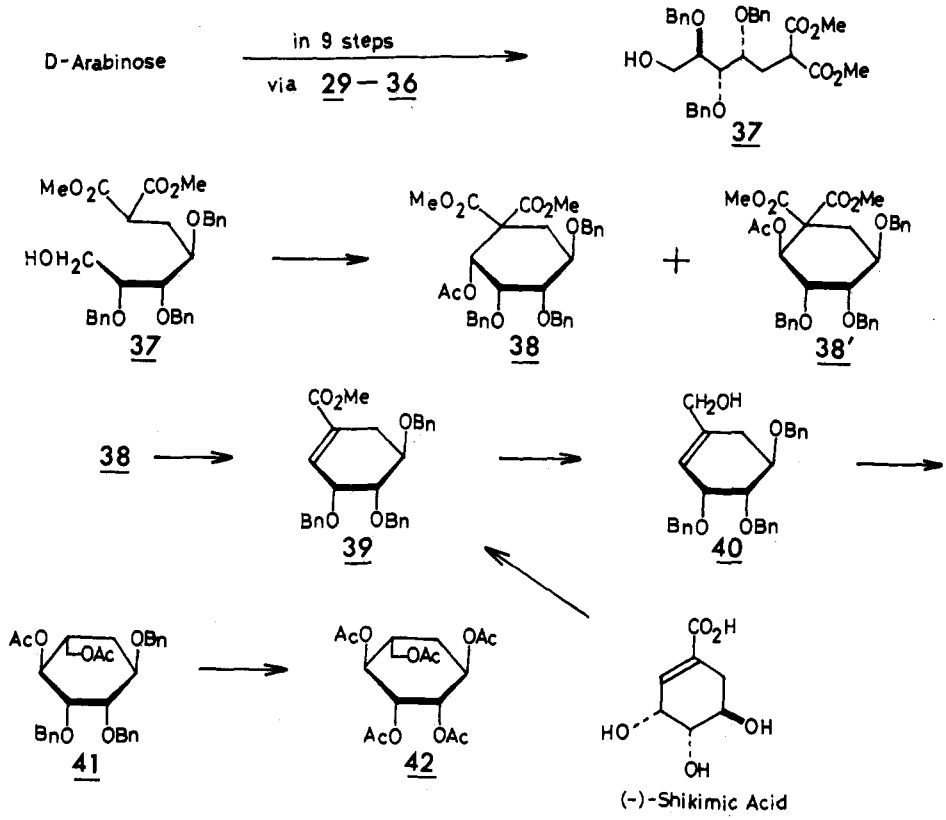
(16) Ogawa, S.; Ara, M.; Kondoh, T.; Saitoh, M.; Masuda, R.; Toyokuni, T.; Suami, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1121.

(17) Ogawa, S.; Tsukiboshi, Y.; Iwasawa, Y.; Suami, T. *Carbohydr. Res.* **1985**, *136*, 77.

(18) Hough, L.; Taylor, T. J. *J. Chem. Soc.* **1955**, 1213.

(19) In the ^{1}H NMR spectra, H-2 (proton on the carbon bearing the acetoxyl group) of **24** appeared at δ 5.28 as a doublet with J = 9 Hz, while that of **24'** appeared at δ 6.10 as a doublet with J = 3 Hz. Consequently, the acetoxyl group in **24** is oriented equatorially in the most stable 1C conformation (H-2 and H-3 were a trans diaxial relationship) and that in **24'** oriented axially (H-2 and H-3 were a cis equatorial–axial relationship). The 6-benzyloxy group in **23** seems to be a stereocontrolling factor in the transition state of the cyclization.

Scheme III



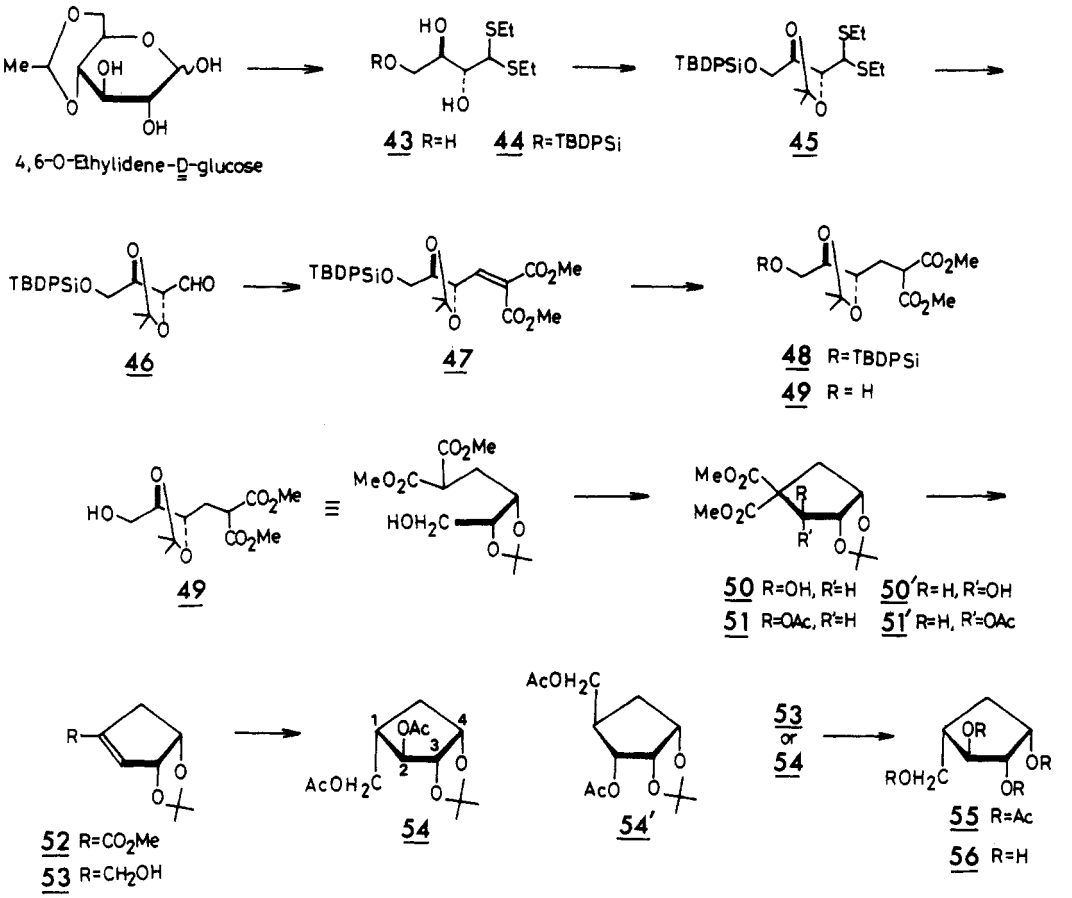
acetylation provided the two pseudohexopyranose derivatives **27** and **27′** and 67% and 11% yield, respectively. On the basis of comparison of the ^{1}H NMR spectrum of the main product **27** with that of the known (1*R*,2*R*,3*S*,4*S*,5*R*)-2-acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexane, the D-enantiomer of **27**, which was synthesized from D-glucose by an independent method,[11e] the structure of **27** was established to be (1*S*,2*S*,3*R*,4*R*,5*S*)-2-acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexane. The ^{1}H NMR spectrum of **27′** accorded with that of the known (1*S*,2*S*,3*S*,4*S*,5*R*)-2-acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexane, the L-enantiomer of **27′** prepared from D-glucose.[11c,e] Therefore, compound **27′** is a derivative of pseudo-α-D-altropyranose. The stereoselectivity of the hydroboration is approximately 6 to 1 with preference for the adduct which is formed by attack of borane from the less hindered side [the opposite side to 3,5-bis(benzyloxy) groups]. O-Debenzylation of **27** and **27′**, successive acetylation provided pentaacetates of pseudo-β-L-glucopyranose (**28**) and of pseudo-α-D-altropyranose (**28′**) in a quantitative and 65% yield, respectively. The structure of **28** was confirmed by comparison of the ^{1}H NMR spectrum with those of the D-enantiomer[4,11e] and the DL-**28**.[16,20] The structure of **28′** was also confirmed by comparison of the ^{1}H NMR spectrum with those of the L-enantiomer[11c,e] and the DL-**28′**.[21]

Synthesis of (1*S*,2*S*,3*R*,4*S*,5*R*)-2,3,4,5-Tetraacetoxy-1-(acetoxymethyl)cyclohexane (42) from D-Arabinose (Scheme III). The same reaction sequence used for the conversion of **1** to **9** was used for conversion of the known 5-*O*-trityl-D-arabinose diethyl dithioacetal (**30**)[22] to compound **37** via compounds **31**–**36**. The overall yield from **30** to **37** was 37% in seven steps. Oxidative (PCC) cyclization of **37** followed by acetylation gave two stereoisomers **38** and **38′** in 48% and 5% yield, respectively. On the other hand, we have synthesized **38** and **38′** from D-lyxose as a synthetic intermediate for optically pure shikimic acid.[11b] The ^{1}H NMR spectra of **38** and **38′** of the present work were identical with those of **38** and **38′** prepared from D-lyxose. The main isomer **38** has the 2*R*,3*R*,4*S*,5*R* configuration and **38′** has the 2*S*,3*R*,4*S*,5*R* configuration. The present route to **38** and **38′** from D-arabinose provides an alternative synthetic route for shikimic acid. Thermal demethoxycarbonylation of **38** accompanied by β-elimination of the acetoxyl group gave **39** in 46% yield. Lithium aluminum hydride reduction of **39** afforded compound **40** in 56% yield. However, diisobutylaluminum hydride reduction of **39** gave **40** in 93% yield. Hydroboration of **40** and successive oxidation followed by acetylation furnished a fully protected pseudo-α-L-mannopyranose **41** in 66% yield. The other possible isomer, a derivative of pseudo-β-D-allopyranose, could not be detected. The hydroboration proceeded stereoselectively from the less hindered side. O-Debenzylation of **41** followed by acetylation provided pentaacetate **42** of pseudo-α-L-mannopyranose in 97% yield. The structure of **42** was confirmed by comparison of the ^{1}H NMR spectrum with that of the known DL-**42**.[16]

Synthesis of (1*S*,2*S*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)cyclopentane (56) from D-Erythrose (Scheme IV). Next, our attempts were focused on synthesis of optically pure pseudopentofuranoses. As a starting aldose, we chose D-erythrose diethyl dithioacetal (**43**), which was prepared from 4,6-*O*-ethylidene-D-glucose by the literature procedure.[23] The key intermediate **49** for cyclization was prepared as follows. Selective O-sily-

(20) Suami, T.; Ogawa, S.; Nakamoto, K.; Kasahara, I. *Carbohydr. Res.* **1977**, *58*, 240.
(21) Suami, T.; Ogawa, S.; Ishibashi, T.; Kasahara, I. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1388.
(22) Bristow, N. W.; Lythgoe, B. *J. Chem. Soc.* **1949**, 2306.
(23) Perlin, A. S. *Methods Carbohydr. Chem.* **1962**, *1*, 64. Ballou, C. E.; Fischer, H. O. L.; MacDonald, D. L. *J. Am. Chem. Soc.* **1955**, *77*, 5967.

Scheme IV



lation at the primary hydroxyl group in **43** and successive O-isopropylidenation furnished **45** (68% from 4,6-*O*-ethylidene-D-glucose). Dethioacetalization (**45** to **46**), Knoevenagel condensation with dimethyl malonate (**46** to **47**), and successive 1,4-conjugate addition of hydride from $NaBH_4$ (**47** to **48**) followed by de-O-silylation provided the intermediate **49** in 51% overall yield from **45**.

Oxidative (PCC) cyclization of the intermediate **49** afforded a mixture of cyclopentane-1,1-dicarboxylates **50** and **50'**, which was directly acetylated to afford a mixture of **51** and **51'** in 73% yield. The diastereomers **50** and **50'** were separated by repeated chromatography on silica gel, the ratio of **50** and **50'** being approximately 4 to 1. The structures of **51** and **51'**, which were prepared from pure **50** and **50'**, were assigned as depicted on the basis of their ^1H NMR spectra. Thermal demethoxycarbonylation of the mixture **51** and **51'** accompanied by β-elimination provided 1-cyclopentene-1-carboxylate **52**, which was a somewhat volatile compound. Diisobutylaluminum hydride reduction of **52** afforded 1-cyclopentene-1-methanol **53** in 67% yield. Hydroboration of **53** with borane–THF and oxidative workup followed by acetylation gave a derivative of pseudo-β-L-arabinofuranose **54** in 73% yield. The structure of **54** was established on the basis of the ^1H NMR spectrum, in which the proton on the carbon bearing the acetoxyl group (H-2) appeared at δ 5.07 as a double doublet with J = 1 and 2 Hz supporting the trans relationships of H-2 to both H-1 and H-3.[24] The other possible stereoisomer, a derivative of pseudo-α-D-ribofuranose **54'**, was isolated in 0.7% yield. Therefore, the stereoselectivity of the hydroboration was estimated to be 100 to 1 with predominant attack of borane to **53** from the less hindered convex face. Hydrolysis of **54** in 80% aqueous acetic acid followed by acetylation gave tetraacetate **55** of pseudo-β-L-arabinofuranose in 79% yield. The compound **55** was prepared in an improved yield (64% from **53**) by direct acid hydrolysis of the hydroboration–oxidation product and successive acetylation. Deprotection of **55** with sodium methoxide in methanol provided pseudo-β-L-arabinofuranose (**56**) in 97% yield.

In summary, we have developed in the present work a general transformation of some aldoses to pseudohexopyranoses and pseudopentofuranoses. This newly developed approach might also be applicable to the synthesis of other pseudo-sugars.

Experimental Section

General Procedures. Reactions were carried out at ambient temperature unless otherwise stated. Evaporations were performed under diminished pressure at below 40 °C (bath). Melting points were determined with a Mitamura Riken micro melting point apparatus and are uncorrected. Specific rotations were measured in a 10-mm cell with a Jasco DIP-4 polarimeter. Column chromatography was performed on Kieselgel 60 (Merck), and thin-layer chromatography (TLC) was performed on a glass plate coated with Kieselgel 60 GF_{254} (Merck) followed by detection by UV light and charring with sulfuric acid. Preparative TLC (PTLC) was performed on a glass plate (20 × 20 cm) coated with Kieselgel PF_{254} (Merck), and compounds were extracted with $CHCl_3$. IR spectra were recorded with a Hitachi Model 225 (KBr) or with a Jasco Model A-202 ($CHCl_3$) spectrometer. ^1H NMR spectra were recorded with a Varian EM-390 (90 MHz) spectrometer in $CDCl_3$ (internal Me_4Si). High-resolution mass spectra were obtained with a Hitachi Model M-80 spectrometer. Elemental analyses were performed by Saburo Nakada and Akio Takahashi of our university to whom our thanks are due.

Dichloromethane (CH_2Cl_2) and dimethylformamide (DMF) were dried over CaH_2 and then distilled. Pyridine was distilled

(24) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, 2nd ed*; Pergamon: Oxford, 1969; pp 286–289.

over NaOH. Tetrahydrofuran (THF) was distilled over $LiAlH_4$ and then over sodium–benzoquinone.

Selective Tritylation of Diethyl Dithioacetals 1, 15, and 29 of D-Ribose, D-Xylose, and D-Arabinose. 5-*O*-Trityl-D-ribose Diethyl Dithioacetal (2), 5-*O*-Trityl-D-xylose Diethyl Dithioacetal (16), and 5-*O*-Trityl-D-arabinose Diethyl Dithioacetal (30). Tritylation of 1[14] in pyridine (20 mmol/25 mL) with trityl chloride (1.3 mol equiv) in the presence of 4-(dimethylamino)pyridine (0.2 mol equiv) at 70 °C, extractive workup of the reaction mixture (ethyl acetate), evaporation of the combined extracts after drying over Na_2SO_4, and column chromatography (ethyl acetate/toluene 1:20, containing 1% triethylamine] afforded **2** (92%) as a pale yellow syrup. **2**: TLC R_f 0.87 (ethyl acetate/toluene, 1:1); $[\alpha]^{25}_D$ −3.3° (*c* 0.92, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3450, 3010, 1450, 1210, 1050 cm^{-1}; ^{1}H NMR δ 1.22 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.57, 2.64 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 2.80–3.07 (3 H, m, 3 × OH), 3.28–3.98 (5 H, m, H-2, 3, 4, 5, 5′), 4.16 (1 H, d, *J* = 3 Hz, H-1), 7.10–7.52 (15 H, m, $C(C_6H_5)_3$). Anal. Calcd for $C_{28}H_{34}O_4S_2$: C, 67.45; H, 6.86; S, 12.86. Found: C, 67.61; H, 6.86; S, 13.00.

By the analogous reaction conditions, extractive workup, and chromatographic purification on silica gel (ethyl acetate/toluene, 1:40, containing 1% triethylamine), compound **15**[18] was converted to **16** in 78% yield as a pale yellow syrup. **16**: TLC R_f 0.70 (ethyl acetate/toluene, 1:1); $[\alpha]^{22}_D$ +24.0° (*c* 1.04, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3480, 3010, 1490, 1450, 1210, 1080 cm^{-1}; ^{1}H NMR δ 1.21 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.61, 2.67 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.00–3.15 (3 H, m, 3 × OH), 3.21–4.24 (6 H, m, H-1,2,3,4,5,5′), 7.15–7.55 (15 H, m, $C(C_6H_5)_3$).

Analogously as described above, compound **29** was converted to the known **30**[22] in 81% yield after a silica gel chromatography (ethyl acetate/hexane, 1:5, containing 1% triethylamine). **30**: TLC R_f 0.32 (ethyl acetate/hexane, 1:3); $[\alpha]^{23}_D$ −29.8° (*c* 1.06, $CHCl_3$) [lit.[22] $[\alpha]^{15}_D$ −37.5° (*c* 3.1, $CHCl_3$)]; IR $\nu_{max}^{CHCl_3}$ 3460, 3000, 1450, 1200, 1070 cm^{-1}; ^{1}H NMR δ 1.22 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.59, 2.65 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 2.70–2.98 (3 H, m, 3 × OH), 3.33–4.22 (6 H, m, H-1,2,3,4,5,5′), 7.18–7.56 (15 H, m, $C(C_6H_5)_3$).

O-Benzylation of Compounds 2, 16, and 30 and Successive Acid Hydrolysis for Removal of the *O*-Trityl Group. 2,3,4-Tri-*O*-benzyl-D-ribose Diethyl Dithioacetal (4), 2,3,4-Tri-*O*-benzyl-D-xylose Diethyl Dithioacetal (18), and 2,3,4-Tri-*O*-benzyl-D-arabinose Diethyl Dithioacetal (32). A solution of **2** in DMF (32 mmol/70 mL) containing sodium hydride (5 mol equiv, 60% emulsion in mineral oil, prewashed with hexane and then dried) was added benzyl bromide (5 mol equiv). After completion of the reaction (TLC), ethanol was added for decomposition of the excess base and then evaporated. The residue was extracted with CH_2Cl_2 and then the combined extracts were dried (Na_2SO_4) and evaporated to afford crude **3**. The crude **3** in a mixture of ethyl acetate and methanol (1:1, v/v) was hydrolyzed in the presence of *p*-toluenesulfonic acid monohydrate (1.5–2.0 mol equiv, based on **2**). After completion of the hydrolysis (TLC), the solution was neutralized with saturated aqueous $NaHCO_3$ and evaporated. The residue in water was extracted with ethyl acetate, and the combined extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:10) to afford **4** (61%) as a colorless syrup. **4**: TLC R_f 0.21 (ethyl acetate/hexane, 1:5); $[\alpha]^{24}_D$ +28.3° (*c* 0.53, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3500, 3000, 1450, 1205, 1095, 1070 cm^{-1}; ^{1}H NMR δ 1.19 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.59, 2.62 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.60–4.25 (6 H, m, H-1,2,3,4,5,5′), 4.52–5.01 (6 H, m, 3 × $OCH_2C_6H_5$), 7.37 (15 H, s, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{30}H_{38}O_4S_2$ *m/z* 526.2210, found, M, 526.2222. Anal. Calcd for $C_{30}H_{38}O_4S_2$: C, 68.41; H, 7.27. Found: C, 68.58; H, 7.27.

By the analogous reaction conditions, workup as in the case of **4** and chromatographic purification on silica gel (ethyl acetate/toluene, 1:20), compound **16** was converted to **18** in 67% yield as a colorless syrup. **18**: TLC R_f 0.35 (ethyl acetate/toluene, 1:20); $[\alpha]^{22}_D$ −9.4° (*c* 0.96, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3680, 3590, 3020, 1205, 1045 cm^{-1}; ^{1}H NMR δ 1.19 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.18 (1 H, br s, OH), 2.58 (4 H, q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.55–4.21 (6 H, m, H-1,2,3,4,5,5′), 4.60–4.90 (6 H, m, 3 × $OCH_2C_6H_5$), 7.26–7.43 (15 H, m, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{30}H_{38}O_4S_2$ *m/z* 526.2209, found, M, 526.2216. Anal. Calcd for $C_{30}H_{38}O_4S_2$: C, 68.41; H, 7.27. Found: C, 68.58; H, 7.28.

Analogously as described above, compound **30** was converted to **32** in 64% yield as a colorless syrup. **32**: TLC R_f 0.46 (ethyl acetate/hexane, 1:3); $[\alpha]^{21}_D$ +8.1° (*c* 1.41, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3500, 3010, 2970, 2870, 1450, 1205, 1090 cm^{-1}; ^{1}H NMR δ 1.20 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.03–2.28 (1 H, m, OH), 2.63, 2.70 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.60–4.47 (6 H, m, H-1,2,3,4,5,5′), 4.55–4.93 (6 H, m, 3 × $OCH_2C_6H_5$), 7.26–7.48 (15 H, m, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{30}H_{38}O_4S_2$ *m/z* 526.2209, found, M, 526.2215. Anal. Calcd for $C_{30}H_{38}O_4S_2$: C, 68.41; H, 7.27. Found: C, 68.52; H, 7.19.

O-*tert*-Butyldiphenylsilylation of Compounds 4, 18, and 32. 2,3,4-Tri-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-D-ribose Diethyl Dithioacetal (5), 2,3,4-Tri-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-D-xylose Diethyl Dithioacetal (19), and 2,3,4-Tri-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-D-arabinose Diethyl Dithioacetal (33). To a stirred solution of **4** in DMF (10 mmol/50 mL) were added *tert*-butylchlorodiphenylsilane (1.3 mol equiv) and imidazole (1.3 mol equiv). After completion of the reaction (TLC), the mixture was diluted with ethyl acetate and washed with water. The organic layer was dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:50) to yield **5** in 98% yield as a colorless syrup. **5**: TLC R_f 0.65 (ethyl acetate/hexane, 1:9); $[\alpha]^{26}_D$ −3.3° (*c* 0.98, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3020, 2910, 2850, 1650, 1600, 1580, 1490, 1445, 1420, 1385 cm^{-1}; ^{1}H NMR δ 1.07 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.17 (6 H, t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.60, 2.63 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.87–4.28 (6 H, m, H-1,2,3,4,5,5′), 4.50–4.97 (6 H, m, 3 × $OCH_2C_6H_5$), 7.30 (15 H, s, 3 × $OCH_2C_6H_5$), 7.60–7.77 (10 H, m, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{46}H_{56}O_4S_2Si$: C, 72.21; H, 7.38. Found: C, 72.29; H, 7.30.

Compound **18** was converted to **19** (98%, a colorless syrup) as described in the case of **5** (ethyl acetate/hexane, 1:25 for silica gel chromatography). **19**: TLC R_f 0.84 (ethyl acetate/hexane, 1:8); $[\alpha]^{23}_D$ −2.4° (*c* 1.34, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3060, 3000, 2960, 2930, 2860, 1455, 1430, 1390, 1340, 1260, 1105 cm^{-1}; ^{1}H NMR δ 1.05 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.10, 1.14 (3 H × 2, each t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.49, 2.67 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.59–4.29 (6 H, m, H-1,2,3,4,5,5′), 4.40–4.80 (6 H, m, 3 × $OCH_2C_6H_5$), 7.20–7.30 (15 H, m, 3 × $OCH_2C_6H_5$), 7.29–7.76 (10 H, m, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{46}H_{56}O_4S_2Si$: C, 72.21; H, 7.38. Found: C, 72.24; H, 7.31.

Compound **32** was silylated to afford **33** (93%, as a colorless syrup) as described above. **33**: TLC R_f 0.33 (ethyl acetate/hexane, 1:30); $[\alpha]^{20}_D$ −3.3° (*c* 1.22, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3060, 2930, 2860, 1450, 1425, 1110 cm^{-1}; ^{1}H NMR δ 1.07 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.15, 1.18 (3 H × 2, each t, *J* = 8 Hz, 2 × SCH_2CH_3), 2.57, 2.67 (2 H × 2, each q, *J* = 8 Hz, 2 × SCH_2CH_3), 3.66–4.91 (12 H, m, H-1,2,3,4,5,5′, 3 × $OCH_2C_6H_5$), 7.15–7.83 (25 H, m, 3 × $OCH_2C_6H_5$, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{46}H_{56}O_4S_2Si$: C, 72.21; H, 7.38. Found: C, 72.41; H, 7.39.

Dethioacetalization of Compound 5 and Successive Knoevenagel Condensation of 6 with Dimethyl Malonate. Methyl (4*S*,5*S*,6*R*)-4,5,6-Tris(benzyloxy)-7-[(*tert*-butyldiphenylsilyl)oxy]-2-(methoxycarbonyl)-2-heptenoate (7). To a stirred solution of **5** (293 mg, 0.38 mmol) in a mixture of acetonitrile and water (10:1, 5.5 mL) were added mercury(II) chloride (416 mg, 1.53 mmol) and calcium carbonate (153 mg, 1.53 mmol). After the mixture was stirred for 30 min, the resulting insoluble materials were removed through Celite pad, and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with 1 M KI solution (100 mL × 2) and 30% $Na_2S_2O_3$ solution (100 mL). The organic layer was dried (Na_2SO_4) and evaporated to afford crude **6** [TLC R_f 0.41 (ethyl acetate/hexane, 1:10)], which was subjected to the Knoevenagel reaction without purification. A solution of the crude **6** in a mixture of pyridine (2 mL) and acetic anhydride (1 mL) containing dimethyl malonate (0.44 mL, 3.86 mmol) was stirred for 42 h. The mixture was evaporated, and the residue was partitioned between ethyl acetate (50 mL) and water (50 mL). The aqueous layer was extracted with ethyl acetate (50 mL × 2). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:25) affording **7** (251 mg, 85%) as a colorless syrup. **7**: TLC R_f 0.50 (ethyl acetate/

hexane, 1:5); $[\alpha]^{29}_D$ −5.6° (c 0.78, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 2930, 2860, 1735, 1455, 1440, 1430, 1360, 1255, 1110 cm^{-1}; ^1H NMR δ 1.03 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 3.46, 3.71 (3 H × 2, each s, 2 × $COOCH_3$), 3.73–4.86 (11 H, m, H-4,5,6,7,7′, 3 × $OCH_2C_6H_5$), 7.10 (1 H, d, J = 9 Hz, H-3), 7.20–7.72 (25 H, m, 3 × $OCH_2C_6H_5$, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{47}H_{52}O_8Si$: C, 73.03; H, 6.78. Found: C, 72.72; H, 6.65.

Hydrogenation of Compound 7. Methyl (4*S*,5*S*,6*R*)-4,5,6-Tris(benzyloxy)-7-[(*tert*-butyldiphenylsilyl)oxy]-2-(methoxycarbonyl)heptanoate (8). A solution of **7** (59 mg, 0.07 mmol) in ethanol (3 mL) was hydrogenated in the presence of Raney nickel T-4 at atmospheric hydrogen pressure for 1 h. After removal of the catalyst, the filtrate was evaporated. The residue was purified on PTLC (ethyl acetate/hexane, 1:6) to afford **8** (45 mg, 78%) as a colorless syrup. **8**: TLC R_f 0.36 (ethyl acetate/hexane, 1:8); $[\alpha]^{29}_D$ −27.6° (c 1.08, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3050, 2950, 2850, 1750, 1740, 1590, 1500, 1450, 1390, 1260 cm^{-1}; ^1H NMR δ 1.07 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 2.10–2.38 (2 H, m, H-3,3′), 3.50, 3.60 (3 H × 2, each s, 2 × $COOCH_3$), 3.61–4.90 (12 H, m, H-2,4,5,6,7,7′, 3 × $OCH_2C_6H_5$), 7.21–7.81 (25 H, m, 3 × $OCH_2C_6H_5$, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{47}H_{54}O_8Si$: C, 72.84; H, 7.02. Found: C, 72.98; H, 7.03.

O-Desilylation of Compound 8. Methyl (4*S*,5*S*,6*R*)-4,5,6-Tris(benzyloxy)-7-hydroxy-2-(methoxycarbonyl)heptanoate (9). A solution of **8** (43 mg, 0.05 mmol) in THF (2 mL) with tetrabutylammonium fluoride (1 M in THF, 0.11 mL) was stirred for 2.5 h then evaporated. The residue was purified on PTLC (ethyl acetate/hexane, 1:2) affording **9** (20 mg, 68%) as a colorless syrup. **9**: TLC R_f 0.22 (ethyl acetate/hexane, 1:4), $[\alpha]^{29}_D$ −7.2° (c 1.00, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3550, 3000, 2960, 2880, 1730, 1440, 1270, 1200, 1150 cm^{-1}; ^1H NMR δ 2.00–2.35 (3 H, m, H-3,3′, OH), 3.54, 3.63 (3 H × 2, each s, 2 × $COOCH_3$), 3.45–3.96 (6 H, m, H-2,4,5,6,7,7′), 4.29–4.91 (6 H, m, 3 × $OCH_2C_6H_5$), 7.27–7.35 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{31}H_{36}O_8$: C, 69.38; H, 6.76. Found: C, 69.11; H, 6.79.

In a large-scale experiment, 5.12 g of compound **5** was converted to 1.73 g (overall 48% yield) of **9**. In this case, each crude **6**, **7**, and **8** was subjected to the next step without silica gel chromatography. The compound **9** was purified on silica gel column.

Conversion of Compound 19 to Methyl (4*S*,5*R*,6*R*)-4,5,6-Tris(benzyloxy)-7-hydroxy-2-(methoxycarbonyl)heptanoate (23). Compound **19** (2.20 g) was converted to **23** (826 mg, 53% overall yield) by the analogous reaction conditions as in preparation of **9** from **5**. Knoevenagel condensation of **20** was performed as follows. A solution of the crude **20** in pyridine (7 mL) with dimethyl malonate (2.62 mL) in the presence of triethylamine (0.04 mL) was stirred for 30 h, and then acetic anhydride (5 mL) was added. The mixture was stirred for an additional 40 h until the reaction was complete.

The crude **23** was finally purified on silica gel chromatography (ethyl acetate/hexane, 1:4). **20**: TLC R_f 0.24 (ethyl acetate/hexane, 1:10). **21**: TLC R_f 0.41 (ethyl acetate/hexane, 1:5). **22**: TLC R_f 0.41 (ethyl acetate/hexane, 1:5). **23**: TLC R_f 0.47 (ethyl acetate/hexane, 2:3); $[\alpha]^{21}_D$ −5.5° (c 1.01, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3550, 3000, 2960, 2880, 1730, 1450, 1240, 1165, 1060 cm^{-1}; ^1H NMR δ 1.94–2.50 (3 H, m, H-3,3′, OH), 3.63, 3.64 (3 H × 2, each s, 2 × $COOCH_3$), 3.41–3.95 (6 H, m, H-2,4,5,6,7,7′), 4.36–4.77 (6 H, m, 3 × $OCH_2C_6H_5$), 7.30–7.45 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{31}H_{36}O_8$: C, 69.38; H, 6.76. Found: C, 69.34; H, 6.78.

Conversion of Compound 33 to Methyl (4*R*,5*S*,6*R*)-4,5,6-Tris(benzyloxy)-7-hydroxy-2-(methoxycarbonyl)heptanoate (37). Compound **33** (308 mg) was converted to **37** (133 mg, 62% overall yield) by the analogous reaction conditions as in preparation of **9** from **5**. Each intermediate (**34**–**36**) was used to the next step after extractive workup. Knoevenagel reaction of **34** was performed as described in case of **21**. **34**: TLC R_f 0.35 (ethyl acetate/hexane, 1:10). **35**: TLC R_f 0.50 (ethyl acetate/hexane, 1:5). **36**: TLC R_f 0.44 (ethyl acetate/hexane, 1:6). **37**: TLC R_f 0.38 (ethyl acetate/hexane, 1:2); $[\alpha]^{20}_D$ +4.3° (c 1.52, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3570, 3000, 2960, 2880, 1730, 1450, 1435, 1260, 1230, 1155, 1060 cm^{-1}; ^1H NMR δ 2.10–2.40 (3 H, m, H-3,3′, OH), 3.61, 3.64 (3 H × 2, each s, 2 × $COOCH_3$), 3.17–4.06 (6 H, m, H-2,4,5,6,7,7′), 4.46–4.81 (6 H, m, 3 × $OCH_2C_6H_5$), 7.27–7.48 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{31}H_{36}O_8$: C, 69.38; H, 6.76. Found: C, 69.10; H, 6.77.

4-*O*-(*tert*-Butyldiphenylsilyl)-D-erythrose Diethyl Dithioacetal (44). 4,6-*O*-Ethylidene-D-glucose (10.00 g, 48.5 mmol) was converted to crude D-erythrose diethyl dithioacetal (**43**) (10.12 g) according to the reported procedure.[23] To a stirred solution of the crude **43** in DMF (50 mL) were added *tert*-butylchlorodiphenylsilane (15.13 mL, 58.2 mmol) and imidazole (7.92 g, 116 mmol), and the mixture was stirred for 2 h. The mixture was diluted with ethyl acetate (300 mL) and washed with water (200 mL × 2), 0.1 M aqueous HCl (200 mL), and saturated NaCl (200 mL) successively. The organic layer was dried (Na_2SO_4) and evaporated. The residue was crystallized from hexane (30 mL), affording **44** (10.49 g) as needles. The mother liquor was evaporated, and the residue was chromatographed on silica gel (ethyl acetate/hexane, 1:40) to afford an additional **44** (3.60 g, totally 14.09 g, 68%). **44**: TLC R_f 0.60 (ethyl acetate/hexane, 1:5); mp 61–62 °C; $[\alpha]^{26}_D$ −17.2° (c 1.30, $CHCl_3$); IR ν_{max}^{KBr} 3500, 3420, 2960, 2860, 1430, 1265, 1190, 1100 cm^{-1}; ^1H NMR δ 1.08 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.25, 1.27 (3 H × 2, each t, J = 7 Hz, 2 × SCH_2CH_3), 2.53–2.73 (2 H, m, 2 × OH), 2.61, 2.70 (2 H × 2, each q, J = 7 Hz, 2 × SCH_2CH_3), 3.70–4.03 (4 H, m, H-2,3,4,4′), 4.20 (1 H, d, J = 3 Hz, H-1), 7.30–7.80 (10 H, m, $OSi(C_6H_5)_2C(CH_3)_3$); high-resolution mass spectrum, calcd for $C_{24}H_{36}O_3S_2Si$ m/z 464.1873, found, M, 464.1880. Anal. Calcd for $C_{24}H_{36}O_3S_2Si$: C, 62.02; H, 7.81. Found: C, 62.01; H, 7.85.

4-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-isopropylidene-D-erythrose Diethyl Dithioacetal (45). To a stirred solution of **44** (32.10 g, 69.1 mmol) in acetone (170 mL) were added 2,2-dimethoxypropane (25.5 mL, 207 mmol) and D-camphorsulfonic acid (1.61 g, 6.91 mmol), and the mixture was stirred for 4 h. The solution was neutralized with saturated aqueous $NaHCO_3$ and evaporated. The residue was partitioned between CH_2Cl_2 (600 mL) and water (800 mL). The aqueous layer was extracted with CH_2Cl_2 (600 mL × 2). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:50) affording **45** (34.70 g, quantitatively) as a colorless syrup. **45**: TLC R_f 0.69 (ethyl acetate/hexane, 1:10); $[\alpha]^{26}_D$ −12.7° (c 1.35, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 2940, 2860, 1430, 1385, 1115 cm^{-1}; ^1H NMR δ 1.06 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.15, 1.20 (3 H × 2, each t, J = 7 Hz, 2 × SCH_2CH_3), 1.37, 1.49 (3 H × 2, each s, $C(CH_3)_2$), 2.62 (4 H, q, J = 7 Hz, 2 × SCH_2CH_3), 3.79–4.50 (5 H, m, H-1,2,3,4,4′), 7.28–7.82 (10 H, m, $OSi(C_6H_5)_2C(CH_3)_3$); high-resolution mass spectrum, calcd for $C_{27}H_{40}O_3S_2Si$ m/z 504.2185, found, M, 504.2176. Anal. Calcd for $C_{27}H_{40}O_3S_2Si$: C, 64.23; H, 7.99. Found: C, 64.50; H, 7.89.

Conversion of Compound 45 to Methyl (4*S*,5*R*)-6-Hydroxy-4,5-(isopropylidenedioxy)-2-(methoxycarbonyl)-hexanoate (49). To a solution of **45** (34.70 g, 68.7 mmol) in a mixture of acetonitrile (500 mL) and water (54 mL) were added mercury(II) chloride (82.11 g, 302 mmol) and calcium carbonate (34.38 g, 344 mmol), and the mixture was stirred for 1 h. The resulting insoluble materials were removed by filtration through Celite pad, and the filtrate was evaporated to ca. 50 mL. The Celite pad was washed with ethyl acetate (1200 mL). The concentrate and washing were combined and washed with 1 M aqueous KI (600 mL × 5), 30% aqueous $Na_2S_2O_3$ (600 mL × 2), and saturated aqueous NaCl (600 mL) successively. The organic layer was dried (Na_2SO_4) and evaporated to afford crude 4-*O*-(*tert*-butyldiphenylsilyl)-2,3-*O*-isopropylidene-aldehydo-D-erythrose (**46**) [TLC R_f 0.52 (ethyl acetate/hexane, 1:5)], which was subjected to the next step directly. To a stirred solution of the crude **46** in pyridine (140 mL) were added dimethyl malonate (23.6 mL, 206 mmol) and acetic anhydride (105 mL). The mixture was stirred for 41 h and diluted with ethyl acetate (1000 mL). The solution was washed with water (500 mL × 4), saturated aqueous $NaHCO_3$ (300 mL × 2), saturated aqueous NaCl (500 mL × 3), and then water (500 mL) successively. The organic layer was dried (Na_2SO_4) and evaporated to afford crude methyl (4*S*,5*R*)-6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-(isopropylidenedioxy)-2-(methoxycarbonyl)-2-hexenoate (**47**), which was used to the next step without purification. In a small-scale experiment, the crude **47** was purified by silica gel chromatography (ethyl acetate/hexane, 1:20) affording pure **47** as a colorless syrup. **47**: TLC R_f 0.43 (ethyl acetate/hexane, 1:5); $[\alpha]^{26}_D$ +18.5° (c 0.94, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2960, 2940, 2860, 1730, 1650, 1440, 1385, 1265, 1215 cm^{-1}; ^1H NMR δ 1.06 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.39,

1.52 (3 H × 2, each s, $C(CH_3)_3$), 3.52–3.96 (2 H, m, H-6,6′), 3.78, 3.83 (3 H × 2, each s, 2 × $COOCH_3$), 4.34–4.57 (1 H, m, H-5), 5.11 (1 H, t, J = 8 Hz, H-4), 7.30–7.85 (11 H, m, H-3, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{28}H_{36}O_7Si$: C, 65.59; H, 7.08. Found: C, 65.39; H, 7.12.

To a stirred solution of the above crude **47** in methanol (280 mL) was added sodium borohydride (5.20 g, 137 mmol), and the mixture was stirred for 2.5 h. The mixture was neutralized with 1 M aqueous HCl at 0 °C and evaporated. The residue was partitioned between ethyl acetate (500 mL) and water (600 mL), and the aqueous layer was extracted with ethyl acetate (500 mL × 2). The combined organic layers were dried (Na_2SO_4) and evaporated to afford crude methyl (4*S*,5*R*)-6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-(isopropylidenedioxy)-2-(methoxycarbonyl)hexanoate (**48**), which was used to the next step without purification. In a small-scale experiment, the crude **48** was purified by PTLC (ethyl acetate/hexane, 1:5) to give pure **48** as a colorless syrup: $[\alpha]^{26}_D$ −7.4° (*c* 0.76, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2960, 2860, 1750, 1440, 1430, 1385, 1375, 1205, 1160, 1100 cm^{-1}; ^1H NMR δ 1.06 (9 H, s, $OSi(C_6H_5)_2C(CH_3)_3$), 1.27, 1.33 (3 H × 2, each s, $C(CH_3)_2$), 1.90–2.50 (2 H, m, H-3,3′), 3.53–4.33 (5 H, m, H-2,4,5,6,6′), 3.72, 3.75 (3 H × 2, each s, 2 × $COOCH_3$), 7.27–7.85 (10 H, m, $OSi(C_6H_5)_2C(CH_3)_3$). Anal. Calcd for $C_{28}H_{38}O_7Si$: C, 65.34; H, 7.44. Found: C, 65.48; H, 7.39.

To a stirred solution of the above crude **48** in THF (250 mL) was added tetrabutylammonium fluoride (1 M in THF, 82.4 mL, 82.4 mmol), and the mixture was stirred for 2 h and evaporated. The residue was chromatographed on silica gel (550 g, ethyl acetate/hexane, 1:10 to 1:2), and fractions corresponding to R_f 0.33 (ethyl acetate/hexane, 1:1) were evaporated to afford **49** (9.60 g, 51% from **45**) as a colorless syrup. **49**: $[\alpha]^{27}_D$ −5.2° (*c* 1.07, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3580, 2990, 2950, 1730, 1440, 1385, 1370, 1160, 1030 cm^{-1}; ^1H NMR δ 1.33, 1.45 (3 H × 2, each s, $C(CH_3)_2$), 2.00–2.22 (2 H, m, H-3,3′), 2.28 (1 H, br s, OH), 3.47–4.33 (5 H, m, H-2,4,5,6,6′), 3.75, 3.80 (3 H × 2, each s, 2 × $COOCH_3$). Anal. Calcd for $C_{12}H_{20}O_7$: C, 52.16; H, 7.30. Found: C, 51.92; H, 7.21.

Cyclization of Compound 9 by Pyridinium Chlorochromate (PCC) Oxidation and Successive Acetylation. Dimethyl (2*S*,3*R*,4*S*,5*S*)-2-Acetoxy-3,4,5-tris(benzyloxy)cyclohexane-1,1-dicarboxylate (10). To a stirred solution of **9** (102 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) were added PCC (123 mg, 0.57 mmol) and molecular sieves (4A, powder, 50 mg). The mixture was stirred for 2 h and applied on a silica gel short column (3 g). The column was eluted with ether, and the ethereal elutes corresponding to R_f 0.65 to 0.38 (ethyl acetate/hexane, 1:3) were evaporated. The residue was acetylated with acetic anhydride (1 mL) in pyridine (2 mL) for 70 h. The mixture was evaporated, and the residue was partitioned between ethyl acetate (20 mL) and water (20 mL). The aqueous layer was extracted with ethyl acetate (20 mL × 2). The combined extracts were dried (Na_2SO_4) and evaporated. The residue was purified by PTLC (ethyl acetate/hexane, 1:3) affording **10** (75 mg, 69%), mp 134–136 °C. **10**: TLC R_f 0.40 (ethyl acetate/hexane, 1:3); $[\alpha]^{32}_D$ +12.1° (*c* 0.97, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3025, 2950, 2850, 1745, 1730, 1490, 1450, 1430, 1360, 1260, 1220, 1060 cm^{-1}; ^1H NMR δ 1.92 (3 H, s, $OCOCH_3$), 2.20–2.73 (2 H, m, H-6,6′), 3.64 (6 H, s, 2 × $COOCH_3$), 3.43–4.08 (3 H, m, H-3,4,5), 4.43–4.90 (6 H, m, 3 × $OCH_2C_6H_5$), 5.77 (1 H, d, J = 12 Hz, H-2), 7.30 (15 H, s, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{33}H_{36}O_9$: C, 68.73; H, 6.29. Found: C, 68.57; H, 6.35.

Cyclization of Compound 23 by PCC Oxidation and Successive Acetylation. Dimethyl (2*S*,3*R*,4*R*,5*S*)- (24) and (2*R*,3*R*,4*R*,5*S*)-2-Acetoxy-3,4,5-tris(benzyloxy)cyclohexane-1,1-dicarboxylates (24′). Compound **23** (115 mg) was treated with PCC (138 mg) and molecular sieves (50 mg) for 11 h. The mixture was passed through silica gel column by using ether for elution. After evaporation of the elute, the residue was acetylated with acetic anhydride (1.5 mL) in pyridine (3 mL) for 4 days. Extractive workup and PTLC purification as described above afforded **24** (42 mg, 34%) and **24′** (25 mg, 21%). **24** as a colorless syrup: TLC R_f 0.54 (ethyl acetate/hexane, 2:5); $[\alpha]^{21}_D$ −3.4° (*c* 1.12, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 1730, 1450, 1435, 1360, 1255, 1070 cm^{-1}; ^1H NMR δ 1.90 (3 H, s, $OCOCH_3$), 1.95–2.61 (2 H, m, H-6,6′), 3.68 (6 H, s, 2 × $COOCH_3$), 3.41–4.38 (3 H, m, H-3,4,5), 4.58–4.88 (6 H, m, 3 × $OCH_2C_6H_5$), 5.28 (1 H, d, J = 9 Hz, H-2), 7.23–7.39 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{33}H_{36}O_9$: C, 68.73; H, 6.29. Found: C, 68.52; H, 6.29. **24′** as a colorless syrup: TLC R_f 0.61 (ethyl acetate/hexane, 2:5); $[\alpha]^{21}_D$ −12.8° (*c* 1.27, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 2860, 1745, 1450, 1435, 1370, 1220, 1090 cm^{-1}; ^1H NMR δ 2.05 (3 H, s, $OCOCH_3$), 2.13–2.70 (2 H, m, H-6,6′), 3.63, 3.68 (3 H × 2, each s, 2 × $COOCH_3$), 3.25–3.83 (3 H, m, H-3,4,5), 4.45–4.90 (6 H, m, 3 × $OCH_2C_6H_5$), 6.10 (1 H, d, J = 3 Hz, H-2), 7.23–7.41 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{33}H_{36}O_9$: C, 68.73; H, 6.29. Found: C, 68.52; H, 6.25.

Cyclization of Compound 37 by PCC Oxidation and Successive Acetylation. Dimethyl (2*R*,3*R*,4*S*,5*R*)- (38) and (2*S*,3*R*,4*S*,5*R*)-2-Acetoxy-3,4,5-tris(benzyloxy)cyclohexane-1,1-dicarboxylates (38′). Compound **37** (133 mg) was oxidized with PCC (214 mg) and molecular sieves (50 mg) for 15 h. After acetylation of the cyclized products and purification by PTLC (ethyl acetate/hexane, 1:5), **38** (69 mg, 48%) and **38′** (7 mg, 5%) were obtained. **38** as a colorless syrup: TLC R_f 0.58 (ethyl acetate/hexane, 2:5); $[\alpha]^{21}_D$ −21.6° (*c* 1.02, $CHCl_3$) (lit.[11b] $[\alpha]^{25}_D$ −22.8° (*c* 0.64, $CHCl_3$)). The ^1H NMR spectrum of **38** was superimposable with that of the authentic sample.[11b] **38′** as a colorless syrup: TLC R_f 0.67 (ethyl acetate/hexane, 2:5); $[\alpha]^{21}_D$ −13.3° (*c* 1.13, $CHCl_3$) (lit.[11b] $[\alpha]^{25}_D$ −17.5° (*c* 0.71, $CHCl_3$)). The ^1H NMR spectrum was superimposable with that of the authentic sample.[11b]

Cyclization of Compound 49 by PCC Oxidation and Successive Acetylation. Dimethyl (2*S*,3*S*,4*S*)- (50) and (2*R*,3*S*,4*S*)-2-Hydroxy-3,4-(isopropylidenedioxy)cyclopentane-1,1-dicarboxylates (50′) and Their 2-Acetoxy Derivatives 51 and 51′. To a stirred solution of **49** (2.38 g, 8.61 mmol) in CH_2Cl_2 (50 mL) were added PCC (5.57 g, 25.8 mmol) and molecular sieves (4A, powder, 2.40 g). The mixture was stirred for 2 h and charged on silica gel (150 g). The column was eluted with ether to afford a mixture of **50** and **50′** as a semicrystalline syrup, which was acetylated with acetic anhydride (23 mL) in pyridine (36 mL) for 19 h. The mixture was evaporated and the residue was chromatographed on silica gel (90 g, ethyl acetate/hexane, 1:6). Fractions corresponding to R_f 0.49 (ethyl acetate/hexane, 1:2) were evaporated to afford an inseparable mixture of **51** and **51′** (1.99 g, 73%) as a colorless syrup. In a small-scale experiment (**49**, 400 mg), the crude **50** and **50′** were separated by repeated silica gel chromatography (ethyl acetate/hexane, 1:16) to afford pure **50** (128 mg, 32%) and **50′** (32 mg, 8%). **50**: TLC R_f 0.38 (ethyl acetat/hexane, 1:2); mp 94.5–96 °C; $[\alpha]^{27}_D$ −15.4° (*c* 1.31, $CHCl_3$); IR ν_{max}^{KBr} 3490, 3000, 2960, 1735, 1445, 1385, 1295, 1260, 1235, 1210, 1160, 1060 cm^{-1}; ^1H NMR δ 1.24, 1.36 (3 H × 2, each s, $C(CH_3)_2$), 2.52 (2 H, d, J = 3 Hz, H-5,5′), 2.97–3.13 (1 H, br s, OH), 3.75 (6 H, s, 2 × $COOCH_3$), 4.47 (1 H, dd, J = 6 and 2.5 Hz, H-3), 4.67–4.90 (2 H, m, H-2,4); high-resolution mass spectrum, calcd for $C_{12}H_{19}O_7$ m/z 275.1130, found; M + H, 275.1134. Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.61. Found: C, 52.47; H, 6.64. **50′**: TLC R_f 0.43 (ethyl acetate/hexane, 1:2); mp 90.5–92 °C; $[\alpha]^{21}_D$ +39.9° (*c* 1.57, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3500, 2990, 2955, 1720, 1435, 1385, 1275, 1200, 1160, 1090 cm^{-1}; ^1H NMR δ 1.32, 1.42 (3 H × 2, each s, $C(CH_3)_2$), 2.11 (1 H, dd, J = 15 and 5 Hz, H-5), 2.70 (1 H, d, J = 15 Hz, H-5′), 3.80, 3.82 (3 H × 2, each s, 2 × $COOCH_3$), 4.13–4.58 (2 H, m, H-3, OH), 4.58–4.80 (2 H, m, H-2,4); high-resolution mass spectrum, calcd for $C_{12}H_{18}O_7$ m/z 274.1050, found, M, 274.1046. Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.61. Found: C, 52.41; H, 6.53.

Each **50** and **50′** were acetylated in the usual manner to provide **51** (90%) and **51′** (96%). **51** as a colorless syrup: $[\alpha]^{28}_D$ −36.8° (*c* 1.12, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2995, 2980, 1740, 1435, 1385, 1380, 1280, 1220, 1160, 1110 cm^{-1}; ^1H NMR δ 1.24, 1.36 (3 H × 2, each s, $C(CH_3)_2$), 2.01 (3 H, s, $OCOCH_3$), 2.67 (2 H, d, J = 5 Hz, H-5,5′), 3.67, 3.77 (3 H × 2, each s, 2 × $COOCH_3$), 4.42 (1 H, d, J = 5 Hz, H-3), 4.53–4.87 (1 H, m H-4), 5.85 (1 H, s, H-2); high-resolution mass spectrum, calcd for $C_{14}H_{21}O_8$ m/z 317.1235, found, M + H, 317.1236. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 52.92; H, 6.21. **51′**: mp 74.5–76 °C; $[\alpha]^{19}_D$ +105.8° (*c* 1.44, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2985, 2950, 1730, 1430, 1285, 1220, 1100 cm^{-1}; ^1H NMR δ 1.29, 1.45 (3 H × 2, each s, $C(CH_3)_2$), 2.08 (3 H, s, $OCOCH_3$), 2.45 (1 H, dd, J = 14 and 7 Hz, H-5), 2.75 (1 H, dd, J = 7 and 5 Hz, H-5′), 3.73, 3.75 (3 H × 2, each s, 2 × $COOCH_3$), 4.57–4.97 (2 H, m, H-3,4), 5.53 (1 H, d, J = 5 Hz, H-2). Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.28; H, 6.19.

Demethoxycarbonylation Accompanied by β-Elimination of the Acetoxyl Groups of Compounds 10, 24, 24′, and 38.

Methyl (3*R*,4*S*,5*S*)- (11), (3*R*,4*R*,5*S*)- (25), and (3*R*,4*S*,5*R*)-3,4,5-Tris(benzyloxy)-1-cyclohexene-1-carboxylates (39). A solution of **10** (145 mg, 0.05 mmol) in aqueous Me_2SO (water/Me_2SO, 1:10, v/v, 6.6 mL) containing NaCl (59 mg) was heated from 120 to 170 °C for 1 h. After cooling to ambient temperature, the solution was diluted with ethyl acetate (80 mL) and washed with water (80 mL × 3). The organic layer was dried (Na_2SO_4) and evaporated. The residue was purified by PTLC (ethyl acetate/hexane, 1:4) affording **11** (81 mg, 70%) as a colorless syrup. **11**: TLC R_f 0.56 (ethyl acetate/hexane, 1:4); $[\alpha]^{29}_D$ −53.3° (*c* 1.11, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2950, 2860, 1710, 1450, 1350, 1260, 1065 cm^{-1}; ^1H NMR δ 2.07–2.31 (1 H, m, H-6), 2.57–2.83 (1 H, m, H-6′), 3.74 (3 H, s, $COOCH_3$), 3.60–4.27 (3 H, m, H-3,4,5), 4.50–4.95 (6 H, m, 3 × $OCH_2C_6H_5$), 6.78–6.88 (1 H, m, H-2), 7.35 (15 H, s, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{29}H_{30}O_5$ *m/z* 458.2091, found, M, 458.2083.

By the analogous reaction conditions described above, **24** and **24′** were converted to **25** in 50% and 66% yield, respectively. The mixture of **24** and **24′** (approximately 3 to 2) (960 mg) was also converted to **25** (365 mg) in 48% yield. **25**: colorless syrup; TLC R_f 0.55 (ethyl acetate/hexane, 1:4); $[\alpha]^{22}_D$ −32.8° (*c* 0.90, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 2870, 1710, 1655, 1495, 1455, 1440, 1340, 1255, 1090 cm^{-1}; ^1H NMR δ 2.30–2.95 (2 H, m, H-6,6′), 3.74 (3 H, s, $COOCH_3$), 3.57–4.36 (3 H, m, H-3,4,5), 4.68–5.04 (6 H, m, 3 × $OCH_2C_6H_5$), 6.76–6.90 (1 H, m, H-2), 7.26–7.46 (15 H, m, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{29}H_{30}O_5$ *m/z* 458.2090, found, M, 458.2086.

Compound **38** (430 mg) was converted to **39** (157 mg, 46%) by the analogous reaction conditions and workup as case of **11**. **39**: colorless syrup; TLC R_f 0.53 (ethyl acetate/hexane, 1:4); $[\alpha]^{18.5}_D$ −104.0° (*c* 1.18, $CHCl_3$) (lit.[11b] $[\alpha]^{26}_D$ −114° (*c* 0.15, $CHCl_3$)). The ^1H NMR spectrum of **39** was superimposable with that of the authentic sample.[11b]

Lithium Aluminum Hydride Reduction of Compounds 11 and 25. (3*R*,4*S*,5*S*)- (12) and (3*R*,4*R*,5*S*)-3,4,5-Tris(benzyloxy)-1-cyclohexene-1-methanols (26). To a stirred suspension of lithium aluminum hydride (52 mg, 1.38 mmol) in THF (8 mL) was added a THF (7 mL) solution of **11** (317 mg, 0.69 mmol) at −15 °C, and the mixture was stirred at the temperature for 15 min. To the mixture was added ethyl acetate (5 mL) and stirred for 20 min at ambient temperature. The resulting insoluble solids were removed through Celite pad, and the filtrate was evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:3) affording **12** (261 mg, 88%) as a colorless syrup. **12**: TLC R_f 0.47 (ethyl acetate/toluene, 1:1); $[\alpha]^{28}_D$ −49.8° (*c* 1.23, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3600, 3000, 2860, 1660, 1495, 1450, 1360, 1180, 1080 cm^{-1}; ^1H NMR δ 2.15–2.53 (2 H, m, H-6,6′), 3.34–3.71 (2 H, m, H-3,5), 3.90–4.25 (4 H, m, H-4, CH_2OH), 4.50–4.93 (6 H, m, 3 × $OCH_2C_6H_5$), 5.57–5.65 (1 H, m, H-2), 7.35 (15 H, s, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{28}H_{30}O_4$ *m/z* 430.2141, found M, 430.2127. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 77.75; H, 7.13.

By the analogous reaction conditions, compound **25** (365 mg) was converted to **26** (300 mg) in 88% yield. **26**: colorless syrup: TLC R_f 0.14 (ethyl acetate/hexane, 1:3); $[\alpha]^{22}_D$ −41.4° (*c* 1.16, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3600, 3000, 2860, 1490, 1455, 1360, 1075 cm^{-1}; ^1H NMR δ 2.10–2.60 (2 H, m, H-6,6′), 3.63–4.28 (6 H, m, H-3,4,5, CH_2OH), 4.54–5.03 (6 H, m, 3 × $OCH_2C_6H_5$), 5.66 (1 H, br s, H-2), 7.33 (15 H, s, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{28}H_{30}O_4$ *m/z* 430.2143, found, M, 430.2154. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 78.25; H, 7.10.

Diisobutylaluminum Hydride Reduction of Compound 39. (3*R*,4*S*,5*R*)-3,4,5-Tris(benzyloxy)-1-cyclohexene-1-methanol (40). To a stirred solution of **39** (220 mg, 0.48 mmol) in CH_2Cl_2 (15 mL) was added diisobutylaluminum hydride (1.5 M toluene, 2.16 mL, 3.24 mmol) at −78 °C, and the mixture was stirred for 3 h. The mixture was quenched with saturated aqueous NH_4Cl (1 mL) and 4% aqueous HCl (2 mL) and diluted with water (100 mL). The aqueous mixture was extracted with CH_2Cl_2 (100 mL × 3). The extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:3) affording **40** (192 mg, 93%) as a colorless syrup. **40**: TLC R_f 0.64 (ethyl acetate/tluene, 1:1); $[\alpha]^{19.5}_D$ −61.7° (*c* 1.54, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3580, 3000, 2920, 2860, 2490, 1450, 1360, 1090 cm^{-1}; ^1H NMR δ 1.67–2.68 (2 H, m, H-6,6′), 3.24–4.31 (6 H, m, H-3, 4,5,CH_2OH), 4.53–4.89 (6 H, m, 3 × $OCH_2C_6H_5$), 5.66–5.79 (1 H, m, H-2), 7.34 (15 H, s, 3 × $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{28}H_{30}O_4$: *m/z* 430.2142, found, M, 430.2147. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 77.94; H, 7.00.

Demethoxycarbonylation of Mixture of 51 and 51′ and Successive Diisobutylaluminum Hydride Reduction. (3*R*,4*S*)-3,4-(Isopropylidenedioxy)-1-cyclopentene-1-methanol (53). An aqueous Me_2SO solution (Me_2SO, 29 mL, and water, 2 mL) of a 4 to 1 mixture of **51** and **51′** (850 mg, 2.7 mmol) containing NaCl (471 mg, 8.1 mmol) was heated from 110 to 160 °C for 4 h, and the solution was kept stirring at 160 °C for 6 h. After cooling to ambient temperature, the solution was diluted with CH_2Cl_2 (150 mL). The solution was washed with water (150 mL × 3), dried (Na_2SO_4), and evaporated to ca. 15 mL. The concentrate contained methyl (3*R*,4*S*)-3,4-(isopropylidenedioxy)-1-cyclopentene-1-carboxylate (**52**) and was subjected to the next step without purification. In a small-scale experiment, the concentrate was passed through silica gel column (hexane and then ethyl acetate/hexane, 1:20) to give **52** as a colorless syrup: $[\alpha]^{20}_D$ −45.9° (*c* 1.03, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2930, 1720, 1620, 1435, 1375, 1300, 1210, 1180, 1150, 1100 cm^{-1}; ^1H NMR δ 1.34, 1.38 (3 H × 2, each s, $C(CH_3)_2$), 2.07–2.87 (2 H, m, H-5,5′), 3.77 (3 H, s, $COOCH_3$), 4.80 (1 H, dt, *J* = 6 and 3 Hz, H-4), 5.17 (1 H, dt, *J* = 6 and 2 Hz, H-3), 6.61 (1 H, q, *J* = 2 Hz, H-2). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.92; H, 7.08.

To a stirred solution of the above crude **52** (concentrate) in CH_2Cl_2 (30 mL) was added diisobutylaluminum hydride (1.5 M in toluene, 7.17 mL, 10.8 mmol) at −78 °C. The mixture was stirred at the temperature for 2 h and quenched with saturated aqueous NH_4Cl (2.4 mL), 4% aqueous HCl (1.2 mL), and water (2.4 mL) successively. After warming to ambient temperature, the mixture was diluted with CH_2Cl_2 (250 mL) and washed with water (250 mL). The aqueous layer was extracted with CH_2Cl_2 (250 mL × 5). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (20 g, ethyl acetate/hexane, 1:7 to 1:4), and fractions corresponding to R_f 0.33 (ethyl acetate/hexane 1:1) were evaporated to afford **53** (308 mg, 67%) as a colorless syrup: $[\alpha]^{21}_D$ −16.9° (*c* 1.09, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3600, 3440, 2990, 2930, 2860, 1715, 1650, 1445, 1425, 1380, 1370, 1270, 1150 cm^{-1}; ^1H NMR δ 1.35, 1.41 (3 H × 2, each s, $C(CH_3)_2$), 2.37 (1 H, br s, OH), 2.40–2.63 (2 H, m, H-5,5′), 4.18 (2 H, s, CH_2OH), 4.80 (1 H, dt, *J* = 7 and 3 Hz, H-4), 5.13 (1 H, dt, *J* = 7 and 2 Hz, H-3), 5.69 (1 H, q, *J* = 2 Hz, H-2). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.45; H, 8.21.

Hydroboration of Compound 12, Oxidative Treatment and Successive Acetylation. (1*S*,2*S*,3*R*,4*S*,5*S*)-2-Acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexane (13). To a stirred solution of **12** (233 mg, 0.54 mmol) in THF (8 mL) was added borane–THF complex (1.0 M in THF, 3.24 mL, 3.24 mmol) at 0 °C. The mixture was stirred at the temperature for 4 h and then quenched with water (1 mL). To the mixture were added 3 M aqueous NaOH (2 mL) at 0 °C and 35% aqueous H_2O_2 (3 mL) at ambient temperature. The mixture was stirred for 14 h, neutralized with 3 M HCl, and then evaporated. The residue was partitioned between ethyl acetate (80 mL) and water (80 mL), and the aqueous layer was extracted with ethyl acetate (80 mL × 2). The combined extracts were dried (Na_2SO_4) and evaporated. The resulting syrup was acetylated with acetic anhydride (3 mL) in pyridine (3 mL) for 35 h. The mixture was evaporated, and the residue was partitioned between ethyl acetate (80 mL) and water (80 mL). The aqueous layer was extracted with ethyl acetate (80 mL × 2). The combined extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:15), affording **13** (189 mg, 66%) as a colorless syrup. **13**: TLC R_f 0.27 (ethyl acetate/toluene, 1:8); $[\alpha]^{16}_D$ +6.3° (*c* 1.08, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2870, 1735, 1450, 1365, 1240, 1085 cm^{-1}; ^1H NMR δ 1.60–2.08 (3 H, m, H-1,6,6′), 1.97, 2.01 (3 H × 2, each s, 2 × $OCOCH_3$), 3.26 (1 H, dd, *J* = 10 and 3.5 Hz, H-3), 3.20–3.47 (1 H, m, H-5), 3.98 (2 H, d, *J* = 6 Hz, CH_2OAc), 4.10 (1 H, t, *J* = 3.5 Hz, H-4), 4.42–4.88 (6 H, m, 3 × $OCH_2C_6H_5$), 5.35 (1 H, t, *J* = 9 Hz, H-2), 7.20–7.48 (15 H, m, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 72.25; H, 6.81.

O-Debenzylation of Compound 13 and Successive Acetylation. (1*S*,2*S*,3*R*,4*S*,5*S*)-2,3,4,5-Tetraacetoxy-1-(acetoxymethyl)cyclohexane, Pseudo-β-L-mannopyranose Pentaacetate (14). A solution of **13** (158 mg, 0.30 mmol) in methanol (5 mL) containing a drop of acetic acid (pH 4) was hydrogenolyzed in the presence of palladium black in a Parr apparatus for 14 h. The catalyst was removed by filtration, and the filtrate was evaporated. The residue was acetylated with acetic anhydride (1.5 mL) in pyridine (1.5 mL) for 14 h. The mixture was evaporated, and the residue was chromatographed on silica gel (ethyl acetate/hexane, 1:4) affording **14** (59 mg, 52%) as colorless syrup. **14**: TLC R_f 0.27 (ethyl acetate/hexane, 2:3); $[\alpha]^{19.5}_D$ −1.1° (*c* 1.26, $CHCl_3$) (lit.[6] pseudo-β-D-mannopyranose pentaacetate, $[\alpha]^{20}_D$ +2.9° (*c* 1.28, $CHCl_3$)). The ^1H NMR spectrum of **14** was superimposable with that of the known DL-**14**.[16] High-resolution mass spectrum, calcd for $C_{17}H_{25}O_{10}$ *m/z* 389.1446, found, M + H, 389.1454. Anal. Calcd for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23. Found: C, 52.31; H, 6.28.

Hydroboration of Compound 26, Oxidative Treatment and Successive Acetylation. (1*S*,2*S*,3*R*,4*R*,5*S*)- (27) and (1*R*,2*R*,3*R*,4*R*,5*S*)-2-Acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexanes (27′). Hydroboration of **26** (116 mg) with borane–THF complex (1.08 mL) at 0 °C for 30 min and then at ambient temperature for 1 h and oxidation with 35% aqueous H_2O_2 (1.5 mL) in the presence of 3 M aqueous NaOH (3 mL) followed by acetylation, provided **27** (96 mg, 67%) and **27′** (16 mg, 11%) after PTLC separation (ethyl acetate/hexane, 2:9). **27**: TLC R_f 0.29 (ethyl acetate/hexane, 1:4); mp 64–66 °C; $[\alpha]^{20.5}_D$ −5.3° (*c* 1.13, $CHCl_3$); IR ν_{max}^{KBr} 3010, 2940, 2900, 1735, 1450, 1370, 1240, 1060 cm^{-1}. The ^1H NMR spectrum of **27** was superimposable with that of the known 1*R*,2*R*,3*S*,4*S*,5*R* enantiomer.[11e] Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 71.96; H, 6.87. **27′**: colorless syrup; TLC R_f 0.33 (ethyl acetate/hexane, 1:4); $[\alpha]^{23}_D$ +14.0° (*c* 1.00, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2920, 2870, 1730, 1450, 1370, 1240, 1065 cm^{-1}. The ^1H NMR spectrum of **27′** was superimposable with that of the known 1*S*,2*S*,3*S*,4*S*,5*R* enantiomer.[11c,e] Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 71.89; H, 6.80.

O-Debenzylation of Compounds 27 and 27′ and Successive Acetylation. (1*S*,2*S*,3*R*,4*R*,5*S*)- (28) and (1*R*,2*R*,3*R*,4*R*,5*S*)-2,3,4-Tetraacetoxy-1-(acetoxymethyl)cyclohexanes (28′), Pseudo-β-L-glucopyranose Pentaacetate and Pseudo-α-D-altropyranose Pentaacetate. Hydrogenolysis of compound **27** (76 mg) followed by acetylation as described in preparation of **14** afforded **28** as crystals in a quantitative yield. **28**: TLC R_f 0.34 (ethyl acetate/hexane, 2:3); mp 111–112 °C, mp for the D-enantiomer (lit.[4] mp 115–116 °C, lit.[11e] mp 114–116 °C); $[\alpha]^{19}_D$ −7.4° (*c* 1.78, $CHCl_3$) ($[\alpha]_D$ for the D-enantiomer, lit.[4] $[\alpha]^{20}_D$ +13.8° (*c* 1.0, $CHCl_3$), lit.[11e] $[\alpha]^{23}_D$ +4.4° (*c* 1.23, $CHCl_3$)); IR $\nu_{max}^{CHCl_3}$ 3020, 2940, 1745, 1420, 1365, 1240, 1030 cm^{-1}. The ^1H NMR spectrum of **28** was superimposable with those of the D-**28**[11e] and the DL-**28**.[16,20] High-resolution mass spectrum, calcd for $C_{17}H_{25}O_{10}$ *m/z* 389.1446, found, M + H, 389.1444. Anal. Calcd for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23. Found: C, 52.77; H, 6.17.

Analogously, compound **27′** (25 mg) was converted to **28′** in 65% yield as a colorless syrup.[25] **28′**: TLC R_f 0.30 (ethyl acetate/hexane, 2:3); $[\alpha]^{24}_D$ +14.4° (*c* 1.36, $CHCl_3$) ($[\alpha]_D$ for the L-enantiomer, lit.[11c,e] $[\alpha]^{27}_D$ −13.7° (*c* 1.36, $CHCl_3$)); IR $\nu_{max}^{CHCl_3}$ 3020, 2940, 2850, 1440, 1430, 1370, 1235, 1040 cm^{-1}. The ^1H NMR spectrum of **28′** was superimposable with those of the known L-**28′**[11c,e] and the DL-**28′**.[21] High-resolution mass spectrum, calcd for $C_{17}H_{25}O_{10}$ *m/z* 389.1445, found, M + H, 389.1443. Anal. Calcd for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23. Found: C, 52.38; H, 6.14.

Hydroboration of Compound 40, Oxidative Treatment and Successive Acetylation. (1*S*,2*S*,3*R*,4*S*,5*R*)-2-Acetoxy-1-(acetoxymethyl)-3,4,5-tris(benzyloxy)cyclohexane (41). Hydroboration of **40** (226 mg) with borane–THF (3.68 mL) at 0 °C for 15 min and then at ambient temperature for 2 h and oxidation with 35% aqueous H_2O_2 (6 mL) in the presence of 3 M aqueous NaOH (4 mL) followed by acetylation, provided **41** (185 mg, 66%) as a colorless syrup. **41**: TLC R_f 0.52 (ethyl acetate/hexane, 1:3); $[\alpha]^{25}_D$ −18.8° (*c* 1.04, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2900, 1725, 1450, 1265, 1240, 1200, 1100 cm^{-1}; ^1H NMR δ 1.50–2.18 (2 H, m, H-6,6′), 2.00, 2.02 (3 H × 2, each s, 2 × $OCOCH_3$), 3.60–4.10 (6 H, m, H-1,3,4,5, CH_2OAc), 4.35–4.91 (6 H, m, 3 × $OCH_2C_6H_5$), 5.37 (1 H, t, *J* = 12 Hz, H-2), 7.31 (15 H, s, 3 × $OCH_2C_6H_5$). Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 71.91; H, 6.81.

O-Debenzylation of Compound 41 and Successive Acetylation. (1*S*,2*S*,3*R*,4*S*,5*R*)-2,3,4,5-Tetraacetoxy-1-(acetoxymethyl)cyclohexane, Pseudo-α-L-mannopyranose Pentaacetate (42). Hydrogenolysis of compound **41** (80 mg) followed by acetylation as described above afforded **42** (57 mg, 97%) as crystals. **42**: TLC R_f 0.38 (ethyl acetate/hexane, 2:3); mp 84–86 °C; $[\alpha]^{28}_D$ −38.5° (*c* 1.04, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2980, 2940, 1740, 1370, 1240, 1035 cm^{-1}. The ^1H NMR spectrum of **42** was superimposable with that of the known DL-**42**.[16] High-resolution mass spectrum, calcd for $C_{17}H_{25}O_{10}$ *m/z* 389.1446, found, M + H, 389.1457. Anal. Calcd for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23. Found: C, 52.40; H, 6.15.

Hydroboration of Compound 53, Oxidative Treatment and Successive Acetylation. (1*S*,2*S*,3*S*,4*S*)- (54) and (1*R*,2*R*,3*S*,4*S*)-2-Acetoxy-1-(acetoxymethyl)-3,4-(isopropylidenedioxy)cyclopentanes (54′). To a stirred solution of **53** (1.02 g, 5.99 mmol) in THF (45 mL) was added borane–THF complex (1.0 M in THF, 24.0 mL, 24.0 mmol) at 0 °C, and the mixture was stirred at the temperature for 2.5 h. To the mixture were added water (16 mL) and 3 M aqueous NaOH (28 mL) at 0 °C. After the mixture was warmed to ambient temperature, 35% aqueous H_2O_2 (30 mL) was added. The mixture was stirred for 2 h, and unsaturated aqueous sodium sulfite (30 mL) was added and the solution then evaporated. To the residue was added ethanol (200 mL), and the insoluble solids were removed by filtration. The filtrate was evaporated, and the residue was applied on silica gel (40 g, ethanol/toluene, 1:10). Fractions corresponding to R_f 0.51 to 0.29 (ethanol/toluene, 1:5), in which a compound possessing R_f 0.37 was predominant, were combined and evaporated. The residue was acetylated with acetic anhydride (16 mL) in pyridine (16 mL) for 24 h. The mixture was diluted with ethyl acetate (200 mL) and washed with water (100 mL), saturated aqueous $NaHCO_3$ (60 mL × 4), and saturated aqueous NaCl (100 mL) successively. The organic layer was dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:10). Fractions corresponding to R_f 0.66 (ethyl acetate/hexane, 2:3) were evaporated to afford **54** (1.19 g, 73%), and fractions corresponding to R_f 0.63 were evaporated to afford **54′** (0.012 g, 0.7%). **54**: colorless syrup; $[\alpha]^{14}_D$ +7.9° (*c* 1.07, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2980, 2920, 1730, 1430, 1365, 1230, 1155, 1030 cm^{-1}; ^1H NMR δ 1.27, 1.50 (3 H × 2, each s, $C(CH_3)_2$), 2.03, 2.06 (3 H × 2, each s, 2 × $OCOCH_3$), 1.67–2.63 (3 H, m, H-1,5,5′), 4.18 (2 H, dd, *J* = 6 and 1.5 Hz, CH_2OAc), 4.48 (1 H, dd, *J* = 6 and 1 Hz, H-3), 4.75 (1 H, dt, *J* = 6 and 2 Hz, H-4), 5.07 (1 H, dd, *J* = 2 and 1 Hz, H-2). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.50; H, 7.31. **54′**: mp 57.5–58.5 °C; $[\alpha]^{26}_D$ +102.5° (*c* 0.71, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 2850, 1730, 1455, 1440, 1385, 1375, 1235, 1210, 1165, 1130 cm^{-1}; ^1H NMR δ 1.32, 1.49 (3 H × 2, each s, $C(CH_3)_2$), 1.80–2.76 (3 H, m, H-1,5,5′), 2.07, 2.13 (3 H × 2, each s, 2 × $OCOCH_3$), 4.15 (2 H, dd, *J* = 5 and 2 Hz, CH_2OAc), 4.37–4.82 (3 H, m, H-2,3,4). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.10; H, 7.34.

(1*S*,2*S*,3*S*,4*S*)-2,3,4-Triacetoxy-1-(acetoxymethyl)cyclopentane (55). From 53. After hydroboration of **53** (153 mg), oxidative workup with 35% aqueous H_2O_2, addition of aqueous sodium sulfite, and evaporation of the reaction mixture, the residue was dissolved in 90% aqueous acetic acid (20 mL), and the solution was refluxed for 3 h and then evaporated. The residue was acetylated with acetic anhydride (10 mL) in pyridine (10 mL) for 3 h. The mixture was evaporated. The residue was partitioned between ethyl acetate (100 mL) and water (100 mL), and the aqueous layer was extracted with ethyl acetate (100 mL × 2). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ethyl acetate/hexane, 1:6), and fractions corresponding to R_f 0.48 (ethyl acetate/hexane, 1:1) were evaporated to afford **55** (181 mg, 64%) as a colorless syrup. **55**: $[\alpha]^{23}_D$ +4.1° (*c* 1.07, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2960, 2930, 2870, 2860, 1735, 1455, 1365, 1230, 1040 cm^{-1}; ^1H NMR δ 1.57–2.57 (3 H, m, H-1,5,5′), 2.08 (12 H, s, 4 × $OCOCH_3$), 4.17 (2 H, dd, *J* = 6.5 and 3.5 Hz, CH_2OAc), 5.07–5.40 (3 H, m, H-2,3,4); high-

(25) The L-enantiomer of **28′**, pseudo-α-L-altropyranose pentaacetate, was obtained as crystals (mp 84–85 °C);[11c,e] however, we could not obtain compound **28′** as crystals up to now.

resolution mass spectrum, calcd for $C_{14}H_{21}O_8$ m/z 317.1234, found M + H, 317.1222. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.11; H, 6.37. Found: C, 53.31; H, 6.61.

From **54**. Compound **54** (8 mg) was hydrolyzed with 80% aqueous acetic acid at ambient temperature for 48 h and evaporated. The residue was acetylated. Compound **55** (7 mg, 79%) was obtained after silica gel chromatography.

(1*S*,2*S*,3*S*,4*S*)-2,3,4-Trihydroxy-1-(hydroxymethyl)-cyclopentane (56). To a stirred solution of **55** (142 mg, 0.45 mmol) in methanol (4 mL) was added sodium methoxide (1 M in methanol, 1.3 mL, 1.3 mmol), and the mixture was stirred at 0 °C for 3 h. The solution was neutralized with Amberlite IR 120 (H^+), and the resin was removed by filtration to afford **56** (64 mg, 97%) as crystals. **56**: mp 103-104 °C; $[\alpha]^{23}_D$ -8.8° (*c* 0.56, MeOH); ^{1}H NMR (CD_3OD) δ 1.23-1.67 (1 H, m, H-1), 1.70-2.40 (2 H, m, H-5,5'), 3.30-5.43 (5 H, m, H-2,3,4, CH_2OH); high-resolution mass spectrum, calcd for $C_6H_{13}O_4$ m/z 149.0812, found M + H, 149.0783. Anal. Calcd for $C_6H_{12}O_4 \cdot {}^1/_4H_2O$: C, 47.20; H, 8.26. Found: C, 47.12; H, 8.16.

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Total Synthesis of (+)-Codonopsinine and Its Stereoisomers: Stereochemical Assignment of Natural (-)-Codonopsinine

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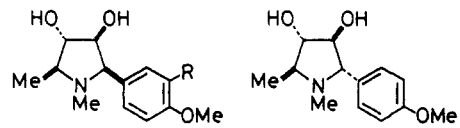
(+)-Codonopsinine [(+)-**1b**], the enantiomer of natural (-)-codonopsinine, and its stereoisomers, (2*R*,3*S*,4*S*,5*S*)-**1a**, (2*R*,3*S*,4*S*,5*R*)-**1c**, and (2*S*,3*S*,4*S*,5*R*)-**1d**, were synthesized in enantiomerically pure forms from diethyl L-tartrate via the common intermediate 4-*O*-benzyl-2,3-*O*-bis(methoxymethyl)-L-threose (**3**), thus leading to both stereochemical revision of codonopsinine from **1a** to **1b** and confirmation of the absolute configuration of natural codonopsinine to be 2*R*,3*R*,4*R*,5*R* [(-)-**1b**].

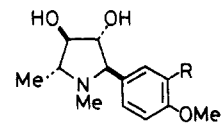
Codonopsinine and codonopsine, a new class of the 1,2,3,4,5-pentasubstituted pyrrolidine alkaloids isolated[1,2] from *Codonopsis clematidea*, have been shown to have structures assigned as **1** and **2**, respectively, by Russian workers.[3,4] In animal tests the latter has been found to possess hypotensive pharmacological activity with no effect on the central nervous system.[5] Shortly after the structure elucidation, in 1972 the Russian group[6] reported the relative stereochemistry for these alkaloids to be 2*R**,3*S**,4*S**,5*S** as shown in **1a** and **2a**, based on analyses of ^{1}H NMR coupling constants using the Karplus equation. However, vicinal coupling constants have been shown to be unreliable for assigning configurations of substituted pyrrolidines.[7] Thus, it seemed to us that the proposed assignments rested on dubious spectral interpretation, and hence, additional verification was desirable. In view of this, we recently reinvestigated the relative structure of codonopsinine by means of NOE experiments and chemical correlation that led to the revised structure **1b** for codonopsinine.[8] That study also revealed that the phthalimide intermediate for the synthesis of (+)-codonopsinine, originally assigned structure **6**,[9] actually possessed structure **7**, based on X-ray crystallographic analysis. In order to provide direct evidence for the structure of codonopsinine, we aimed to synthesize codonopsinine (**1b**) and all possible diastereoisomers (e.g., **1a**, **1c**, **1d**) with the vicinal hydroxy groups in the threo configuration (3*S*,4*S*) by utilizing the structurally established intermediates **6** and **7**.

In this paper, we describe the total synthesis of (+)-codonopsinine [(+)-**1b**] in detail[10] and its stereoisomers **1a**,

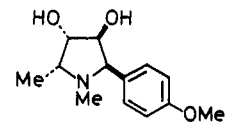


1a R = H
2a R = OMe

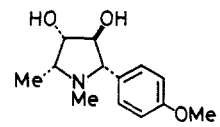
(+)-**1b**



(-)-**1b** R = H
(-)-**2b** R = OMe



1c



1d

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(10) In the preceding communication,[9] (+)-codonopsinine [(+)-**1b**] synthesized was represented by the wrong formula **1a**.

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