1270, 1160, 1075, 990, 735 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$) correspond excellently with the data reported for authentic 4;[2] MS *m/e* 342 (M^+), 283 (100), 255, 128, 127. UV (MeOH) λ_{max} 432, 408, 388, 364, 274, 226 nm. Anal. Calcd for $C_{21}H_{14}N_2O_3$: C, 73.67; H, 4.12; N, 8.18. Found: C, 73.57; H, 4.11; N, 8.18.

Fascaplysin (1). Peracetic acid (32%, 0.6 mL, 3 mmol) was added slowly to a stirred ice-cooled solution of 7 (0.26 g, 1 mmol), in THF (15 mL). The dark red solution was stirred at 0 °C for 20 min, and excess peracetic acid was decomposed by addition of a catalytic amount of 10% Pd/C. After 15 min the mixture was filtered through a pad of Celite, which was washed thoroughly with MeOH. The MeOH extract was concentrated in vacuo, and the residue was absorbed on silica gel and purified by vacuum liquid chromatography[31] (silica gel 60, Merck, 230–400 mesh, elution with gradually increasing amounts of AcOH [0–5%] in EtOH). The eluent was concentrated and redissolved in MeOH. Concentrated aqueous HCl (0.3 mL) was added, and the solution was allowed to stand for 1 h, concentrated, and dried (60 °C, ~1 Torr) to give 1 (0.26 g, 85%) as a red brown solid, which was identical (FTIR, ^1H NMR, MS, UV, and TLC) with an authentic sample.[32]

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Registry No. 1, 114719-57-2; 4, 132938-12-6; 5, 132911-52-5; 7, 222-22-0; 15, 129697-27-4; 17, 120-72-9; 18, 22980-09-2; 19, 65610-76-6; 20, 496-15-1; 21, 129697-28-5; 22, 129697-29-6; 25, 129697-31-0; 26, 141271-95-6; 27, 129697-33-2; 28, 141250-38-6; 29, 129697-30-9.

(31) (a) Pelletier, S. W.; Chokshi, H. P.; Desai, H. K. *J. Nat. Prod.* **1986**, *49*, 892. (b) Coll, J. C.; Bowden, B. F. *J. Nat. Prod.* **1986**, *49*, 934.

(32) A sample of fascaplysin and spectra were kindly provided by Professor Chris Ireland, University of Utah.

Synthesis of a Branched-Chain Inosose Derivative, a Versatile Synthon of N-Substituted Valiolamine Derivatives from D-Glucose[1]

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The synthesis of (1*S*)-(1(OH),2,4/1,3)-2,3,4-tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-5-oxo-1,2,3,4-cyclohexanetetrol (**7**), which is an important synthon for the synthesis of valiolamine (**8**)[2] and its N-substituted derivatives such as AO-128 (**9**)[3] having strong α-D-glucosidase inhibitory activity, is described. This branched-chain inosose derivative **7** has been prepared from the D-glucono-1,5-lactone derivative **2** which is readily available from D-glucose (**1**). The key step in the synthesis involves the stereospecific intramolecular carbocyclic ring closure of the 1-deoxy-2,6-heptodiulose derivatives **5a** and **5b** obtained by the oxidation of 2,3,4,6-tetra-*O*-benzyl-1-*C*-[bis(methylthio)methyl]-D-glucitol (**4a**) and 2,3,4,6-tetra-*O*-benzyl-1-*C*-(dichloromethyl)-D-glucitol (**4b**). The resulting branched-chain bis(methylthio)inosose derivative **6a** and dichloroinosose derivative **6b** have been converted to the desired branched-chain inosose derivative **7** by desulfurization of **6a** and dechlorination of **6b**.

Introduction

Valiolamine (**8**), (1*S*)-(1(OH),2,4,5/1,3)-5-amino-1-*C*-(hydroxymethyl)-1,2,3,4-cyclohexanetetrol is a pseudo-amino sugar first isolated from the fermentation broth of *Streptomyces hygroscopicus* subsp. *limoneus* and later semisynthesized by stereospecific conversion of valienamine to valiolamine.[2]

Valiolamine and its N-substituted derivatives have potent α-D-glucosidase inhibitory activity, and one of these derivatives, *N*-[2-hydroxy-1-(hydroxymethyl)ethyl]valiolamine (**9**; AO-128) is presently undergoing clinical trials as an oral antidiabetic agent.[3]

In this paper, we report a stereospecific synthetic method for preparing (1*S*)-(1(OH),2,4/1,3)-2,3,4-tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-5-oxo-1,2,3,4-cyclohexanetetrol (**7**), an important key compound in the synthesis of valiolamine and its N-substituted derivatives, which has been synthesized via its 6,6-bis(methylthio) and 6,6-dichloro derivatives (**6a** and **6b**) starting from 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**) which is readily available from D-glucose (**1**).

It is known that an intramolecular cyclization reaction (Wordworth–Emmons reaction) of the 1-deoxy-1-(dimethoxyphosphoryl)-D-*xylo*-2,6-heptodiulose derivative, obtained by chain-extension of tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**) with lithium dimethyl methylphosphonate, results in the formation of an unsaturated inosose derivative, because an elimination reaction in the β-hydroxy

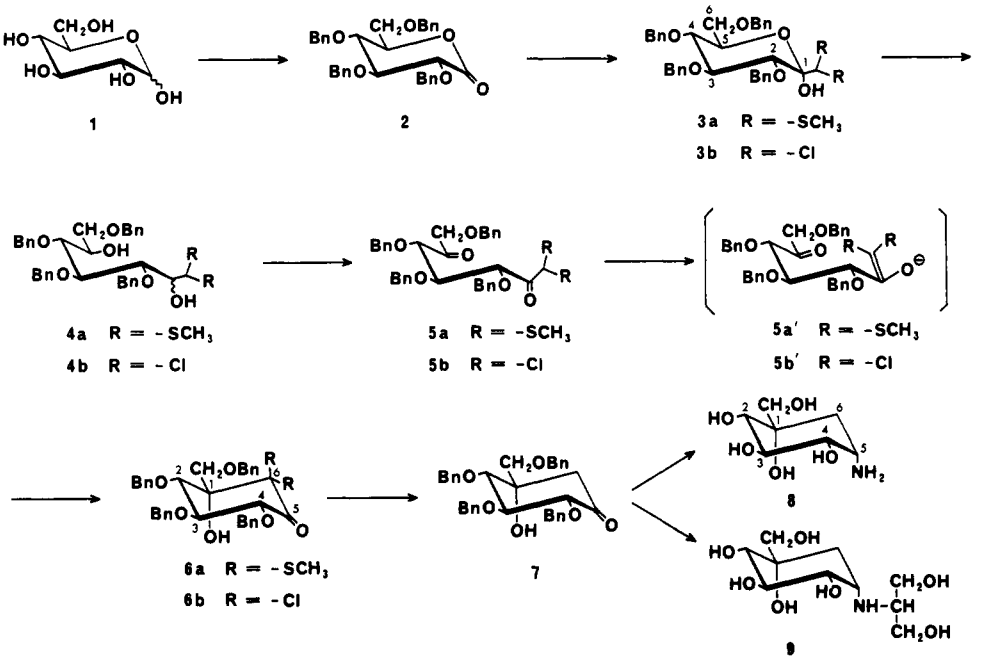
(1) Part of this work and related experimental results are disclosed in the following patent application: Horii, S.; Fukase, H. (Takeda Chemical Industries, Ltd.). Eur. Pat. Appl. EP 260,121, 1988; *Chem. Abstr.* **1988**, *109*, 129587v. Portions of this work were presented in Sept 1989 at the 198th National Meeting of the American Chemical Society. See: *Abstracts of Papers*. 198th National Meeting of the American Chemical Society; Washington, DC, 1989; Abstr. CARB 19.

(2) Horii, S.; Fukase, H.; Kameda, Y. *Carbohydr. Res.* **1985**, *140*, 185.

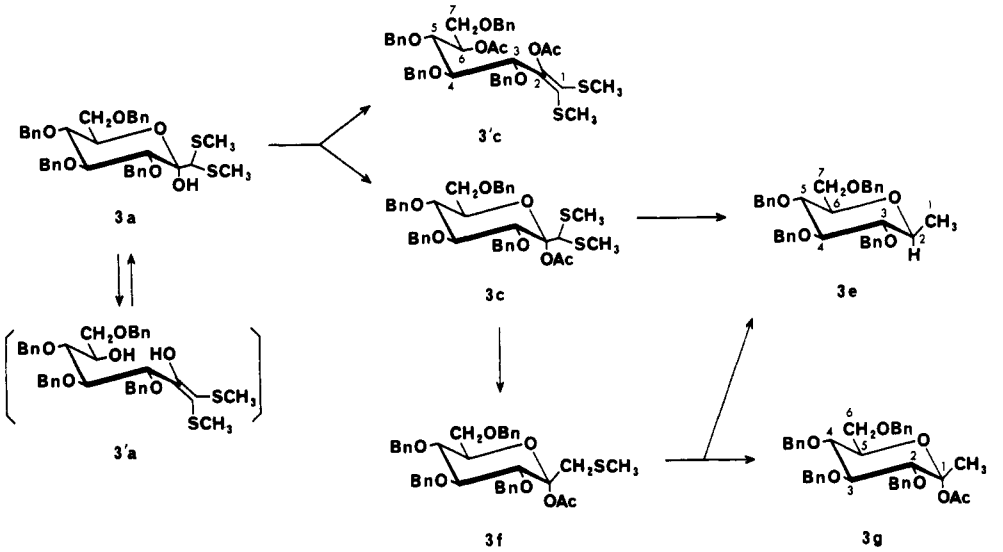
(3) Horii, S.; Fukase, H.; Matsuo, T.; Kameda, Y.; Asano, N.; Matsui, K. *J. Med. Chem.* **1986**, *29*, 1038. AO-128 is the preclinical study code number of **9**.

0022-3263/92/1957-3642$03.00/0

Scheme I



Scheme II



ketone system occurs.[4] To avoid this elimination and to get a saturated inosose, we planned to mask the α-protons of the β-hydroxy ketone system.

For this purpose, we chose bis(methylthio)methyl carbanion and dichloromethyl carbanion[5] as reagents for the chain extension of the D-glucono-1,5-lactone derivative **2**.

Results and Discussion

The reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**) with 2 equiv of bis(methylthio)methyl carbanion which was generated by treatment of bis(methylthio)methane with *n*-butyllithium[5a] gave the 1-*C*-[bis(methylthio)methyl]-D-glucopyranose derivative **3a** as a single tautomer. The formation of diadducts was not detected in the reaction mixture. On the other hand, unconsumed starting material was detected in the reaction with an equimolecular amount of bis(methylthio)methyl carbanion and the reaction resulted in a low yield.

The necessity of using 2 equiv of the carbanion can be explained as follows. The excess carbanion reagent is consumed in opening of the hemiacetal ring, and the resulting enol form **3'a** is resistant to the formation of diadducts. The mono[bis(methylthio)methyl] derivative presumably exists as the mono anion of the pyranose form **3a** and/or the dianion of the enolate form **3'a** in the reaction mixture, but it does not exist in the keto form which can react with the second carbanion to form the di[bis(methylthio)methyl] derivative.

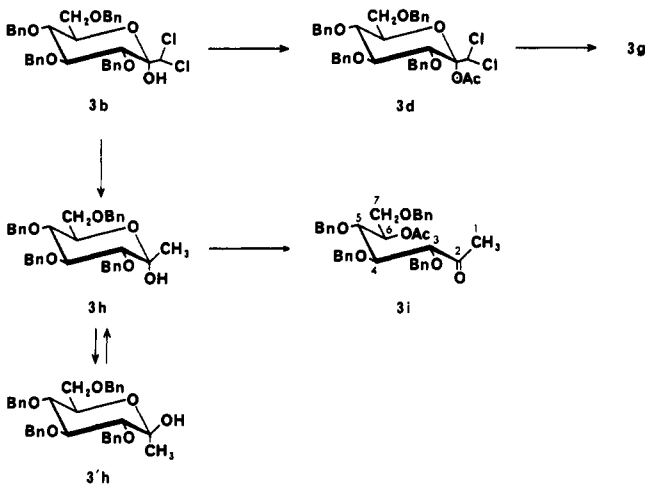
Similarly, reaction of **2** with 2 equiv of dichloromethyl carbanion, which was generated in situ from dichloromethane with LDA,[5c] gave the 1-*C*-(dichloromethyl) derivative **3b** in good yield.

The spectral data of **3a** and **3b** indicated that both products exist in a cyclic hemiacetal form, and their anomeric configuration was proved to be α as follows.

(4) (a) Horii, S.; Fukase, H. (Takeda Chem. Ind. Ltd.). Jpn. Pat. Appl. JP 63-119438, 1988 (*Eur. Pat. Appl.* EP 240,175; *Chem. Abstr.* **1988**, *109*, 55166h). (b) Paulsen, H.; von Deyn, W. *Liebigs Ann. Chem.* **1987**, 125.

(5) (a) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231. (b) Horton, D; Priebe, W. *Carbohydr. Res.* **1981**, *94*, 27; (c) Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010.

Scheme III



The configuration of the 1-*C*-[bis(methylthio)methyl] derivative **3a** was first assigned by converting it to the 2,6-anhydroheptitol **3e** via the 1-*O*-acetate **3c** by a method similar to that described by Horton and Prieb.[5b] Details of the assignment are given in the Experimental Section.

Furthermore, desulfurization of the bis(methylthio)-methyl derivative **3c**, via the mono(methylthio)methyl derivative **3f** by a two-step reduction with tri-*n*-butyltin hydride (Bu_3SnH) in the presence of AIBN and then Raney nickel gave the 1-*O*-acetyl-1-*C*-methylglucopyranose derivative **3g**, together with the 2,6-anhydro-1-deoxy-heptitol derivative **3e** which was identical to that obtained as a single product by the one-stage reduction of **3c** with Raney nickel as described above.

The α-anomeric configuration of the 1-*C*-(dichloro-methyl) derivative **3b** was elucidated by converting it to the 1-*O*-acetyl-1-*C*-methylglucopyranose derivative **3g**. Acetylation of **3b** with acetic anhydride (Ac_2O)/4-(dimethylamino)pyridine/triethylamine (Et_3N) gave the 1-*O*-acetate **3d**, and then dechlorination of **3d** with Bu_3SnH/AIBN afforded **3g** which was identical to that derived from the 1-*C*-[bis(methylthio)methyl] derivative **3a**.

In the ^1H NMR spectra, the C-3 and C-5 resonances of the 1-*O*-acetyl derivatives **3c** and **3d** were observed at higher field and the C-2 and C-4 resonances at lower field in comparison to the corresponding resonances of **3a** and **3b**. Such chemical shifts can be explained by the shielding and deshielding effects caused by acetylation of the anomeric free hydroxyl groups of **3a** and **3b**, thus supporting their α-anomeric configuration.

Dechlorination of **3b** with Bu_3SnH/AIBN gave the 1-*C*-methyl derivative as a mixture of the α-anomer **3h** and the β-anomer **3'h** (approximately 15:1, estimated by ^1H NMR). The exclusive presence of the α-anomer in **3a,b** and the 15:1 ratio of the α-anomer **3h** to the β-anomer **3'h** in the dechloro derivative can be explained by the favored equatorial orientation of the bulky C-1 substituents.

The anomeric hydroxyl group of the 1-*C*-(dichloro-methyl) derivative **3b** was more easily acetylated with Ac_2O/4-(dimethylamino)pyridine/Et_3N (30 min, at ice-bath temperature) than that of the 1-*C*-[bis(dimethyl-thio)methyl] derivative **3a** (24 h, at ice-bath temperature) as described above. In contrast to **3b**, acetylation of **3h** with the same reagent combination gave the acyclic 6-*O*-acetylheptulose derivative **3i**, the anomeric hydroxyl group of **3h** not being acetylated. The different courses of these reactions correlate with the difference in the electron-withdrawing power of the C-1 substituents.

Oxidation of the heptulose derivatives **3a** and **3b** to the heptodiulose derivatives **5a** and **5b** was next attempted. However, direct oxidation of the hydroxyl group which is masked by stable pyranose ring formation was unsuccessful with reagent combinations which include DMSO, and accordingly it was thought that pyranose ring opening prior to oxidation would be a viable alternative.

Therefore, the D-*gluco*-2-heptulose derivatives **3a** and **3b** were reduced with lithium aluminum hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$), respectively, to yield the acyclic heptitol derivatives **4a** and **4b** as a mixture of the epimers at the newly formed carbinol chiral center. The 1-deoxy-1,1-bis(methylthio)heptitol derivative **4a** was separated into **4'a** and **4''a** by silica gel chromatography in the approximate ratio of 13:1. The absolute configuration of the main epimer **4'a** was determined by converting it to the known (1*R*)-1-deoxy-D-*glycero*-D-*gulo*-heptitol (**4'd**)[6] ($[\alpha]^{24}_D$ +6.6° (*c* 1, H_2O)) via its tetra-*O*-benzyl derivative **4'c** by reductive desulfurization with Raney nickel and then removal of the *O*-benzyl protecting groups with palladium black and formic acid. The minor epimer **4''a** was converted to the deoxyheptitol **4''d** having a specific rotation of $[\alpha]^{24}_D$ −1.1° (*c* 1, H_2O), which can be assigned to 7-deoxy-D-*glycero*-L-*gulo*-heptitol, in the same manner as was **4'a**. The 1,1-dichloroheptitol derivative **4b** was shown to be an approximately 2:1 mixture of (1*R*)- and (1*S*)-isomers by converting it to the tetra-*O*-benyldeoxy-heptitol derivatives **4'c** and **4''c** with Bu_3SnH/AIBN followed by chromatographic separation on a silica gel column.

The epimeric mixture **4a** was nevertheless subjected to the next reaction without resolution of the two isomers, as this chiral center disappears in the next oxidation reaction.

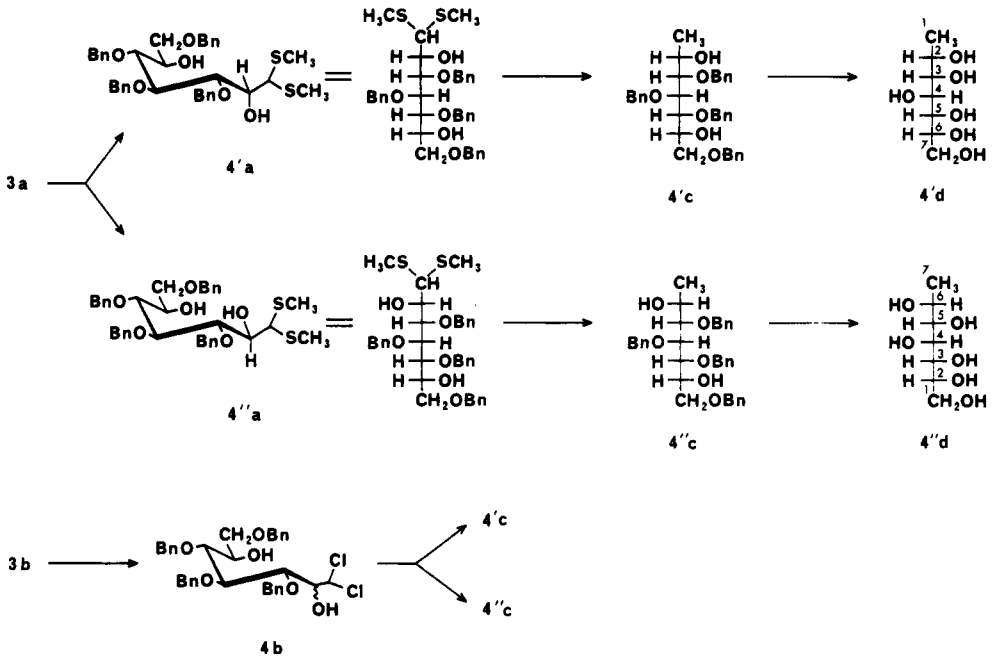
The oxidation of the unprotected hydroxyl groups of the heptose dithioacetal derivative **4a** with DMSO, trifluoro-acetic anhydride (TFAA), and Et_3N (Swern oxidation) gave the 2,6-dioxoheptose 1,1-dithioacetal derivative **5a** which was too labile to isolate; however, the partially purified compound showed reasonable spectral data. Chromatographic purification of **5a** with silica gel was unsuccessful, but nevertheless yielded the desired branched-chain α,α-bis(methylthio)inosose derivative **6a**. It is thought that this was produced by the intramolecular aldol condensation of **5a** while in contact with silica gel. The 2,6-dioxo-heptose 1,1-dithioacetal derivative **5a** more easily underwent intramolecular aldol condensation, through its intermediate enolate anion **5a'**, in the presence of sodium acetate and 18-crown-6 in toluene to stereoselectively give **6a**. However, treatment with potassium carbonate and 18-crown-6 gave the undesired epimer **6c** as the main product in the approximate ratio 1:4 (**6a** to **6c**). The reason for this unexpected result is not yet understood.

On the other hand, Swern oxidation of the 1-deoxy-1,1-dichloroheptose derivative **4b** followed by an intramolecular aldol condensation reaction gave the branched-chain α,α-dichloroinosose derivative **6b**. In this oxidation reaction, the δ-dicarbonyl heptose **5b** was formed only as a transient intermediate, and it was not possible to isolate it because it spontaneously cyclized to give the desired branched-chain dichloroinosose derivative **6b** via the enolate anion **5b'** generated in the presence of excess base.

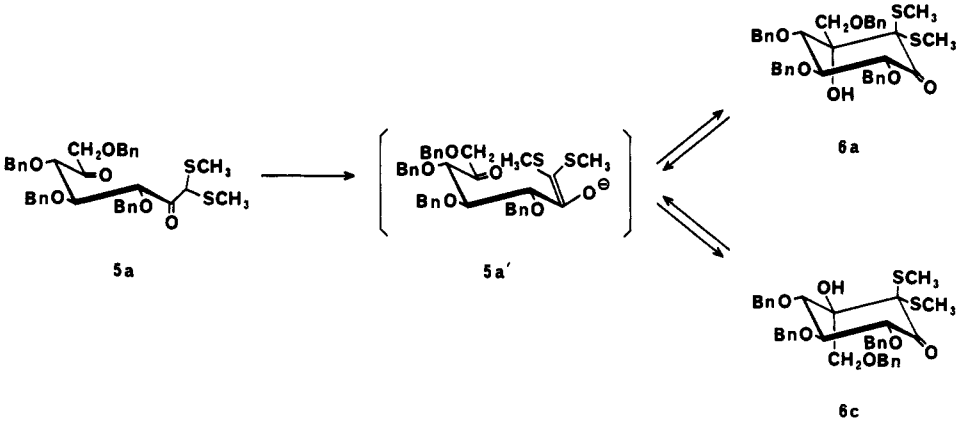
The carbonyl groups of **5a** and **5b** which are conjugated with the electron-withdrawing bis(methylthio) and dichloro

(6) (a) Zissis, E.; Richtmyer, N. K.; Hudson, C. S. *J. Am. Chem. Soc.* **1951**, *73*, 4714. (b) Gillies, D. G.; Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1155.

Scheme IV



Scheme V



groups, respectively, preferentially undergo enolization compared to the other carbonyl groups, and the intermediate enolate anions **5a'** and **5b'** play an important role in the regiospecific aldol condensation.

The two epimers **6a** and **6c** of the branched-chain α,α-bis(methylthio)inosose derivatives are in equilibrium via the open-chain enolate anion **5a'** in the presence of bases such as *n*-butyllithium and potassium carbonate. For example, the reaction of **6a** with potassium carbonate in the presence of 18-crown-6 gave an approximately 1:4 mixture of **6a** and **6c**. The reaction of **6a** with *n*-butyllithium gave an approximately 1:1 mixture of **6a** and **6c**.

As mentioned above, intramolecular aldol condensation of **5a** with sodium acetate stereospecifically gave the branched-chain bis(methylthio)inosose derivative **6a**, but the simultaneous formation of the epimer **6c** was observed in the presence of potassium carbonate. The ^{1}H NMR coupling constants showed that **6a** and **6c** have three vicinal equatorial secondary alcohol groups as a common stereochemical configuration unit (J 8.7–9.7 Hz), yet they differ in their specific rotations. Therefore, they should differ only in the configuration of the quaternary carbon atom attached to the hydroxymethyl group, and either of them should have the same configuration as that of the branched-chain dichloroinosose derivative **6b** which was stereospecifically obtained by the intramolecular aldol condensation of the probable transient intermediate **5b**.

After desulfurization of **6a**, the carbonyl group of the resulting branched-chain inosose derivative **7** was stereospecifically converted to an axial secondary alcohol group [^{1}H NMR δ 4.18 ($J_{4,5}$ 3.1 Hz, $J_{5,6ax}$ 2.9 Hz, $J_{5,6eq}$ 3.2 Hz)] with $NaBH_4$ at −15 to −20 °C to give the branched-chain inositol derivative **10a**.

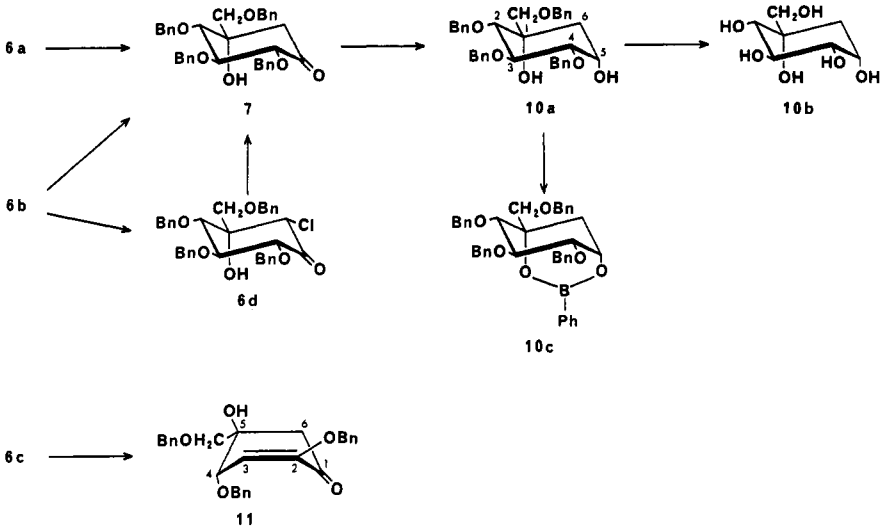
The two unprotected hydroxyl groups of **10a** were reacted with phenylboric acid and *p*-toluenesulfonic acid to give the crystalline cyclic phenylboronate ester **10c**. Formation of a cyclic ester shows that the two unprotected hydroxyl groups, that is the tertiary alcohol group and the newly formed hydroxyl group, are in a *Z*-axial arrangement.

Deprotection of the *O*-benzyl groups of **10a** with palladium black and formic acid gave (1*S*)-(1(OH),2,4,5/1,3)-1-*C*-(hydroxymethyl)-1,2,3,4,5-cyclohexanepentol (**10b**), the pseudosugar in which the amino group of valiolamine (**8**) is replaced by a hydroxyl group.

In contrast to **6a**, desulfurization of its epimer **6c** was accompanied by elimination of the benzyloxyl group to give the 2-cyclohexenone derivative **11** [IR 3486 (OH), 1698 (α,β-unsaturated CO) cm^{-1}].

The branched-chain dichloroinosose derivative **6b** was converted by reductive dehalogenation with Bu_3SnH/AIBN to the branched-chain inosose derivative **7** which

Scheme VI



was identical to that derived from the branched-chain bis(methylthio)inosose derivative **6a**.

Reduction of **6b** with zinc and acetic acid gave the branched-chain monochloroinosose derivative **6d**. In the infrared spectra, the carbonyl of the monochloro derivative **6d** absorbs at nearly the same place as that in the dichloro derivative **6b**, and these are shifted to a higher frequency relative to that in the unhalogenated derivative **7** by 25 cm^{-1}. This shift shows that the chloro group of **6d** is in an equatorial position (*R*-configuration)[7] [IR (KBr) 1735 cm^{-1} for **7**, 1760 cm^{-1} for **6b**, and 1759 cm^{-1} for **6d**]. The equatorial position of chloro group of **6d** was also ascertained by the long-range spin–spin couplings (*J* 0.8 Hz)[8] between the tertiary hydroxyl proton and the axial proton on the chlorine-bearing carbon which are separated by four single bonds. Reductive dehalogenation of **6d** with Bu_3SnH/AIBN gave **7**.

The branched-chain inosose derivative **7** was also synthesized in five steps from the D-glucono-1,5-lactone derivative **2** by a method similar to that described above for the bis(methylthio)methyl series, except for the use of 1,3-dithian-2-yl carbanion instead of bis(methylthio)methyl carbanion for one-carbon elongation. As the bis(methylthio)methyl method (26.7% overall yield from **2**) provides better yields than the 1,3-dithian-2-yl method (8.1% overall yield from **2**) and the two methods proceeded fundamentally in a similar manner, further details of the 1,3-dithian-2-yl method are not described in this text. Experimental details of the 1,3-dithian-2-yl series can be found in the supplementary material.

The dichloromethyl series (44.5% overall yield from **2**) is a more practical method for preparation of the branched-chain inosose derivative **7** than the bis(alkylthio)methyl series because it can avoid the foul odor of sulfur-containing reagents. Furthermore, the dichloroinosose derivative **6b**, a key compound for the synthesis of **7** in the dichloromethyl method, can be obtained readily from the D-glucono-1,5-lactone derivative **2** in a one-flask procedure as described in the Experimental Section.

Valiolamine (**8**) was synthesized by reduction of the ketoxime of the branched-chain inosose derivative **7**, and N-substituted valiolamine derivatives such as AO-128 (**9**) were synthesized by reductive amination of the branched-chain inosose derivative **7**.[1] This method is especially useful when synthons of *N*-substituent moieties are easily available as corresponding amino compounds. Details of the conversion of **7** to **8** and **9** will be discussed in a subsequent paper,[9] together with the total synthesis of validoxylamine G and validamycin G which are validamycin congeners having **7** as their constituents.

Experimental Section

Melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 67.8 MHz, respectively. Chromatography columns of silica gel were prepared with Kieselgel (70–230 mesh). Column chromatography was monitored by refractive index, if necessary. Ratios for mixtures of solvents are expressed by volume (v/v), unless otherwise indicated. Organic solutions were dried over anhydrous sodium sulfate before evaporation, if necessary. Solutions were evaporated under reduced pressure using a rotary evaporator.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-[bis(methylthio)methyl]-D-glucopyranose (3a). A solution of *n*-butyllithium in *n*-hexane (1.6 M solution, 37.5 mL, 60 mmol) was added dropwise to a solution of bis(methylthio)methane (6.13 mL, 60 mmol) in THF (150 mL) under argon at −65 to −70 °C with stirring, and the resulting mixture was stirred for an additional 2.5 h at −20 to −30 °C. The mixture was again cooled to −65 to −70 °C, and a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone[10] (**2**, 16.2 g, 30 mmol) in THF (60 mL) was added dropwise with stirring. After being stirred for 1 h at the same temperature, the reaction mixture was quenched with 10% (w/v) aqueous NH_4Cl (300 mL). The resulting oily substance was extracted with EtOAc (300 mL × 2) and washed with H_2O, 2 N HCl, and saturated aqueous $NaHCO_3$, and then the solvent was evaporated. Crystallization of the residue from Et_2O/petroleum ether (1:10) gave 1-*C*-[bis(methylthio)-methyl]-D-glucopyranose derivative **3a** (16.0 g, 82%) as white crystals: mp 96–97 °C; $[\alpha]^{25}_D$ −24.6° (*c* 1, $CHCl_3$); IR (KBr) 3394 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 1.97 and 2.15 (each 3 H, s, $-SCH_3$ × 2), 3.55 (1 H, dd, *J* 1, 7, 11.2 Hz) and 3.74 (1 H, dd, *J* 4.4, 11.2 Hz) (6-H), 3.64 (1 H, dd, *J* 8.6, 9.9 Hz, 4-H), 3.89 (1 H, s, –SCHS–), 3.98 (1 H, ddd, *J* 1.7, 4.4, 9.9 Hz, 5-H), 4.10 (1 H, t*, *J* 8.6, 9.4 Hz, 3-H), 4.16 (1 H, br d, *J* 9.4 Hz, 2-H), 4.44 (1 H, br s, –OH) (*apparent splitting pattern); ^{13}C NMR ($CDCl_3$) δ 12.72 (q, $-SCH_3$), 14.80 (q, $-SCH_3$), 61.44 (d, –SCHS–), 68.96 (t, 6-C), 71.98 (d, 5-C); 73.24 (t), 74.97 (t), 75.49 (t) and 75.54 (t) ($PhCH_2$– × 4); 78.56 (d), 79.38 (d), and 84.10 (d) (2, 3, 4-C); 98.86 (s, 1-C); 127.36–128.39, 138.38 (s), 138.44 (s), 138.56 (s), and 138.66 (s) (C_6H_5– × 4). Anal. Calcd for $C_{37}H_{42}O_6S_2$: C, 68.70; H, 6.54; S, 9.91. Found: C, 68.61; H, 6.62; S, 9.64.

(7) (a) Corey, E. J. *J. Am. Chem. Soc.* **1953**, *75*, 2301; (b) Allinger, N. L.; Blatter, H. M. *J. Org. Chem.* **1962**, *27*, 1523.
(8) Meinwald, J.; Lewis, A. *J. Am. Chem. Soc.* **1961**, *83*, 2769.
(9) Fukase, H.; Horii, S. *J. Org. Chem.*, the subsequent paper in this issue.
(10) Kuzuhara, H.; Fletcher, H. G., Jr. *J. Org. Chem.* **1967**, *32*, 2531.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-(dichloromethyl)-D-glucopyranose (3b). To a solution of diisopropylamine (2.8 mL, 20 mmol) in THF (20 mL) was added a solution of *n*-butyllithium in *n*-hexane (1.6 M solution, 12.5 mL, 20 mmol) dropwise with stirring under argon at −5 to −10 °C, and stirring was continued for 1 h at the same temperature. The resulting LDA solution was added dropwise to a solution of **2** (5.4 g, 10 mmol) in CH_2Cl_2 (30 mL) with stirring under argon at −70 to −75 °C, and stirring was continued for 1 h at the same temperature. The mixture was partitioned between CH_2Cl_2 (200 mL) and 2 N HCl (100 mL). The organic layer was washed with H_2O and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (400 mL) with toluene/EtOAc (20:1). The eluate was evaporated, and petroleum ether (100 mL) was added to the residue. The mixture was refrigerated overnight to give 1-*C*-(dichloromethyl)-D-glucopyranose derivative **3b** (5.9 g, 94%) as colorless crystals: mp 72–73 °C; $[\alpha]^{23}_D$ +20.2° (*c* 1, $CHCl_3$); IR (KBr) 3402 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 3.29 (1 H, d, *J* 1.1 Hz, –OH), 3.73 (1 H, dd, *J* 1.8, 11.6 Hz) and 3.84 (1 H, dd, *J* 3.9, 11.6 Hz) (6-H), 3.75 (1 H, dd, *J* 8.9, 9.8 Hz, 4-H), 3.99 (1 H, ddd, *J* 1.8, 3.9, 9.8 Hz, 5-H), 4.00 (1 H, dd, *J* 1.1, 8.9 Hz, 2-H), 4.07 (1 H, t, *J* 8.9 Hz, 3-H), 5.81 (1 H, s, $-CHCl_2$); ^{13}C NMR ($CDCl_3$) δ 67.98 (t, 6-C), 73.34 (d, 5-C), 74.37 (d, $-CHCl_2$); 73.32 (t), 75.03 (t), 75.43 (t) and 75.63 (t) ($PhCH_2$– × 4); 78.07 (d), 78.09 (d) and 83.66 (d) (2, 3, 4-C); 97.55 (s, 1-C); 127.42–128.53, 137.47 (s), 138.07 (s), 138.30 (s), and 138.46 (s) (C_6H_5– × 4). Anal. Calcd for $C_{35}H_{36}Cl_2O_6$: C, 67.42; H, 5.82; Cl, 11.37. Found: C, 67.81; H, 5.80; Cl, 11.62.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-[bis(methylthio)methyl]-D-glucitol (4a) [(1*R*)-Isomer 4′a and (1*S*)-Isomer 4″a]. $LiAlH_4$ (2.8 g, 74 mmol) was added by portions to a solution of 1-*C*-[bis(methylthio)methyl]-D-glucopyranose derivative **3a** (14.0 g, 21.6 mmol) in THF (140 mL) with stirring under cooling in an ice–water bath. The mixture was stirred for an additional 3 h at room temperature and then quenched with MeOH (50 mL) under cooling in an ice bath. After removal of the organic solvents, EtOAc (200 mL) and H_2O (200 mL) were added to the residue, and then the aqueous layer was made acidic with 2 N HCl with stirring. The EtOAc layer was separated, and the aqueous layer was extracted with EtOAc (200 mL). The extracts were combined and washed with H_2O and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (500 mL) with toluene/EtOAc (6:1) to give (1*R*)-isomer **4′a** (11.5 g, 82%) as a colorless syrup from the earlier eluted fractions and (1*S*)-isomer **4″a** (0.9 g, 6%) as a colorless syrup from the later eluted fractions.

4′a: $[\alpha]^{25}_D$ −5.8° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.12 (6 H, s, $-SCH_3$ × 2), 2.84 (1 H, d, *J* 5.2 Hz, 5-OH), 3.44 (1 H, dd, *J* 0.5, 2.6 Hz, 1-OH), 3.62 (2 H, d, *J* 4.8 Hz, 6-H), 3.85 (1 H, dd, *J* 0.5, 2.7 Hz, –SCHS–), 3.93 (1 H, dd, *J* 3.5, 6.2 Hz, 4-H), 4.03 (1 H, t*, *J* 3.5, 4.2 Hz, 3-H), 4.05–4.10 (1 H, m, 5-H), 4.15 (1 H, dd, *J* 4.2, 8.3 Hz, 2-H), 4.23 (1 H, td*, *J* 2.6, 2.7, 8.3 Hz, 1-H) (*apparent splitting pattern). Anal. Calcd for $C_{37}H_{44}O_6S_2$: C, 68.49; H, 6.83; S, 9.88. Found: C, 68.78; H, 6.92; S, 9.76.

4″a: $[\alpha]^{26}_D$ −12.7° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.97 (3 H, s, CH_3S–), 1.99 (3 H, s, CH_3S–), 2.96 (1 H, d, *J* 5.2 Hz, –OH), 3.05 (1 H, d, *J* 5.1 Hz, –OH), 3.58–3.69 (3 H, m, 1-H, 6-H), 3.73 (1 H, dd, *J* 3.0, 6.9 Hz, 4-H), 3.80 (1 H, d, *J* 9.1 Hz, –SCHS–), 4.08–4.15 (1 H, m, 5-H), 4.18 (1 H, dd, *J* 3.0, 8.3 Hz, 3-H), 4.37 (1 H, dd, *J* 1.5, 8.3 Hz, 2-H). Anal. Calcd for $C_{37}H_{44}O_6S_2$: C, 68.49; H, 6.83; S, 9.88. Found: C, 68.82; H, 6.99; S, 9.58.

A Mixture of (1*R*)- and (1*S*)-Isomers of 2,3,4,6-Tetra-*O*-benzyl-1-*C*-(dichloromethyl)-D-glucitol (4b). To a solution of the 1-*C*-(dichloromethyl)-D-glucopyranose derivative **3b** (5.0 g, 8 mmol) in diethylene glycol dimethyl ether (50 mL) was added $NaBH_4$ (0.5 g, 13 mmol). The mixture was stirred for 5 h at room temperature and then concentrated, and then H_2O (100 mL) was added to the residue. The resulting oily substance was extracted with EtOAc (200 mL × 2). The extract was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (250 mL). The column was washed with toluene/EtOAc (20:1) and then eluted with toluene/EtOAc (10:1) to give the dichloroheptitol derivative **4b** (4.7 g, 94%) as a colorless syrup: ^1H NMR ($CDCl_3$ + D_2O) δ 3.63** (d, *J* 4.2 Hz) and 3.64* (d, *J* 4.5 Hz) (total 2 H, 6-H), 3.72** (dd, *J* 2.8, 7.1 Hz) and 3.91* (dd, *J* 3.7, 6.6 Hz) (total 1 H, 4-H), 3.80* (dd, *J* 4.5, 8.7 Hz) and 4.25** (dd, *J* 2.2, 7.8 Hz) (total 1 H, 2-H), 3.96** (dd, *J* 2.2, 6.8 Hz) and 4.17* (dd, *J* 1.9, 8.7 Hz) (total 1 H, 1-H), 4.00–4.15 (2 H, m, 3-H, 5-H), 5.66** (d, *J* 6.8 Hz) and 5.98* (d, *J* 1.9 Hz) (total 1 H, $-CHCl_2$) [*the signals of the (1*R*)-isomer, **the signals of the (1*S*)-isomer]. Anal. Calcd for $C_{35}H_{38}Cl_2O_6$: C, 67.20; H, 6.12; Cl, 11.33. Found: C, 67.49; H, 6.31, Cl: 11.19.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-[bis(methylthio)methyl]-D-*xylo*-5-hexosulose (5a). A solution of TFAA (6.4 mL) in CH_2Cl_2 (5 mL) was added dropwise to a solution of DMSO (4.4 mL) in CH_2Cl_2 (40 mL) at −65 to −70 °C with stirring, and stirring was continued for 20 min at the same temperature. To the stirred mixture was added dropwise a solution of 1-*C*-[bis(methylthio)-methyl]-D-glucitol derivative **4a** (a mixture of the (1*R*)- and (1*S*)-isomers **4′a** and **4″a**, 6.5 g, 10 mmol) in CH_2Cl_2 (40 mL) at −65 to −70 °C, and then the reaction mixture was stirred for an additional 1 h at the same temperature. A solution of Et_3N (11.6 mL) in CH_2Cl_2 (40 mL) was added dropwise with stirring, and the stirring was continued for 15 min at −65 to −70 °C. The reaction mixture was removed from the cooling bath and allowed to warm to 0 °C with stirring. The reaction mixture was partitioned between CH_2Cl_2 (150 mL) and ice–water (150 mL). The organic layer was separated and washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then evaporated to give crude 5-hexosulose derivative **5a** (6.7 g) as a pale yellow syrup: IR ($CHCl_3$) 1729 (CO), 1715 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (3 H, s, CH_3S–), 1.99 (3 H, s, CH_3S–), 4.01 and 4.12 (each 1 H, ABq, *J* 18.0 Hz, 6-H), 4.13 (1 H, dd, *J* 3.7, 4.9 Hz, 3-H), 4.19 (1 H, d, *J* 3.7 Hz, 4-H), 4.72 (1 H, d, *J* 4.9 Hz, 2-H), 4.97 (1 H, s, –SCHS–).

(1*S*)-(1(OH),2,4/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-5-oxo-6,6-bis(methylthio)-1,2,3,4-cyclohexanetetrol (6a). To a solution of the crude 5-hexosulose derivative **5a** (6.7 g, 10 mmol) in toluene (200 mL) were added sodium acetate (5.8 g) and 18-crown-6 (0.1 g). The mixture was stirred for 16 h at room temperature. The reaction mixture was filtered, and the solid was washed with toluene. The filtrate and the washings were combined, washed with 2 N HCl and saturated aqueous $NaHCO_3$, and then concentrated to give bis(methylthio)inosose derivative **6a** as a colorless syrup. To the syrup was added Et_2O/petroleum ether (1:5, 120 mL). The mixture was refrigerated overnight to give colorless crystals of **6a** (5.3 g, 82% from **4a**): mp 97–98 °C; $[\alpha]^{22}_D$ −35.6° (*c* 1, $CHCl_3$); IR (KBr) 3324 (OH), 1732 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83 and 2.12 (each 3 H, s, CH_3S– × 2), 2.86 (1 H, s, –OH), 3.79 and 3.87 (each 1 H, ABq, *J* 9.3 Hz, $-CH_2O$–), 4.08 (1 H, t, *J* 9.3 Hz, 3-H), 4.66 (1 H, d, *J* 9.3 Hz, 2-H) 5.05 (1 H, d, *J* 9.3 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ 12.98 (q) and 15.49 (q) (CH_3S– × 2), 71.83 (t, $-CH_2O$–), 73.73 (s, 6-C); 73.24 (t), 74.03 (t), 75.85 (t) and 75.89 (t) ($PhCH_2$– × 4); 79.44 (d), 82.69 (d) and 82.86 (d) (2, 3, 4-C); 80.78 (s, 1-C); 127.54–128.46, 137.48 (s), 137.49 (s), 138.18 (s) and 138.47 (s) (C_6H_5– × 4); 199.04 (s, 5-C). Anal. Calcd for $C_{37}H_{40}O_6S_2$: C, 68.92; H, 6.25; S, 9.95. Found: C, 69.11; H, 6.26; S, 10.07.

(1*S*)-(1(OH),2,4/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-6,6-dichloro-5-oxo-1,2,3,4-cyclohexanetetrol (6b). (a) From 1-*C*-(Dichloromethyl)-D-glucitol Derivative 4b. A solution of TFAA (9.6 mL) in CH_2Cl_2 (40 mL) was added dropwise to a solution of DMSO (7.4 mL) in CH_2Cl_2 (80 mL) with stirring at −65 to −75 °C, and the resulting mixture was stirred for an additional 30 min. To this mixture was added dropwise a solution of **4b** (10.6 g, 17 mmol) in CH_2Cl_2 (60 mL). After the reaction mixture was stirred for 1 h, a solution of Et_3N (19 mL) in CH_2Cl_2 (80 mL) was added. The reaction temperature was kept at −65 to −75 °C throughout the above processes. After the reaction mixture was stirred for 15 min, it was removed from the cooling bath and was allowed to warm to 0 °C. Iced CH_2Cl_2 (400 mL) and H_2O (200 mL) were added to the mixture followed by stirring. The CH_2Cl_2 layer was washed with 2 N HCl and aqueous saturated $NaHCO_3$ and then concentrated. Et_2O/petroleum ether (1:10, 110 mL) was added to the residue. The mixture was refrigerated overnight to give the dichloroinosose derivative **6b** (7.03 g, 67%) as white crystals: mp 139–142 °C; $[\alpha]^{23}_D$ + 2.5° (*c* 1, $CHCl_3$); IR (KBr) 3410 (OH), 1760 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.36 (1 H, s, –OH), 3.83 and 3.87 (each 1 H, ABq, *J* 10.1 Hz, $-CH_2O$–), 4.08 (1 H, t, *J* 9.3 Hz, 3-H), 4.31 (1 H, d, *J* 9.3 Hz, 2-H), 4.93 (1 H, d, *J* 9.3 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ 69.34 (t, $-CH_2O$–); 73.77 (t), 73.82 (d), 76.17 (t) and 76.17 (t) ($PhCH_2$– × 4); 78.94 (s, 1-C);

78.92 (d), 81.32 (d) and 81.62 (d) (2, 3, 4-C); 89.72 (s, 6-C); 127.58–128.44, 137.10 (s), 137.19 (s), 137.59 (s) and 138.05 (s) (C_6H_5– × 4); 191.31 (s, 5-C). Anal. Calcd for $C_{35}H_{34}Cl_2O_6$: C, 67.63; H, 5.51; Cl, 11.41. Found: C, 68.00; H, 5.53; Cl, 11.39.

(b) A One-Flask Preparation of 6b from 2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (2). LDA (120 mmol) in THF (100 mL) was added to **2** (21.6 g, 40 mmol) in CH_2Cl_2 (80 mL) under argon at −70 to −75 °C and stirred for 1 h at the same temperature. The reaction mixture was partitioned between CH_2Cl_2 (350 mL) and 2 N HCl (300 mL) with ice cooling. The organic layer was washed with H_2O and then saturated aqueous $NaHCO_3$. The organic layer was concentrated to dryness to give crude 1-*C*-(dichloromethyl)-D-glucopyranose derivative **3b** (26.6 g) as a light yellow syrup. The syrup (26.6 g) was dissolved in THF/diethylene glycol dimethyl ether (1:1, 265 mL). $NaBH_4$ (10.0 g) was added to the solution, and the mixture was stirred overnight at room temperature. The mixture was concentrated, and the residue was partitioned between EtOAc (1.2 L) and H_2O (600 mL). The EtOAc layer was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The resulting colorless syrup (26.9 g) that contained the 1-*C*-(dichloromethyl)-D-glucitol derivative **4b** was dissolved in CH_2Cl_2 (125 mL) and oxidized as described in the method a [TFAA (24.2 mL) in CH_2Cl_2 (75 mL), DMSO (18.6 mL) in CH_2Cl_2 (75 mL) and Et_3N (48 mL) in CH_2Cl_2 (150 mL)]. Crystallization from Et_2O/petroleum ether (1:10, 250 mL) at room temperature overnight gave **6b** (15.6 g, 63%) as white crystals.

(1*R*)-(1(CH_2OH),2,4/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-6,6-bis(methylthio)-5-oxo-1,2,3,4-cyclohexanetetrol (6c). Potassium carbonate (3.0 g) and 18-crown-6 (50 mg) were added to a solution of crude 5-hexosulose derivative **5a** (5.0 g, 7.7 mmol) in toluene, and the resulting mixture was stirred for 18 h at room temperature. The reaction mixture was filtered, and the solid was washed with toluene (100 mL). The filtrate and the washings were combined, washed with 2 N HCl and saturated aqueous $NaHCO_3$, and then concentrated. The residue was chromatographed on a column of silica gel (300 mL) with toluene/EtOAc (20:1) to give the (1*R*)-(1(CH_2OH),2,4/1,3) derivative **6c** (2.5 g, 51% from **4a**) as a colorless syrup from the earlier eluted fraction and the (1*S*)-(1(OH),2,4,5/1,3) derivative **6a** as colorless crystals (crystallization from Et_2O/petroleum ether (1:10)) (490 mg, 10% from **4a**) from the later eluted fraction.

6c: $[\alpha]^{24}_D$ −84.1° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 3550 (OH), 1724 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.92 and 2.17 (each 3 H, s, CH_3S– × 2), 2.32 (1 H, s, –OH), 3.71 and 3.94 (each 1 H, ABq, *J* 8.7 Hz, $–CH_2O–$), 4.33 (1 H, dd, *J* 8.8, 9.6 Hz, 3-H), 4.46 (1 H, d, *J* 9.6 Hz), 2-H), 4.93 (1 H, d, *J* 8.8 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ 11.50 (q) and 13.31 (q) (CH_3S– × 2), 70.64 (t, $–CH_2O–$), 74.48 (s, 6-C); 73.47 (t), 73.81 (t), 75.18 (t) and 76.05 (t) ($PhCH_2$– × 4); 80.48 (s, 1-C); 81.22 (d), 83.18 (d) and 83.25 (d) (2, 3, 4-C); 127.38–128.57, 137.22 (s), 138.00 (s), 138.36 (s) and 138.43 (s) (C_6H_5– × 4), 197.02 (s, 5-C). Anal. Calcd for $C_{37}H_{40}O_6S_2$: C, 68.92; H, 6.25; S, 9.95. Found: C, 68.89; H, 6.38; S, 9.98.

(1*S*)-(1(OH),2,4,6/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-6-chloro-5-oxo-1,2,3,4-cyclohexanetetrol (6d). Zinc dust (2.0 g) was added by portions to a suspension of the dichloro inosose derivative **6b** (2.0 g, 3.2 mmol) in AcOH (10 mL) with stirring, keeping the reaction temperature at 15–20 °C, and stirring was continued for 1 h at the same temperature. Et_2O (50 mL) was added to the mixture, and then the solid was removed by filtration and washed with Et_2O (50 mL). The filtrate and the washings were combined, washed with H_2O and saturated aqueous $NaHCO_3$, and then concentrated. Et_2O/petroleum ether (1:5, 60 mL) was added to the residue, and the mixture was allowed to stand overnight at room temperature to give the monochloro inosose derivative **6d** (1.24 g, 66%) as colorless crystals: mp 103.5–106 °C; $[\alpha]^{24}_D$ + 62.6° (*c* 1, $CHCl_3$); IR (KBr) 3470 (OH), 1759 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.29 (1 H, d, *J* 0.8 Hz, –OH), 3.55 and 3.65 (each 1 H, ABq, *J* 8.6 Hz, $–CH_2O–$), 4.04 (1 H, t, *J* 9.3 Hz, 3-H), 4.12 (1 H, d, *J* 9.3 Hz, 2-H), 4.19 (1 H, dd, *J* 0.9, 9.3 Hz, 4-H), 4.89 (1 H, t*, *J* 0.8, 0.9 Hz, 6-Hax) (*apparent splitting pattern); ^{13}C NMR ($CDCl_3$) δ 65.20 (d, 6-C), 69.31 (t, $–CH_2O–$); 73.24 (t), 73.46 (t), 76.00 (t) and 76.20 (t) ($PhCH_2$– × 4); 77.14 (s, 1-C); 79.00 (d), 82.46 (d) and 84.31 (d) (2, 3, 4-C); 127.66–128.46, 137.22 (s), 137.26 (s), 137.52 (s) and 138.17 (s) (C_6H_5– × 4); 196.13 (s, 5-C). Anal. Calcd for $C_{35}H_{35}ClO_6$: C, 71.60; H, 6.01; Cl, 6.04. Found: C, 71.63; H, 5.99; Cl, 6.00.

(1*S*)-(1(OH),2,4/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-5-oxo-1,2,3,4-cyclohexanetetrol (7). (a) From the Bis(methylthio)inosose Derivative 6a. To a solution of **6a** (5.2 g, 8.0 mmol) in dioxane (150 mL) was added Raney Ni (15.0 g). The suspension was stirred for 30 min at room temperature. The reaction mixture was filtered, and the solid was washed with dioxane. The filtrate and the washings were combined and then concentrated. The residue was chromatographed on a column of silica gel (250 mL) with toluene/EtOAc (6:1) to give the desulfurized branched-chain inosose derivative **7** (1.9 g, 43%) as colorless crystals (crystallization from Et_2O/petroleum ether (1:2)): mp 84–85 °C; $[\alpha]^{22}_D$ +45.1° (*c* 1, $CHCl_3$); IR (KBr) 3440 (OH), 1735 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (1 H, d, *J* 2.0 Hz, –OH), 2.47 (1 H, d, *J* 14.5 Hz, 6-Heq), 2.84 (1 H, ddd, *J* 0.9, 2.0, 14.5 Hz, 6-Hax), 3.15 and 3.53 (each 1 H, ABq, *J* 8.6 Hz, $–CH_2O–$), 4.01 (1 H, t, *J* 9.0 Hz, 3-H), 4.06 (1 H, d, *J* 9.0 Hz, 2-H), 4.14 (1 H, dd, *J* 0.9, 9.0 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ 45.61 (t, 6-C), 72.85 (t, $–CH_2O–$), 74.12 (s, 1-C); 73.33 (t), 73.33 (t), 75.74 (t) and 75.91 (t) ($PhCH_2$– × 4); 80.07 (d), 83.12 (d) and 85.65 (d) (2, 3, 4-C); 127.60–128.47, 137.44 (s), 137.74 (s), 137.87 (s) and 138.43 (s) (C_6H_5– × 4); 203.87 (s, 5-C). Anal. Calcd for $C_{35}H_{36}O_6$: C, 76.06; H, 6.57. Found: C, 76.11; H, 6.47.

(b) From the Dichloroinosose Derivative 6b. A solution of **6b** (3.0 g, 4.8 mmol), Bu_3SnH (5.0 g, 17 mmol), and AIBN (0.3 g, 1.8 mmol) in toluene (30 mL) was stirred for 1 h at 100 °C. After the mixture was cooled to room temperature, EtOAc (150 mL) was added. The organic solution was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (250 mL) with toluene/EtOAc (6:1). The eluate was concentrated, and Et_2O/petroleum ether (1:6, 35 mL) was added to the residue. The mixture was refrigerated overnight to give the dechlorinated derivative **7** (1.87 g, 71%) as white crystals.

(c) From the Monochloroinosose Derivative 6d. To a solution of **6d** (1.0 g, 1.7 mmol) in toluene (15 mL) were added Bu_3SnH (750 mg, 2.6 mmol) and AIBN (50 mg, 0.3 mmol). The mixture was stirred for 1 h at 100 °C. Treatment of the reaction mixture by a method similar to method b gave **7** (710 mg, 75%) as white crystals.

(d) To a solution of the dichloro derivative **6b** (2.0 g, 3.2 mmol) in THF/MeOH (1:7, 80 mL) were added 5% (w/w) Pd–$BaSO_4$ (0.5 g) and AcONa (2.0 g), and the mixture was hydrogenated with shaking overnight at the pressure of 3–3.5 kg/cm^2 at room temperature. The solid was removed by filtration and washed with THF/MeOH (1:1). The filtrate and the washings were combined and concentrated. The residue was partitioned between EtOAc (100 mL) and H_2O (100 mL). The organic layer was washed with 2 N HCl and concentrated. Et_2O/petroleum ether (1:4, 25 mL) was added to the residue. The mixture was refrigerated overnight to give **7** (710 mg, 40%) as white crystals.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-[bis(methylthio)methyl]-α-D-glucopyranose (3c) and 2,6-Di-*O*-acetyl-3,4,5,7-tetra-*O*-benzyl-1-deoxy-1,1-bis(methylthio)-D-*gluco*-hept-1-enitol (3′c). To a solution of **3a** (1.0 g) in Et_3N (30 mL) were added Ac_2O (2 mL) and 4-(dimethylamino)pyridine (0.1 g). The mixture was stirred for 18 h at 0 °C. The reaction mixture was concentrated, and the residue was partitioned between EtOAc (80 mL) and H_2O (25 mL). The organic layer was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (150 mL) with toluene/EtOAc (20:1) to give the 1-*O*-acetyl derivative **3c** (410 mg, 39%) as a colorless syrup from the earlier eluted fraction and the enol-2,6-di-*O*-acetyl derivative **3′c** (650 mg, 57%) as a colorless syrup from the later eluted fraction.

3c: $[\alpha]^{24}_D$ +74.2° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (3 H, s, acetyl), 2.19 and 2.23 (each 3 H, s, $–SCH_3$ × 2), 3.65 (1 H, dd, *J* 2.7, 11.9 Hz) and 3.77 (1 H, dd, *J* 3.2, 11.9 Hz) (6-H), 3.78 (1 H, dt*, *J* 2.7, 3.2, 9.4 Hz, 5-H), 3.85 (1 H, t*, *J* 9.0, 9.4 Hz, 4-H), 3.93 (1 H, t, *J* 9.0 Hz, 3-H), 4.58 (1 H, d, *J* 9.0 Hz, 2-H), 4.97 (1 H, s, –SCHS–) (*apparent splitting pattern). Anal. Calcd for $C_{39}H_{44}O_7S_2$: C, 68.00; H, 6.44; S, 9.31. Found: C, 68.28; H, 6.36; S, 9.11.

3′c: $[\alpha]^{24}_D$ +93.8° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1763, 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 and 2.16 (each 3 H, s, acetyl × 2), 2.22 (3 H, s, $–SCH_3$), 2.25 (3 H, s, $–SCH_3$), 3.71 (1 H, dd, *J* 6.3, 11.2

Hz) and 3.84 (1 H, dd, *J* 2.7, 11.2 Hz) (7-H), 3.84 (1 H, dd, *J* 3.4, 6.8 Hz, 5-H), 3.87 (1 H, dd, *J* 3.4, 7.1 Hz, 4-H), 5.31–5.36 (1 H, m, 6-H), 5.38 (1 H, d, *J* 7.1 Hz, 3-H). Anal. Calcd for $C_{41}H_{46}O_8S_2$: C, 67.37; H, 6.34; S, 8.77. Found: C, 67.47; H, 6.35; S, 8.54.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-(dichloromethyl)-α-D-glucopyranose (3d). A solution of the dichloroheptulose derivative **3b** (1.0 g, 1.6 mmol) and 4-(dimethylamino)pyridine (0.1 g) in Et_3N (30 mL)/Ac_2O (1.0 mL) was stirred for 30 min at 0 °C to give the mono-*O*-acetate **3d** (1.0 g, 98%) as a colorless syrup: $[\alpha]^{24}_D$ +65.4° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15 (3 H, s, acetyl), 3.72 (1 H, br d, *J* 11.7 Hz) and 3.84 (1 H, dd, *J* 3.0, 11.7 Hz) (6-H), 3.78–3.83 (1 H, m, 5-H), 3.84 (1 H, t*, *J* 8.6, 9.3 Hz, 4-H), 3.95 (1 H, t*, *J* 8.6, 9.2 Hz, 3-H), 4.26 (1 H, d, *J* 9.2 Hz, 2-H), 6.96 (1 H, s, $-CHCl_2$) (*apparent splitting pattern). Anal. Calcd for $C_{37}H_{38}Cl_2O_7$: C, 66.77; H, 5.75; Cl, 10.65. Found: 67.01; H, 5.85; Cl, 10.58.

3,4,5,7-Tetra-*O*-benzyl-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (3e). To a solution of the 1-*O*-acetyl-1-*C*-[bis(methylthio)methyl] derivative **3c** (300 mg, 0.43 mmol) in dioxane (5 mL) was added Raney Ni (500 mg). The suspension was heated at 80 °C for 1 h with stirring to give the 2,6-anhydro derivative **3e** (150 mg, 64%) as a colorless syrup: $[\alpha]^{24}_D$ +10.1° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.32 (3 H, d, *J* 6.1 Hz, 1-H), 3.21 (1 H, t*, *J* 8.9, 9.1 Hz, 3-H), 3.39 (1 H, dq, *J* 9.1, 6.1 Hz, 2-H), 3.44 (1 H, ddd, *J* 2.0, 4.3, 9.4 Hz, 6-H), 3.59 (1 H, t*, *J* 9.1, 9.4 Hz, 5-H), 3.65 (1 H, dd, *J* 4.3, 10.6 Hz) and 3.71 (1 H, dd, *J* 2.0, 10.6 Hz) (7-H), 3.67 (1 H, t*, *J* 8.9, 9.1 Hz, 4-H) (*apparent splitting pattern). Anal. Calcd for $C_{35}H_{38}O_5$: C, 78.04; H, 7.11. Found: C, 78.46; H, 7.11.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-[(methylthio)methyl]-α-D-glucopyranose (3f). To a solution of the 1-*O*-acetyl-1-*C*-[bis(methylthio)methyl] derivative **3c** (400 mg, 0.58 mmol) in toluene (15 mL) were added Bu_3SnH (1.0 g, 3.4 mmol) and AIBN (20 mg, 0.12 mmol). The mixture was heated at 100 °C for 2.5 h with stirring to give the mono(methylthio) derivative **3f** (150 mg, 40%) as a colorless syrup: $[\alpha]^{23}_D$ +42.2° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08 (3 H, s, acetyl), 2.20 (3 H, s, $-SCH_3$), 2.98 and 3.73 (each 1 H, ABq, *J* 14.3 Hz, $-CH_2S-$), 3.59 (1 H, ddd, *J* 1.7, 3.0, 9.7 Hz, 5-H), 3.67 (1 H, dd, *J* 1.7, 10.9 Hz) and 3.79 (1 H, dd, *J* 3.0, 10.9 Hz) (6-H), 3.88 (1 H, t*, *J* 9.3, 9.7 Hz, 4-H), 4.00 (1 H, t, *J* 9.3 Hz, 3-H), 4.21 (1 H, d, *J* 9.3 Hz, 2-H) (*apparent splitting pattern). Anal. Calcd for $C_{38}H_{42}O_7S$: C, 71.00; H, 6.59; S, 4.99. Found: C, 71.28; H, 6.43; S, 4.76.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-α-D-glucopyranose (3g). (a) From the Mono(methylthio) Derivative 3f. To a solution of **3f** (140 mg, 0.22 mmol) in dioxane (5 mL) was added Raney Ni (30 mg). The suspension was heated at 80 °C with stirring for 90 min and then filtered. The solid was washed with dioxane. The filtrate and the washings were combined and then concentrated. The residue was chromatographed on a column of silica gel (100 mL) with toluene/EtOAc (20:1). The earlier eluted fraction was concentrated to give the 2,6-anhydro-1-deoxyheptitol derivative **3e** (45 mg, 38%) as a colorless syrup which was identical to that obtained by desulfurization of the 1-*O*-acetyl-1-*C*-[bis(methylthio)methyl]-α-D-glucopyranose derivative **3c** as described above. The later eluted fraction was concentrated to give the 1-*O*-acetyl-1-*C*-methyl-α-D-glucopyranose derivative **3g** (40 mg, 31%) as a colorless syrup.

3g: $[\alpha]^{24}_D$ +48.7° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (3 H, s, $-CH_3$), 2.08 (3 H, s, acetyl), 3.29 (1 H, d, *J* 9.4 Hz, 2-H), 3.56 (1 H, ddd, *J* 1.8, 3.2, 10.0 Hz, 5-H), 3.68 (1 H, dd, *J* 1.8, 11.1 Hz) and 3.78 (1 H, dd, *J* 3.2, 11.1 Hz) (6-H), 3.81 (1 H, t*, *J* 9.4, 10.0 Hz, 4-H), 3.99 (1 H, t, *J* 9.4 Hz, 3-H) (*apparent splitting pattern). Anal. Calcd for $C_{37}H_{40}O_7$: C, 74.47; H, 6.76. Found: C, 74.66; H, 6.69.

(b) From the Dichloromethyl Derivative 3d. A solution of **3d** (500 mg, 0.75 mmol), Bu_3SnH (850 mg, 3 mmol), and AIBN (50 mg, 0.3 mmol) in toluene (5 mL) was stirred for 1 h at 100 °C to give the dechloro derivative **3g** (315 mg, 70%) as a colorless syrup.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-D-glucopyranose (3h). A solution of the dichloroheptulose derivative **3b** (3.0 g, 4.8 mmol), Bu_3SnH (3.5 g, 12 mmol), and AIBN (0.3 g) in toluene (50 mL) was stirred for 1 h at 100 °C to give the dechlorinated compound **3h** (2.3 g, 86%) as a colorless syrup: $[\alpha]^{23}_D$ +25.8° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 3456 cm^{-1} (OH); ^1H NMR ($CDCl_3$) α-anomer δ 1.41 (3 H, s, $-CH_3$), 2.58 (1 H, s, –OH), 3.36 (1 H, d, *J* 9.3 Hz, 2-H), 3.64 (1 H, t*, *J* 9.3, 10.0 Hz, 4-H), 3.66 (1 H, dd, *J* 2.1, 10.8 Hz) and 3.72 (1 H, dd, *J* 4.0, 10.8 Hz) (6-H), 3.96 (1 H, t, *J* 9.3 Hz, 3-H), 4.00 (1 H, ddd, *J* 2.1, 4.0, 10.0 Hz, 5-H) (*apparent splitting pattern); β-anomer ($^1/_{15}$ H of α-anomer) δ 1.48 (3 H, s, $-CH_3$), 2.79 (1 H, s, –OH); ^{13}C NMR ($CDCl_3$) δ 26.47 (q, $-CH_3$), 68.90 (t, 6-C), 71.44 (d) and 73.37* (d) (5-C); 73.34 (t), 74.62* (t), 74.76 (t), 74.88* (t), 75.48 (t) and 75.56 (t) ($PhCH_2-$ × 4); 78.00* (d), 78.50 (d), 83.28 (d), 83.59 (d), 83.72* (d) and 85.33* (d) (2, 3, 4-C); 97.30 (s) and 99.82* (s) (1-C); 127.50–128.34, 137.94 (s), 138.11* (s), 138.18 (s), 138.30 (s), 138.57* (s) and 138.69 (s) (C_6H_5- × 4) (*signals of β-anomer). Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.79; H, 6.91. Found: 76.02; H, 6.90.

6-*O*-Acetyl-3,4,5,7-tetra-*O*-benzyl-1-deoxy-D-*gluco*-2-heptulose (3i). A solution of the 1-deoxyheptulose derivative **3h** (550 mg, 1 mmol) and 4-(dimethylamino)pyridine (60 mg) in Et_3N (15 mL)/Ac_2O (1.1 mL) was stirred for 24 h at 0 °C to give the acyclic mono-*O*-acetate **3i** (470 mg, 79%) as a colorless syrup: $[\alpha]^{24}_D$ +27.8° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1733, 1716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.99 and 2.02 (each 3 H, s, 1-H, acetyl), 3.68 (1 H, dd, *J* 5.7, 10.6 Hz) and 3.85 (1 H, dd, *J* 4.4, 10.6 Hz) (7-H), 3.94 (1 H, dd, *J* 4.1, 5.9 Hz, 5-H), 4.00 (1 H, d, *J* 4.1 Hz, 3-H), 4.01 (1 H, dd, *J* 4.1, 5.9 Hz, 4-H), 5.18 (1 H, td*, *J* 4.1, 4.4, 5.7 Hz, 6-H) (*apparent splitting pattern). Anal. Calcd for $C_{37}H_{40}O_7$: C, 74.47; H, 6.76. Found: C, 74.61; H, 6.74.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*glycero*-D-*gulo*-heptitol (4′c). A mixture of the 1-*C*-[bis(methylthio)methyl] derivative 4′a (1.0 g, 1.5 mmol) and Raney Ni (1.5 g) in dioxane (15 mL) was stirred at 80 °C for 1 h to give the tetra-*O*-benzyl-1-deoxyheptitol **4′c** (720 mg, 79%) as a colorless syrup: $[\alpha]^{22}_D$ +1.3° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.18 (3 H, d, *J* 6.3 Hz, 1-H), 2.85 (1 H, d, *J* 4.7 Hz, –OH), 2.92 (1 H, d, *J* 5.0 Hz, –OH), 3.57 (1 H, t*, *J* 5.0, 6.0 Hz, 3-H), 3.63 (2 H, d, *J* 4.4 Hz, 7-H), 3.80 (1 H, dd, *J* 3.5, 6.8 Hz, 5-H), 3.89 (1 H, dd, *J* 3.5, 5.0 Hz, 4-H), 3.93–4.07 (2 H, m, 2-H, 6-H) (*apparent splitting pattern). Anal. Calcd for $C_{35}H_{40}O_6$: C, 75.51; H, 7.24. Found: C, 75.76; H, 7.19.

1,3,4,5-Tetra-*O*-benzyl-7-deoxy-D-*glycero*-L-*gulo*-heptitol (4″c). The tetra-*O*-benzyl-7-deoxyheptitol **4″c** (215 mg, 78%) was prepared from the bis(methylthio) derivative **4″a** (320 mg, 0.49 mmol) by desulfurization with Raney Ni (1.0 g) in dioxane (5 mL) at 80 °C for 1 h; a colorless syrup; $[\alpha]^{22}_D$ +2.6° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.06 (3 H, d, *J* 6.4 Hz, 7-H), 2.25 (1 H, d, *J* 7.8 Hz, –OH), 2.94 (1 H, d, *J* 5.5 Hz, –OH), 3.54 (1 H, dd, *J* 2.9, 7.6 Hz, 5-H), 3.66 (2 H, d, *J* 4.3 Hz, 1-H), 3.65–3.79 (1 H, m, 6-H), 3.72 (1 H, dd, *J* 3.2, 6.9 Hz, 3-H), 3.97 (1 H, dd, *J* 3.2, 7.6 Hz, 4-H), 4.02–4.09 (1 H, m, 2-H). Anal. Calcd for $C_{35}H_{40}O_6$: C, 75.51; H, 7.24. Found: 75.48; H, 7.39.

3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*glycero*-D-*gulo*-heptitol (4′c) and 1,3,4,5-Tetra-*O*-benzyl-7-deoxy-D-*glycero*-L-*gulo*-heptitol (4″c). To a solution of the dichloroheptitol derivative **4b** (2.0 g, 3.2 mmol) in toluene (30 mL) were added Bu_3SnH (2.0 g, 6.9 mmol) and AIBN (0.1 g, 0.6 mmol). The mixture was stirred for 7 h at 100 °C. The reaction mixture was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (150 mL) with toluene/EtOAc (9:1) to separate the resulting deoxyheptitol derivatives into the two epimers, **4′c** (1.1 g, 62%) (earlier eluted fraction) and **4″c** (570 mg, 32%) (later eluted fraction) as colorless syrups. The $[\alpha]_D$ and ^1H NMR spectra of **4′c** and **4″c** were identical to those of the compound synthesized by the bis(methylthio)methyl method as described above.

1-Deoxy-D-*glycero*-D-*gulo*-heptitol (4′d). To a solution of the tetra-*O*-benzyl derivative **4′c** (600 mg, 1.1 mmol) in 90% formic acid/MeOH (1:19, 40 mL) was added Pd-black (200 mg). The mixture was stirred under N_2 overnight at room temperature. The catalyst was filtered off and washed with MeOH/H_2O (1:1). The filtrate and the washings were combined and concentrated. The residue was chromatographed on a column of Dowex 1 × 2 (OH^-, 100 mL) with H_2O. The eluate was concentrated and then lyophilized to give the 1-deoxyheptitol **4′d** (194 mg, 92%) as a white solid: $[\alpha]^{24}_D$ +6.6° (*c* 1, H_2O); $[\alpha]^{20}_D$ +6.8° (*c* 1, H_2O);[6a] ^1H NMR (D_2O) δ 1.19 (3 H, d, *J* 6.4 Hz, 1-H), 3.63 (1 H, dd, *J* 4.9, 5.9 Hz, 3-H), 3.63 (1 H, dd, *J* 2.6, 7.6 Hz, 5-H), 3.63 (1 H, dd, *J* 5.9, 11.7 Hz) and 3.81 (1 H, dd, *J* 2.8, 11.7 Hz) (7-H), 3.77 (1 H, m, 6-H), 3.90 (1 H, quint*, *J* 5.9, 6.0 Hz, 2-H), 3.91 (1 H, dd, *J* 2.6, 4.9 Hz,

4-H) (*apparent splitting pattern).[6b] Anal. Calcd for $C_7H_{16}O_6$: C, 42.85; H, 8.22. Found: C, 42.69; H, 8.43.

7-Deoxy-D-*glycero*-L-*gulo*-heptitol (4″d). The 7-deoxyheptitol **4″d** (94 mg, 89%) was prepared as a white solid from the tetra-*O*-benzyl derivative **4″c** (300 mg, 0.54 mmol) by a procedure similar to that described for **4′d**: $[\alpha]^{24}_D$ −1.1° (*c* 1, H_2O); ^1H NMR (D_2O) δ 1.22 (3 H, d, *J* 6.5 Hz, 7-H), 3.55 (1 H, dd, *J* 4.4, 5.4 Hz, 5-H), 3.64 (1 H, dd, *J* 5.6, 11.1 Hz) and 3.81 (1 H, dd, *J* 2.7, 11.1 Hz) (1-H), 3.72 (1 H, dd, *J* 2.4, 7.8 Hz, 3-H), 3.76 (1 H, ddd, *J* 2.7, 5.6, 7.8 Hz, 2-H), 3.91 (1 H, dd, *J* 2.4, 5.4 Hz, 4-H), 3.95 (1 H, dq, *J* 4.4, 6.5 Hz, 6-H). Anal. Calcd for $C_7H_{16}O_6$: C, 42.85; H, 8.22. Found: C, 42.76; H, 8.35.

(1*S*)-(1(OH),2,4,5/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-1,2,3,4,5-cyclohexanepentol (10a). To a stirred solution of the branched-chain inosose derivative **7** (1.0 g, 1.8 mmol) in THF/MeOH (1:4, 20 mL) was added $NaBH_4$ (100 mg, 2.3 mmol) at −15 to −20 °C. The stirring was continued for 30 min at the same temperature, followed by the addition of AcOH (0.2 mL). The reaction mixture was concentrated, and the residue was partitioned between EtOAc (60 mL) and H_2O (30 mL). The organic layer was washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (150 mL) with toluene/EtOAc (3:1). The eluate was concentrated, and then Et_2O/petroleum ether (1:10, 60 mL) was added to the residue. The mixture was allowed to stand in a refrigerator to give the cyclohexanepentol derivative **10a** (910 mg, 91%) as colorless crystals: mp 58–59 °C; $[\alpha]^{22}_D$ +16.2° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.85 (1 H, dd, *J* 2.9, 15.5 Hz, 6-Hax), 2.04 (1 H, dd, *J* 3.2, 15.5 Hz, 6-Heq), 3.19 and 3.50 (each 1 H, ABq, *J* 8.6 Hz, $-CH_2O-$), 3.39 (1 H, d, *J* 5.1 Hz, 5-OH), 3.46 (1 H, dd, *J* 3.1, 9.6 Hz, 4-H), 3.49 (1 H, s, 1-OH), 3.67 (1 H, d, *J* 9.6 Hz, 2-H), 4.14 (1 H, t, *J* 9.6 Hz, 3-H), 4.15–4.21 (1 H, m, 5-H). Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.79; H, 6.91. Found: C, 75.98; H, 6.99.

(1*S*)-(1(OH),2,4,5/1,3)-1-*C*-(Hydroxymethyl)-1,2,3,4,5-cyclohexanepentol (10b). The pseudo-sugar **10b** (185 mg, 89%) was prepared from the *O*-benzyl derivative **10a** (500 mg, 0.9 mmol) by a procedure similar to that described for **4′d**; a white solid; $[\alpha]^{22}_D$ +27.9° (*c* 1, H_2O); ^1H NMR (D_2O) δ 1.73 (1 H, dd, *J* 2.8, 15.5 Hz, 6-Hax), 2.03 (1 H, dd, *J* 3.4, 15.5 Hz, 6-Heq), 3.43 (1 H, d, *J* 9.6 Hz, 2-H), 3.47 and 3.53 (each 1 H, ABq, *J* 11.4 Hz, $-CH_2O-$), 3.50 (1 H, dd, *J* 3.2, 9.9 Hz, 4-H), 3.86 (1 H, t*, *J* 9.6, 9.9 Hz, 3-H), 4.14 (1 H, q*, *J* 2.8, 3.2, 3.4 Hz, 5-H) (*apparent splitting pattern). Anal. Calcd for $C_7H_{14}O_6\ H_2O$: C, 42.86; H, 7.19. Found: C, 42.98; H, 7.08.

(1*S*)-(1(OH),2,4,5/1,3)-2,3,4-Tri-*O*-benzyl-1-*C*-[(benzyloxy)methyl]-1,2,3,4,5-cyclohexanepentol 1,5-Phenylboronate (10c). To a stirred solution of the cyclohexanepentol derivative **10a** (850 mg, 1.5 mmol) in toluene (15 mL) were added phenylboric acid (400 mg, 3.3 mmol) and *p*-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol). The stirring was continued for 18 h at room temperature. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and then concentrated. The residue was chromatographed on a column of silica gel (100 mL) with toluene/EtOAc (5:1). The eluate was concentrated, and petroleum ether was added to the residue. The mixture was allowed to stand in a refrigerator to give the 1,5-phenylboronate **10c** (890 mg, 91%) as colorless crystals: mp 91–92 °C; $[\alpha]^{22}_D$ +13.4° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.97 (1 H, dd, *J* 4.0, 14.6 Hz, 6-Hax), 2.02 (1 H, dd, *J* 2.2, 14.6 Hz, 6-Heq), 3.33 and 3.91 (each 1 H, ABq, *J* 8.7 Hz, $-CH_2O-$), 3.58 (1 H, dd, *J* 2.6, 9.2 Hz, 4-H), 3.75 (1 H, d, *J* 9.2 Hz, 2-H), 3.91 (1 H, t, *J* 9.2 Hz, 3-H), 4.57 (1 H, quint*, *J* 2.2, 2.6, 4.0 Hz, 5-H), 7.25–7.45 (3 H, m) and 7.89 (2 H, dd, *J* 1.5, 8.0 Hz) (phenyl-H) (*apparent splitting pattern). Anal. Calcd for $C_{41}H_{41}BO_6$: C, 76.88; H, 6.45. Found: C, 76.92; H, 6.47.

(4*S*,5*R*)-2,4-Bis(benzyloxy)-5-hydroxy-5-[(benzyloxy)methyl]-2-cyclohexenone (11). To a solution of the branched-chain bis(methylthio)inosose epimer **6c** (2.0 g, 3.1 mmol) in dioxane (30 mL) was added Raney Ni (6.0 g). The suspension was stirred at 80 °C for 1 h. The reaction mixture was filtered, and the solid was washed with dioxane. The filtrate and the washings were combined and then concentrated. The residue was chromatographed on a column of silica gel (200 mL) with toluene/EtOAc (4:1) to give the cyclohexenone derivative **11** (900 mg, 65%) as a colorless syrup: $[\alpha]^{23}_D$ +76.3° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 3486 (OH), 1698 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.58 and 2.86 (each 1 H, ABq, *J* 16.5 Hz, 6-H), 2.84 (1 H, s, −OH), 3.44 and 3.78 (each 1 H, ABq, *J* 9.1 Hz, $-CH_2O-$), 4.21 (1 H, d, *J* 5.2 Hz, 4-H), 5.73 (1 H, d, *J* 5.2 Hz, 3-H). Anal. Calcd for $C_{28}H_{28}O_5$: C, 75.66; H, 6.35. Found: C, 75.82; H, 6.41.

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Registry No. **1**, 50-99-7; **2**, 13096-62-3; **3a**, 140658-49-7; **3b**, 140658-50-0; **3c**, 140658-53-3; **3′c**, 140676-22-8; **3d**, 140658-56-6; **3e**, 95189-55-2; **3f**, 140658-54-4; **3g**, 140658-55-5; **3h**, 137344-41-3; **3′h**, 140849-70-3; **3i**, 140658-57-7; **4′a**, 116308-10-2; **4″a**, 116308-11-3; (*R*)-**4b**, 116308-14-6; (*S*)-**4b**, 116348-71-1; **4′c**, 140658-58-8; **4″c**, 140849-68-9; **4′d**, 5328-46-1; **4″d**, 140849-69-0; **5a**, 140658-51-1; **5b**, 140658-52-2; **6a**, 116308-20-4; **6b**, 116308-18-0; **6c**, 140849-67-8; **6d**, 116308-02-2; **7**, 115250-38-9; **8**, 83465-22-9; **9**, 83480-29-9; **10a**, 140676-23-9; **10b**, 115250-26-5; **10c**, 140676-24-0; **11**, 140658-59-9.

Supplementary Material Available: Complete ^1H NMR data of all compounds described in the Experimental Section and experimental details of the 1,3-dithian-2-yl series (20 pages). Ordering information is given on any current masthead page.