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De novo highly stereocontrolled synthesis of 2,6-dideoxy sugars by use of 2,6-anhydro-2-thio sugars

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ABSTRACT

Representative 2,6-dideoxy sugars, L-cladinose (**1**), L-mycarose (**2**), L-oleandrose (**3**), L-olivose (**4**), and all of their C-3 epimers, 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-L-*arabino*-hexopyranose (**26**), 2,6-dideoxy-3-*C*-methyl-L-*arabino*-hexopyranose (L-olivomycose) (**27**), 2,6-dideoxy-3-*O*-methyl-L-*ribo*-hexopyranose (L-cymarose) (**32**), and 2,6-dideoxy-L-*ribo*-hexopyranose (L-digitoxose) (**33**) have been stereospecifically synthesized through a highly stereoselective addition of a nucleophilic reagent to the C-3 carbonyl groups of methyl 2,6-anhydro-4-*O*-benzyl-2-thio-α-L-*arabino*-hexopyranosid-3-ulose (**11**) or methyl 2,6-anhydro-4-*O*-benzyl-2-thio-β-L-*arabino*-hexopyranosid-3-ulose (**12**) possessing 2,6-anhydro-2-thio structures. Anomers **11** and **12** were both prepared in stereocontrolled fashion by treatment of a common intermediate, methyl 2,6-anhydro-4-*O*-benzyl-3-*O*-tetrahydropyranyl-2-thio-α-L-altropyranoside (**8**) with Lewis acids in methanol followed by oxidation.

INTRODUCTION

Numerous 2,6-dideoxy sugars as the glycosidic components of useful antibiotics have been discovered during the past three decades[1]. Recently, as the mechanisms of action of biologically active natural products have been elucidated more precisely, the glycons as well as the aglycons of these natural products have received considerable attention from the biological standpoint. In connection with projects aimed at development of methodology for stereocontrolled synthesis of natural products, we have recently reported a highly stereoselective and powerful glycosylation method for 2,6-dideoxy sugars by use of 2,6-anhydro-2-thio sugars[2]. Further, in extended studies, we have investigated the efficient use of 2,6-anhydro-2-thio sugars for stereocontrolled synthesis of 2,6-dideoxy sugars, especially, 2,6-dideoxy-3-*C*-branched carbohydrates[3]. We describe here full details of the latter work, which has resulted in syntheses of L-cladinose[4] (**1**), L-mycarose[5] (**2**), L-oleandrose[6] (**3**), L-olivose[7] (**4**), and all of their C-3 epimers, the novel sugar **26**, L-olivomycose[8] (**27**), L-cymarose[9] (**32**) and L-digitoxose[10] (**33**) by using a highly stereocontrolled addition of a nucleophilic reagent to a carbonyl function at C-3 of a 2,6-anhydro-2-thio sugar as the key step.

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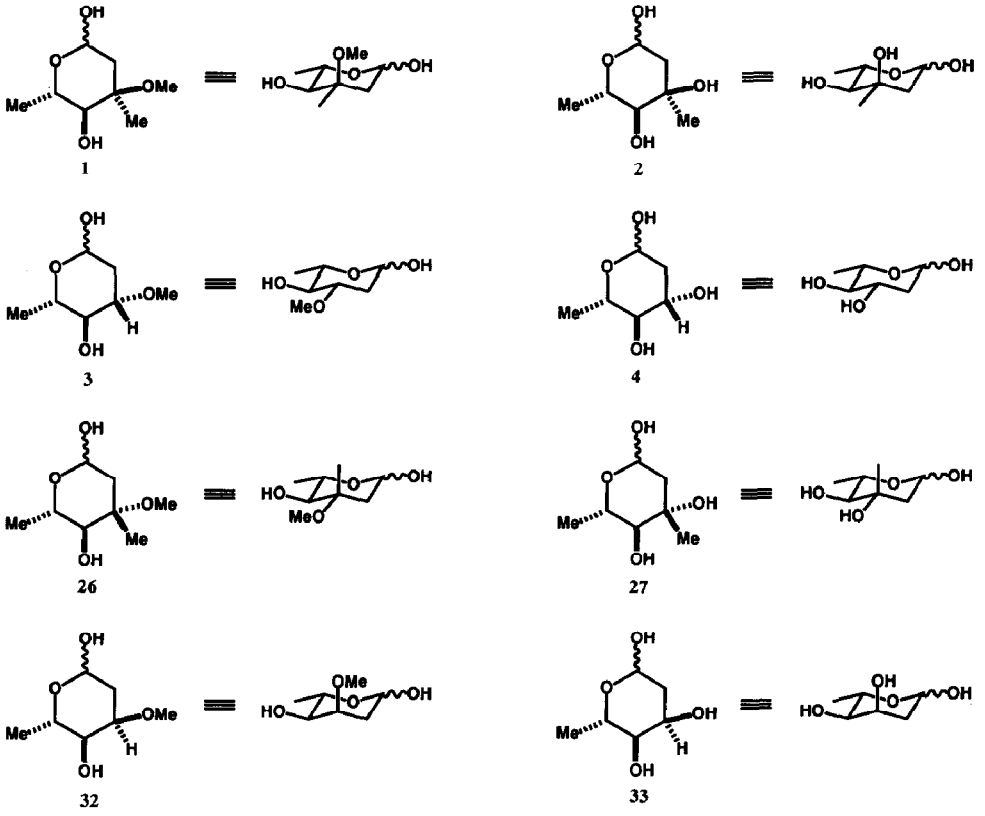
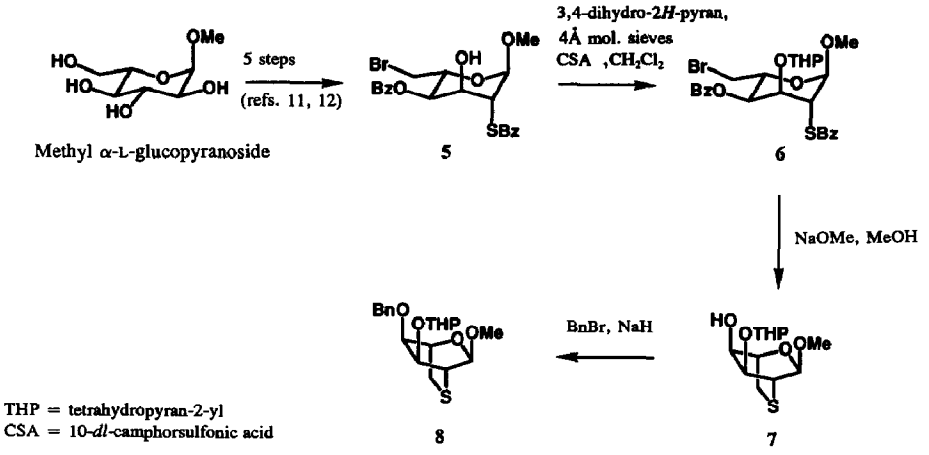


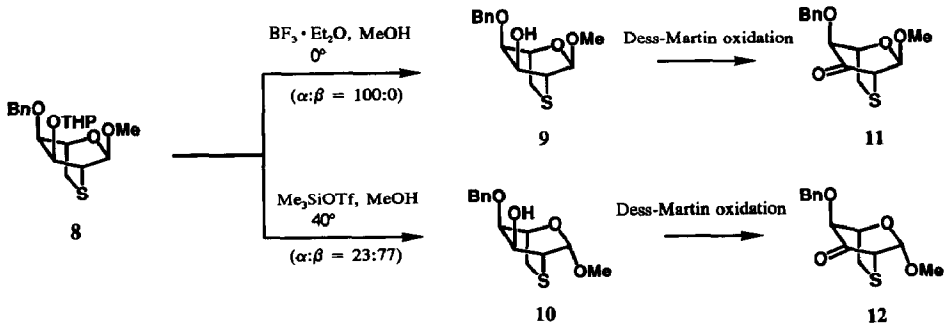
RESULTS AND DISCUSSION

The approach began with the conversion of methyl α-L-glucopyranoside into compound **5** according to the literature[11,12]. No purifications were required in these 5 steps, and **5** was obtained in good overall yield (58%) even on the large scale. Treatment of **5** with 3.0 equiv. of 3,4-dihydro-2*H*-pyran in the presence of catalytic amounts of 10-*dl*-camphorsulfonic acid and 4Å molecular sieves in dichloromethane for 2 h at 0° gave **6** in 97% yield. Basic hydrolysis of **6** with 3.0 equiv. of methanolic sodium methoxide for 3 h at 25° led to formation of a 2,6-anhydro-2-thio bridge with deprotection of benzoyl groups, affording **7** in 98% yield. Standard benzylation of **7** (2.0 equiv. of benzyl bromide and 2.0 equiv. of sodium hydride in *N*,*N*-dimethylformamide for 3 h at 25°) produced **8** in 98% yield.

Treatment of **8** with catalytic amounts of several Lewis acids or methanolic hydrogen chloride caused loss of the THP group with or without reformation of the methyl glycoside. When **8** was treated with 0.2 equiv. of $BF_3 \cdot Et_2O$ in methanol for 0.5 h at 0°, the deprotected α anomer **9** was obtained exclusively in 97% yield. On the other hand, treatment with 0.2 equiv. of trimethylsilyl triflate in methanol for 1.5 h at 40°, gave mainly the thermodynamically more-stable β anomer **10**, in 65% yield, along with 19%

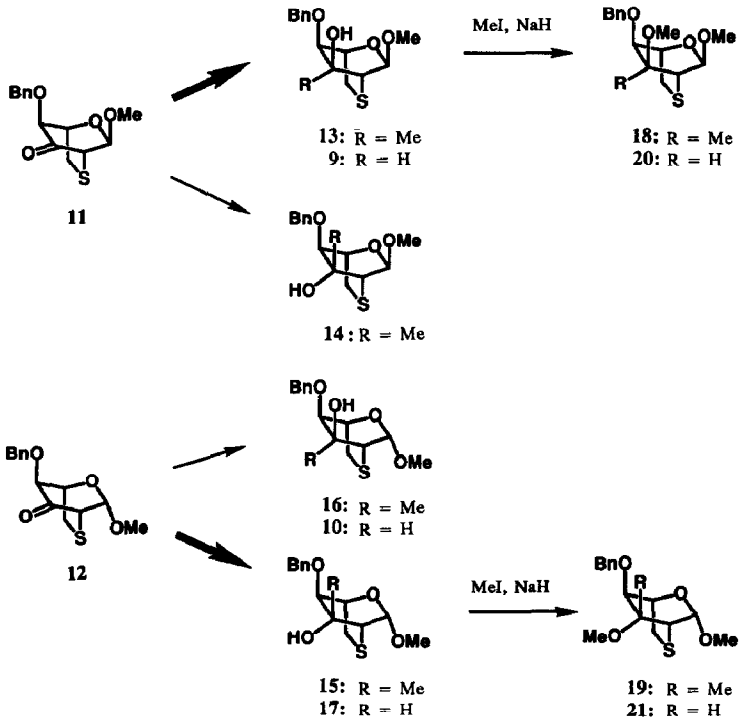


of the α anomer. However, treatment of **8** with trimethylsilyl triflate above 40° generated considerable amounts of an unidentified by-product. Thus, both anomers **9** and **10** could be synthesized in highly stereocontrolled fashion. The combination of the configuration of the anomeric position and the 2,6-anhydro-2-thio structure predictably played a crucial role for the highly stereocontrolled addition of nucleophilic reagents to the carbonyl function at C-3 of compounds **11** and **12**, as described next. The 3-hydroxy products **9** and **10** were each oxidized by periodinane under the Dess–Martin conditions[13] to give the ketones **11** and **12** in 97 and 99% yields, respectively.



At this stage, we examined several nucleophilic additions to the carbonyl functions of **11** and **12**. The addition of Grignard reagent (MeMgBr) to the α anomer **11** at various temperatures gave mainly the α-methyl-β-hydroxy product **13**, whereas treatment of **11** with methyllithium at 0° caused considerable decomposition of **11**. Highly stereocontrolled addition was best effected by treatment of **11** with 4.0 equiv. of methylmagnesium bromide in ether for 1.5 h at $-75° \rightarrow -25°$ and afforded **13** in 85% yield along with 9% of its C-3 epimer **14**. In dramatic contrast, the addition of methylmagnesium bromide or methyllithium to the β anomer **12** generated exclusively the C-3 epimer, the β-methyl-α-hydroxy product **15**, in both instances. The best ster-

eocontrolled addition was observed by treatment of **12** with 3.0 equiv. of methyllithium in ether for 0.5 h at −98° and afforded **15** in 92% yield together with 7% of its C-3 epimer **16**. At this stage, the configurations at C-3 of **13** and **15** were ascertained by the observation of a nuclear Overhauser effect of H-4 upon irradiation at the C-3-Me resonance frequency (see Experimental section). Thus, both C-3-Me epimers could be synthesized in good overall yields with high stereocontrol. Furthermore, the addition of hydride anion from diisobutylaluminum hydride (DIBAL) to **11** and **12** showed similar behavior. The addition of 3.0 equiv. of DIBAL to the α anomer **11** in toluene for 1 h at −78° gave stereospecifically the β-hydroxy product **9** in 97% yield. Treatment of the β anomer **12** with 2.0 equiv. of DIBAL in toluene at −78° produced predominantly the α-hydroxy product **17** in 85% yield, together with 5% of its C-3 epimer **10**. The structure of **17** was also confirmed by n.O.e. experiments (see Experimental section). The results strongly suggest the following mechanism for these reactions. In **12**, the repulsive electronic interaction between the sulfur atom and the nucleophile approaching the C-3 position strongly impedes the reaction. Consequently, the nucleophilic species attacks predominantly the α-face of the carbonyl function of **12** to avoid this disfavored interactions. On the other hand, in structure **11**, because the 1,3-diaxial interaction between the nucleophe and the OMe group at C-1 overcomes the repulsive participation by sulfur, β-attack of the reagent was favored. The effects of different nucleophiles are under current study in detail.



11

13: R = Me
9: R = H

18: R = Me
20: R = H

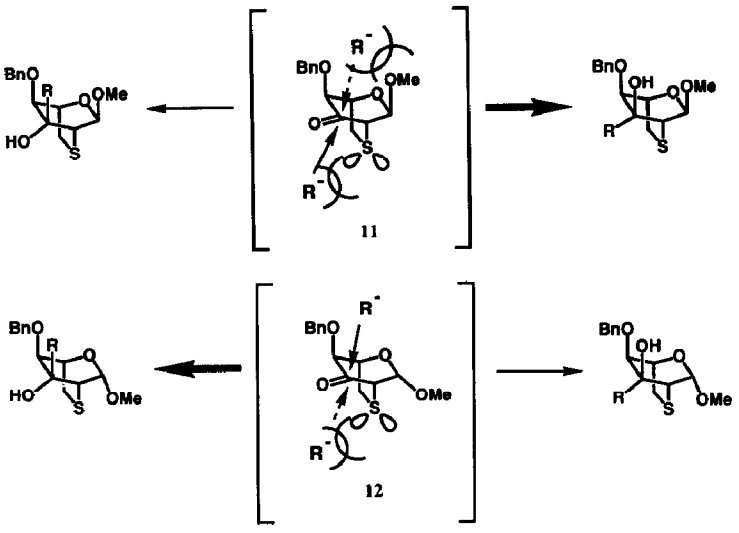
14: R = Me

12

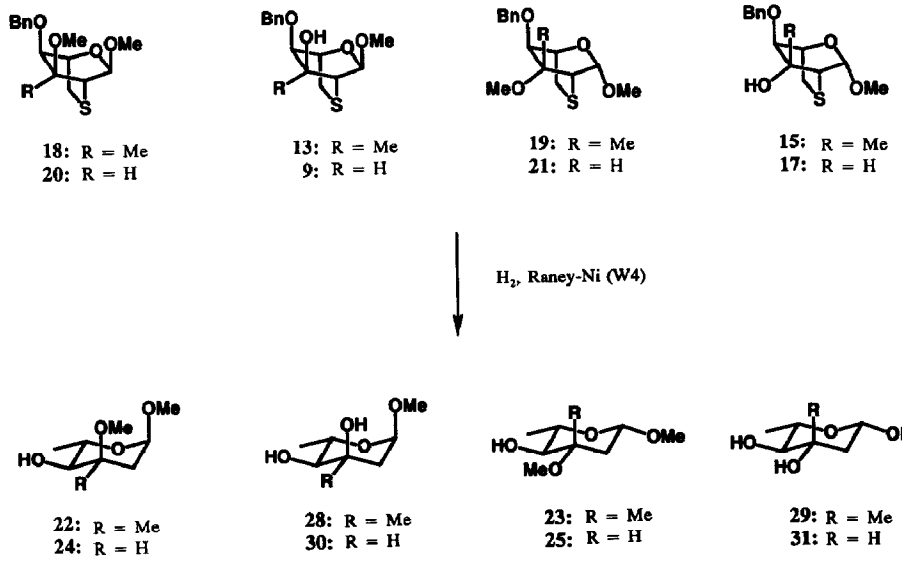
16: R = Me
10: R = H

15: R = Me
17: R = H

19: R = Me
21: R = H



At the next stage, compounds **13**, **15**, **9**, and **17** were *O*-methylated (2.0 equiv. of methyl iodide and 2.0 equiv. of sodium hydride in *N*,*N*-dimethylformamide for 30 min, 25°) to afford **18** (98%), **19** (91%), **20** (94%), and **21** (99%) respectively, and these were subjected to simultaneous desulfurization and *O*-debenzylation by hydrogenolysis [2a] in the presence of Raney-Ni (W4) in ethanol–1,4-dioxane at 40° to give the desired 2,6-dideoxy compounds **22** (refs, **24** 4a–d, 4f), **23**, **24** (refs. 9a, 9e–g, 9i, 9l), and **25** (refs. 6d) in 85, 85, 82, and 78% yields respectively. Finally, acid hydrolyses of the methyl glycosides of **22**, **23** and **25** (0.6M HCl for 24 h) proceeded smoothly to give L-cladinose (**1**), the new C-3 epimer **26** of L-cladinose, L-oleandrose (**3**), and the C-3 epimer **27** of L-oleandrose in 89, 98, 73, and 76% yields respectively.



L-Mycarose (**2**), the C-3 epimer **32** of L-mycarose, L-olivose (**4**), and the C-3 epimer (**33**) of L-olivose were obtained in 81, 63, 74, and 65% overall yields, respectively, by direct hydrogenolyses of **13**, **15**, **9** and **17**, followed by acid hydrolyses of the resulting products, **28** (refs. 4b–d, 5a), **29**, **30** (refs. 10g–i, 10k, 10r), and **31** (refs. 7d–e, 7m).

In conclusion, *de novo* highly stereocontrolled syntheses of 2,6-dideoxy sugars, including the 2,6-dideoxy-3-*C*-branched sugars L-cladinose (**1**), L-mycarose (**2**), L-oleandrose (**3**), L-olivose (**4**), and all of their C-3 epimers, 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-L-*arabino*-hexopyranose (**26**), L-olivomycose (**27**), L-cymarose (**32**), and L-digitoxose (**33**) were achieved by effective assistance of the combination of 2,6-anhydro-2-thio structures and the configurations at the anomeric position.

EXPERIMENTAL

General methods. — Melting points were determined on a Yanaco MP-S3 micro hot-stage and are uncorrected. Optical rotations were measured on a Jasco DIP-360 photoelectric polarimeter in $CHCl_3$ at 25° unless otherwise noted. I.r. spectra were recorded with a Bio-Rad Digilab FTS-65 spectrometer and ^{1}H-n.m.r. spectra with either a Jeol GSX270 or a Jeol GSX400 spectrometer in $CDCl_3$ using Me_4Si as the internal standard unless otherwise noted. Silica-gel t.l.c. and column chromatography were performed on Merck TLC 60F-254 and Merck Kieselgel 60, respectively. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon with oven-dried glassware. In general, organic solvents were purified and dried by the appropriate procedure, and evaporation and concentration were carried out under diminished pressure below 30°, unless otherwise noted.

Methyl 2-S-benzoyl-4-O-benzoyl-6-bromo-2,6-dideoxy-3-O-tetra-hydropyranyl-α-L-altropyranoside (6). — To a stirring suspension of **5** (ref. 12, 5.19 g, 10.8 mmol), 3,4-dihydro-2*H*-pyran (2.95 mL, 32.3 mmol) and 4 Å molecular sieves (16.2 g) in dry CH_2Cl_2 (162 ml) was added 10-*dl*-camphorsulfonic acid (1.50 g, 6.5 mmol) under ice-cooling. After being stirred for 1.5 h under ice-cooling, the mixture was made neutral with Et_3N and then the resulting mixture was filtered to remove the molecular sieves. The filtrate was washed with saturated aqueous NaCl (60 mL), dried over Na_2SO_4, and concentrated to a crude syrup. The syrup was chromatographed on silica gel (610 g) with 5:1 hexane–EtOAc to afford **6** (5.91 g, 97%) as a white foam; R_F 0.29 and 0.31 (5:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz) faster product on t.l.c.: δ 1.25–1.9 (6 H, m, H-2, 3, and 4 of THP), 3.23 (1 H, ddd, *J* 11.6, 4.2, and 4.2 Hz, H-5 of THP), 3.47 (3 H, s, OMe), 3.57 (1 H, dd, *J* 11.0 and 7.2 Hz, H-6), 3.68 (1 H, dd, *J* 11.0 and 2.4 Hz, H-6′), 4.15–4.3 (1 H, m, H-5′ of THP), 4.33 (1 H, d, *J* 3.6 Hz, H-2), 4.39 (1 H, dd, *J* 3.6 and 3.6 Hz, H-3), 4.68 (1 H, ddd, *J* 10.0, 7.2 and 2.4 Hz, H-5), 4.87 (1 H, br s, H-1), 5.08 (1 H, br dd, H-1 of THP), 5.28 (1 H, dd, *J* 10.0 and 3.6 Hz, H-4), and 7.4–8.2 (10 H, Ph × 2); s lower product on t.l.c.: δ 1.25–1.9 (6 H, m, H-2,3, and 4 of THP), 3.52 (3 H, s, OMe), 3.54 (1 H, dd, *J* 11.0 and 7.6 Hz, H-6), 3.64 (1 H, dd, *J* 11.0 and 2.4 Hz, H-6′), 4.1–4.25 (2 H, m, H-5 and H-5′ of THP), 4.31 (1 H, dd, *J* 3.8 Hz, H-3), 4.42 (1 H, dd, *J* 3.8 and 1.0 Hz, H-2), 4.63 (1 H, ddd, *J* 9.9, 7.6 and 2.4 Hz, H-5), 4.69 (1 H, dd, *J* 3.2 and 3.2 Hz, H-1 of

THP), 4.88 (1 H, br s, H-1), 5.24 (1 H, dd, *J* 9.9 and 3.8 Hz, H-4), and 7.4–8.1 (10 H, Ph × 2).

Methyl 2,6-anhydro-3-O-tetrahydropyranyl-2-thio-α-L-altropyranoside (**7**). — To an ice-cold stirring solution of **6** (5.71 g, 10.1 mmol) in dry MeOH (114 mL) was added 5M NaOMe in MeOH (6.06 mL, 30.3 mmol). After being stirred for 3 h at 25° , the mixture was made neutral with solid CO_2. The resulting mixture was extracted with $CHCl_3$ (40 mL × 3) and the extracts were washed with saturated aqueous NaCl (50 mL), dried over Na_2SO_4, and concentrated to a crude syrup. The syrup was chromatographed on silica gel (140 g) with 2:1 hexane–EtOAc to afford **7** (2.72 g, 98%) as a colorless syrup. R_F 0.27 and 0.28 (2:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz) faster product on t.l.c.: δ 1.5–1.95 (6 H, m, H-2, 3, and 4 of THP), 2.61 (1 H, dd, *J* 11.8 and 0.8 Hz, H-6), 2.92 (1 H, br dd, H-2), 3.00 (1 H, dd, *J* 11.8 and 5.9 Hz, H-6′), 3.49 (3 H, s, OMe), 3.45–3.46 (1 H, m, H-5 of THP), 3.73 (1 H, d, *J* 10.2 Hz, OH), 3.9–3.95 (2 H, m, H-4 and H-5′ of THP), 4.38 (1 H, ddd, *J* 5.9, 2.4 and 0.8 Hz, H-5), 4.43 (1 H, ddd, *J* 8.0, 0.8 and 0.8 Hz, H-3), 4.78 (1 H, dd, *J* 4.4 and 3.0 Hz, H-1 of THP), 5.03 (1 H, dd, *J* 2.8 and 0.8 Hz, H-1); slower product on t.l.c.: δ 1.5–1.95 (6 H, m, H-2, 3, and 4 of THP), 2.63 (1 H, dd, *J* 11.4 and 1.6 Hz, H-6), 2.85 (1 H, dd, *J* 2.0 and 1.8 Hz, H-2), 3.02 (1 H, dd, *J* 11.4 and 4.8 Hz, H-6′), 3.45 (3 H, s, OMe), 3.45–3.6 (1 H, m, H-5 of THP), 3.79 (1 H, d, *J* 8.0 Hz, OH), 3.9–4.05 (2 H, m, H-4 and H-5′ of THP), 4.34 (1 H, ddd, *J* 4.8, 2.4 and 1.6 Hz, H-5), 4.39 (1 H, ddd, *J* 7.9, 1.8 and 1.8 Hz, H-3), 4.81 (1 H, dd, *J* 4.2 and 3.4 Hz, H-1 of THP), and 5.07 (1 H, dd, *J* 2.0 and 1.8 Hz, H-1).

Anal. Calc. for $C_{12}H_{20}O_5S$: C, 52.16; H, 7.29. Found: C, 51.84; H, 7.03.

Methyl 2,6-anhydro-4-O-benzyl-3-O-tetrahydropyranyl-2-thio-α-L-altropyranoside (**8**). — To an ice-cold stirring solution of **7** (2.10 g, 7.6 mmol) in dry DMF (42.0 ml) was added NaH (364 mg, 15.2 mmol) portionwise. The mixture was stirred for 1 h at 0° and then benzyl bromide (1.81 mL, 15.2 mmol) was added dropwise. After being stirred at 25° for 1 h, EtOH (1.81 mL) was added to the mixture and then the resulting mixture was poured into ice–water (100 mL). The mixture was extracted with Et_2O (30 mL × 3) and the extracts were washed with saturated aqueous NaCl (40 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (150 g) with 3:1 hexane–EtOAc to afford **8** (2.25 g, 98%) as a colorless syrup, R_F 0.49 and 0.50 (3:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 1.45–1.95 (6 H, m, H-2, 3, and 4 of THP), 2.52 (1 H, dd, *J* 11.8 and 1.8 Hz, H-6), 2.98 (1 H, dd, *J* 2.4 and 1.6 Hz, H-2), 3.04 (1 H, dd, *J* 11.8 and 4.0 Hz, H-6′), 3.45–3.55 (1 H, m. H-5 of THP), 3.49 (3 H, s, OMe), 3.71 (1 H, dd, *J* 8.4 and 1.8 Hz, H-4), 3.95–4.1 (1 H, m, H-5′ of THP), 4.33 (1 H, ddd, *J* 8.4, 2.4 and 1.6 Hz, H-3), 4.39 (1 H, dd, *J* 4.0, 1.8 and 1.8 Hz, H-5), 4.6–4.7 (1 H, m, H-1 of THP), 4.63 and 4.72 (each 1 H, ABq, *J* 12.0 Hz, CH_2Ph), 5.18 (1 H, dd, *J* 1.6 and 1.6 Hz, H-1), and 7.25–7.45 (5 H, Ph).

Anal. Calc. for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15. Found: C, 62.28; H, 7.17.

Methyl 2,6-anhydro-4-O-benzyl-2-thio-α-L-altropyranoside (**9**). — Compound **8** (101 mg, 0.276 mmol) was dissolved in dry MeOH (2.0 mL) and $BF_3 \cdot Et_2O$ (μL, 0.0553 mmol) was added to the solution under ice-cooling. After being stirred for 0.5 h, at 0°, the mixture was made neutral with Et_3N and then concentrated. The residue was

chromatographed on silica gel (8 g) with 3:1 hexane–EtOAc to afford **9** (75.6 mg, 97%) as colorless crystals; m.p. 46.5–47.0° (hexane–EtOAc), $[\alpha]_D$ −110° (*c* 0.89); R_F 0.50 (3:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 2.52 (1H, dd, *J* 11.8 and 1.6 Hz, H-6), 2.86 (1 H, dd, *J* 2.2 and 2.2 Hz, H-2), 2.97 (1 H, dd, *J* 11.8 and 5.0 Hz, H-6'), 3.45 (3 H, s, OMe), 3.68 (1 H, dd, *J* 8.4 and 1.9 Hz, H-4), 3.96 (1 H, d, *J* 12.0 Hz, OH), 4.28 (1 H, dddd, *J* 12.0, 8.4, 2.2, and 1.8 Hz, H-3), 4.37 (1 H, ddd, *J* 5.0, 1.9 and 1.6 Hz, H-5), 4.64 and 4.89 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), and 5.15 (1 H, dd, *J* 2.2 and 1.8 Hz, H-1).

Anal. Calc. for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43. Found: C, 59.72; H, 6.36.

*Methyl 2,6-anhydro-4-O-benzyl-2-thio-β-*L*-altropyranoside* (**10**) *and its anomer* **9**. — Compound **8** (168 mg, 0.458 mmol) was dissolved in dry MeOH (3.4 mL) and Me_3SiOTf (0.018 mL, 0.0965 mmol) was added to the solution. After being stirred for 1.5 h at 40°, the mixture was made neutral with Et_3N and then concentrated. The residue was chromatographed on silica gel (8 g) with 3:1 hexane–EtOAc to afford **10** (84.0 mg, 65%) as colorless crystals and **9** (24.5 mg, 19%). Compound **10** had m.p. 85.5–86.0° (hexane–EtOAc); $[\alpha]_D$ +17° (*c* 0.79); R_F 0.40 (2:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz) δ 2.50 (1 H, ddd, *J* 11.8, 3.6, and 0.3 Hz, H-6), 3.04 (1 H, ddd, *J* 3.8, 3,6 and 0.3 Hz, H-2), 3.27 (1 H, dd, *J* 11.8 and 3.2 Hz, H-6'), 3.53 (3 H, s, OMe), 3.61 (1 H, d, *J* 3.9 Hz, H-4), 3.85 (1 H, d, *J* 7.8 Hz, OH), 4.23 (1 H, dd, *J* 3.6 and 3.2 Hz, H-5), 4.43 (1 H, ddd, *J* 7.8, 3.9, and 3.8 Hz, H-3), 4.71 (2 H, s, CH_2Ph), and 5.16 (1 H, d, *J* 3.6 Hz, H-1).

Anal. Calc. for $C_{14}H_{18}O_4S$: C, 59.55; H, 46.3. Found: C, 59.62; H, 6.45.

*Methyl 2,6-anhydro-4-O-benzyl-2-thio-α-*L*-arabino-hexopyranosid-3-ulose* (**11**). — To a stirred solution **9** (75.9 mg, 0.268 mmol) in dry CH_2Cl_2 (3.0 mL) was added Dess–Martin periodinane[13] (454 mg, 1.07 mmol). After being stirred for 2 h at 25°, the mixture was diluted with ether (3.0 mL) and a mixture (3.0 mL) of 7:1 saturated aqueous $Na_2S_2O_3$–saturated aqueous $NaHCO_3$. The resulting mixture was extracted with ether (3 mL × 3) and extracts were washed with saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous NaCl (5 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (4 g), with 10:1 hexane–EtOAc to afford **11** (72.8 mg, 97%) as a pale-yellow syrup. $[\alpha]_D$ +89.6° (*c* 0.79); R_F 0.47 (10:1 toluene–EtOAc); μ_{max}^{CHCl3} 1741 cm^{-1}; ^{1}H-n.m.r. (270 MHz) δ 2.68 (1 H, dd, *J* 11.6 and 2.0 Hz, H-6), 3.16 (1 H, d, *J* 2.2 Hz, H-2), 3.17 (1 H, dd, *J* 11.6 and 4.0 Hz, H-6'), 3.47 (3 H, s. OMe), 3.80 (1 H, d, *J* 1.8 Hz, H-4), 4.56 (1 H, ddd, *J* 4.0, 2.0 and 1.8 Hz, H-5), 4.82 and 4.97 (each 1H, ABq, *J* 12.2 Hz, CH_2Ph), and 5.24 (1 H, d, *J* 2.2 Hz, H-1).

Anal. Calc. for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 59.89; H, 5.80.

*Methyl 2,6-anhydro-4-O-benzyl-2-thio-β-*L*-arabino-hexopyranosid-3-ulose* (**12**). — By the procedure described in the preparation of **11**, compound **10** (7.1 mg, 0.273 mol) was oxidized by Dess–Martin periodinane (463 mg, 1.09 mmol) to give **12** (72.8 mg, 97%) as a pale-yellow syrup, $[\alpha]_D$ +198° (*c* 0.72); R_F 0.45 (10:1 toluene–EtOAc); ψ_{max}^{CHCl3} 1738 cm^{-1}; ^{1}H-n.m.r. (270 MHz): δ 2.73 (1 H, dd, *J* 11.6 and 3.0 Hz, H-6), 3.32 (1 H, d, *J* 2.8 Hz, H-2), 3.41 (1 H, dd, *J* 11.6 and 2.4 Hz, H-6'), 3.57 (1 H, s, OMe), 4.15 (1 H, d, *J* 1.0 Hz, H-4), 4.46 (1 H, ddd, *J* 3.0, 2.4 and 1.0 Hz, H-5), 4.85 and 5.01 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), and 5.22 (1 H, d, *J* 2.8 Hz, H-1).

Anal. Calc. for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 59.75; H, 5.79.

Methyl 2,6-anhydro-4-O-benzyl-3-C-methyl-2-thio-α-L-altropyranoside (**13**) *and its C-3 epimer* **14**. — To a stirred solution of **11** (125 mg, 0.446 mmol) in dry ether (2.5 mL) was added 3.0M MeMgBr in ether (0.595 mL, 1.78 mmol) at −78° and then the mixture was gradually warmed to −25° over 1.5 h with stirring. To the mixture was added saturated aqueous NH_4Cl (5 mL) and the resulting mixture was extracted with ether (3 mL × 3). The extracts were washed with saturated aqueous NaCl (4 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (13 g) with 10:1 toluene–EtOAc to afford **13** (112 mg, 85%) and its C-3 epimer **14** (11.8 mg, 9%) as pale-yellow syrups. Compound **13** had $[\alpha]_D$ −101° (*c* 0.99); R_F 0.47 (10:1 toluene–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 1.54 (3 H, d, *J* 0.8 Hz, C3-Me), 2.49 (1 H, dd, *J* 11.6 and 1.6 Hz, H-6), 2.60 (1 H, d, *J* 2.0 Hz, H-2), 2.94 (1 H, dd, *J* 11.6 and 4.8 Hz, H-6′), 3.19 (1 H, d, *J* 1.6 Hz, H-4), 3.49 (3 H, s, OMe), 4.33 (1 H, ddd, *J* 4.8, 1.6 and 1.6 Hz, H-5), 4.50 and 4.95 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), 4.65 (1 H, d, *J* 0.8 Hz, OH), and 5.22 (1 H, d, *J* 2.0 Hz, H-1).

Irradiation at the C-3-Me resonance frequency caused n.O.e. of H-2 (8%) and H-4 (10%).

Anal. Calc. for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.88; H, 6.71.

Compound **14** had $[\alpha]_D$ −30.5° (*c* 1.09); R_F 0.44 (10:1 toluene–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 1.58 (3 H, s, C3-Me), 2.62 (1 H, dd, *J* 11.6 and 2.2 Hz, H-6), 2.68 (1 H, d, *J* 0.8 Hz, H-2), 3.03 (1 H, dd, *J* 11.6 and 3.8 Hz, H-6′), 3.32 (1 H, s, H-4), 3.46 (3 H, s, OMe), 3.61 (1 H, br s, OH), 4.29 (1 H, br dd, H-5), 4.64 and 4.74 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), and 5.29 (1 H, d, *J* 0.8 Hz, H-1).

Anal. Calc. for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.56; H, 6.62.

Methyl 2,6-anhydro-4-O-benzyl-3-C-methyl-2-thio-β-L-mannopyranoside (**15**) *and its C-3 epimer* **16**. — To a stirred solution of **12** 106 mg, 0.378 mmol) in dry ether (2.12 mL) was added 1.02M MeLi in ether (0.986 mL, 1.06 mmol) at −98°. After being stirred at same temperature for 0.5 h, saturated aqueous NH_4Cl (5 mL) was added to the mixture which was then extracted with ether (3 mL × 3). The extracts were washed with saturated aqueous NaCl (4 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (5.6 g) with 3:1 hexane–acetone to afford **15** (103 mg, 92%) as a colorless syrup and its C-3 epimer **16** (8.0 mg, 7.1%) as crystals. Compound **15** had $[\alpha]_D$ +50.2° (*c* 0.71): R_F 0.31 (3:1 hexane–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.52 (3 H, d, *J* 0.8 Hz, C3-Me), 2.59 (1 H, ddd, *J* 11.6, 3.2 and 1.0 Hz, H-6), 2.79 (1 H, dd, *J* 3.6 and 1.0 Hz, H-2), 3.26 (1 H, dd, *J* 11.6 and 2.4 Hz, H-6′), 3.54 (1 H, s, H-4), 3.72 (1 H, d, *J* 0.8 Hz, OH), 4.19 (1 H, dd, *J* 3.2 and 2.4 Hz, H-5), 4.63 and 4.73 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), and cuased n.O.e. of H-1 (17%) and H-2 (12%) 5.05 (1 H, d, *J* 3.6 Hz, H-1). Irradiation at the C-3-Me resonance frequency n.O.e. of H-1 (17%) and H-2 (12%).

Anal. Calc. for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.80; H, 6.84.

Compound **16** had m.p. 102.5–103.0° (hexane–EtOAc, needles); $[\alpha]_D$ +53.9° (*c* 0.52); R_F 0.22 (3:1 hexane–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.58 (3 H, s, C-3-Me), 2.50 (1 H, dd, *J* 11.6 and 3.6 Hz, H-6), 2.77 (1 H, dd, *J* 3.6 Hz, H-2), 3.25 (1 H, dd, *J* 11.6 and 2.4 Hz, H-6′), 3.47 (1 H, s, H-4), 3.54 (1 H, s, OMe), 3.63 (1 H, s, OH), 4.21 (1 H, dd, *J* 3.6

and 2.4 Hz, H-5), 4.67 and 4.74 (each 1 H, ABq, *J* 12.0 Hz, CH_2Ph), and 5.28 (1 H, d, *J* 3.6 Hz, H-1).

*Methyl 2,6-anhydro-4-*O*-benzyl-2-thio-α-*L*-*altropyranoside (**9**) *from* **11***. — To a stirred solution of **11** (112 mg, 0,40 mmol) in dry toluene (1.12 mL) was added 1.02M diisobutyl aluminum hydride in toluene (1.18 mL, 1.20 mmol) at −78°. After being stirred for 1 h at −78°, saturated aqueous NH_4Cl (2 mL) was added to the mixture, which was then extracted with $CHCl_3$ (1 mL × 3). The extracts were washed with saturated aqueous NaCl (4 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (13 g) with 3:1 hexane–EtOAc to afford **9** (110 mg, 97%) as the only isolated product.

*Methyl 2,6-anhydro-4-*O*-benzyl-2-thio-β-*L*-mannopyranoside* (**17**) *and its C-3 epimer* **10**. — To a stirred solution of **12** (139 mg, 0.496 mmol) in dry toluene (1.39 mL) was added 1.02M diisobutyl aluminum hydride in toluene (0.97 mL, 0.992 mmol) at −78°. The mixture was stirred for 20 min at −78°, and then saturated aqueous NH_4Cl (2 mL) was added. The mixture was extracted with $CHCl_3$ (1 mL × 3) and the extracts were washed with saturated aqueous NaCl (4 mL), dried over Na_2SO_4, and concentrated to a crude syrup, which was chromatographed on silica gel (13 g) with 3:1 hexane–EtOAc to afford **17** (119 mg, 85%) and **10** (7.0 mg, 5.0%) as colorless syrups. Compound **17** had $[\alpha]_D$ +50.5° (*c* 0.38); R_F 0.38 (3:1 toluene–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 2.59 (1 H, dd, *j* 12.0 and 3.0 Hz, H-6), 2.98 (1 H, dd, *J* 2.4 and 3.0 Hz, H-2), 3.01 (1 H, d, *J* 11.8 Hz, OH), 3.28 (1 H, dd, *J* 12.0 and 3.2 Hz, H-6′), 3.47 (1 H, d, *J* 2.4 Hz, H-4), 3.56 (3 H, s, OMe), 4.10 (1 H, ddd, *J* 11.8, 2.4 and 2.4 Hz, H-3), 4.19 (1 H, dd, *J* 3.2 and 3.0 Hz, H-5), 4.68 and 4.77 (each 1 H, ABq, *J* 12.0 Hz, CH_2Ph), 5.01 (1 H, d, *J* 2.4 Hz, H-1), and 7.25–7.45 (5 H, Ph).

Irradiation at the H-1 resonance frequency caused n.O.e. of H-2 (12%) and H-3 (16%).

Anal. Calc. for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43. Found: C, 59.58; H, 6.27.

O-*Methylation of 2,6-anhydro-3-hydroxy-2-thio compounds*, **13**, **15**, **9**, *and* **17**: *General procedure*. — To an ice-cold stirred solution of the 2,6-anhydro-3-hydroxy-2-thio compound (0.1 mmol) in dry DMF (0.5 mL) was added NaH (0.2 mmol) portionwise. The mixture was stirred for 20 min at 0° and then MeI (0.2 mmol) was added dropwise and, after stirring for 15 min at 25°, the mixture was poured into ice–water. The resulting mixture was extracted with Et_2O and the extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated to the crude products, which were purified by column chromatography. The following 2,6-anhydro-3-*O*-methyl-2-thio sugars were prepared according to this method.

*Methyl 2,6-anhydro-4-*O*-benzyl-3-*C*-methyl-3-*O*-methyl-2-thio-α-*L*-altropyranoside* (**18**): Compound **13** (1.21 g, 4.08 mmol) gave **18** (1.24 g, 98%) as a colorless syrup. $[\alpha]_D$ −128° (*c* 0.84); R_F 0.25 (3:1 toluene–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 1.55 (3 H, s, Me), 2.52 (1 H, dd, *J* 11.6 and 2.4 Hz, H-6), 2.78 (1 H, s, H-2), 3.04 (1 H, dd, *J* 11.6 and 3.6 Hz, H-6′), 3.30 (1 H, s, H-4), 3.34 (3 H, s, OMe), 3.51 (3 H, s, OMe), 4.32 (1 H, dd, *J* 3.6 and 2.4 Hz, H-5), 4.64 and 4.82 (each 1 H, ABq, *J* 12.8 Hz, CH_2Ph), 5.24 (1 H, s, H-1), and 7.25–7.45 (5 H, Ph).

Anal. Calc. for $C_{16}H_{22}O_4S$: C, 61.91; H, 7.14. Found: C, 61.65; H, 6.88.

Methyl 2,6-anhydro-4-O-benzyl-3-C-methyl-3-O-methyl-2-thio-β-L-mannopyranoside (**19**): Compound **15** (2.62 g, 8.84 mmol) gave **19** (2.48 g, 91%) as colorless crystals, m.p. 80.5–81.0° (hexane); $[\alpha]_D$ +68.8° (*c* 0.59); R_F 0.33 (5:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.51 (3 H, s, Me), 2.66 (1 H, dd, *J* 11.8 and 3.2 Hz, H-6), 2.99 (1 H, d, *J* 3.2 Hz, H-2), 3.26 (1 H, dd, *J* 11.8 and 3.2 Hz, H-6'), 3.28 (3 H, s, OMe), 3.55 (3 H, s, OMe), 3.70 (1 H, s, H-4), 4.21 (1 H, dd, *J* 3.2 and 3.2 Hz, H-5), 4.61 and 4.67 (each 1 H, ABq, *J* 12.2 Hz, CH_2Ph), 4.95 (1 H, d, *J* 3.2 Hz, H-1), and 7.25–7.45 (5 H, Ph).

Anal. Calc. for $C_{16}H_{22}O_4S$: C, 61.91; H, 7.14. Found: C, 62.13; H, 6.95.

Methyl 2,6-anhydro-4-O-benzyl-3-O-methyl-2-thio-α-L-altrophyranoside (**20**): Compound **9** (29.2 mg, 0.103 mmol) gave **20** (28.8 mg, 94%) as colorless crystals, m.p. 53.5–54.5° (hexane, needles); $[\alpha]_D$ −95.2° (*c* 1.00); R_F 0.22 (2:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 2.49 (1 H, dd, *J* 12.0 and 2.0 Hz, H-6), 2.95 (1 H, dd, *J* 1.8 and 1.8 Hz, H-2), 3.01 (1 H, dd, *J* 12.0 and 4.0 Hz, H-6'), 3.50 (6 H, s, OMe × 2), 3.72 (1 H, dd, *J* 8.4 and 1.6 Hz, H-4), 3.96 (1 H, ddd, *J* 8.4, 1.8, and 0.6 Hz, H-3), 4.38 (1 H, ddd, *J* 4.0, 2.0, and 1.6 Hz, H-5), 4.69 and 4.81 (each 1 H, ABq, *J* 12.6 Hz, CH_2Ph), 5.16 (1 H, br s, H-1), and 7.25–7.45 (5 H, Ph).

Anal. Calc. for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80. Found: C, 61.09; H, 6.59.

Methyl 2,6-anhydro-4-O-benzyl-2-thio-β-L-mannopyranoside (**21**): Compound **17** (47.6 mg, 0.169 mmol) gave **21** (49.9 mg, 99%) as a colorless syrup. $[\alpha]_D$ +82.6° (*c* 0.53); R_F 0.32 (2:1 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 2.64 (1 H, dd, *J* 12.0 and 3.6 Hz, H-6), 3.07 (1 H, br s, H-2), 3.29 (1 H, dd, *J* 12.0 and 3.2 Hz, H-6'), 3.44 (3 H, s, OMe), 3.56 (3 H, s, OMe), 3.65–3.75 (2 H, m, H-3 and 4), 4.21 (1 H, dd, *J* 3.6 and 3.2 Hz, H-5), 4.62 and 4.66 (each 1 H, ABq, *J* 12.0 Hz, CH_2Ph), 4.94 (1 H, d, *J* 3.4 Hz, H-1), and 7.25–7.45 (5 H, Ph).

Anal. Calc. for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.54; H, 6.79.

Hydrogenolysis with O-debenzylation of 2,6-anhydro-4-O-benzyl-2-thio compounds, **18, 19, 20, 21, 13, 15, 9,** *and* **17**: *General procedure.* — The 2,6-anhydro-2-thio-4-*O*-benzyl-2-thio compound (0.1 mmol) was dissolved in 4:1 EtOH–1,4-dioxane (1.0 mL) and a catalytic amount of Raney-Ni (W4) was added. The mixture was vigorously stirred at 40° for 1–2 h under H_2. After filtration, the catalyst was washed with MeOH and the combined filtrate and washings were concentrated to give the crude products, which were purified by column chromatography or/and distillation under diminished pressure. The following 2,6-dideoxy-4-*O*-hydroxy sugars were prepared according to this method.

Methyl 2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranoside (**22**): Compound **18** (1.44 g, 4.64 mmol) gave **22** (0.74 g, 85%) as a colorless syrup, $[\alpha]_D$ −139° (*c* 0.32, H_2O); the optical rotations of methyl α-cladinoside in refs. 4c and 4d are unfortunately incorrect! These are originally compared with the data in ref. 4a. However, in ref. 4a, the stereochemistry of the anomeric position of methyl cladinoside was not discussed, and we confirmed that the methyl cladinoside obtained from erythromycin A according to the ref. 4a, was a mixture of both anomers (α:β = 1:4.9) by ^{1}H-n.m.r. analysis. R_F 0.51 (2:1 hexane–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.22 (3 H, s, C-3-Me),

1.28 (3 H, d, *J* 6.4 Hz, H-6), 1.53 (1 H, dd, *J* 15.2 and 4.4 Hz, H-2), 2.27 (1 H, d, *J* 15.2 Hz, H-2′), 2.32 (1 H, d, *J* 11.0 Hz, OH), 3.02 (1 H, dd, *J* 11.0 and 9.8 Hz, H-4), 3.26 (3 H, s, OMe), 3.32 (3 H, s, OMe), 3.85 (3 H, dq, *J* 9.8 and 6.4 Hz, H-5), and 4.60 (1 H, d, *J* 4.4 Hz, H-1).

Anal. Calc. for $C_9H_{18}O_4$: C, 56.82; H, 9.54. Found: C, 57.20; H, 9.20.

Methyl 2,6-dideoxy-3-C-methyl-3-O-*methyl-β*-L-arabino-*hexopyranoside* (**23**): Compound **19** (0.96 g, 3.09 mmol) gave **23** (0.50 g, 85%) as colorless crystals; m.p. 82.0–83.0° (EtOAc–hexane, needles) [lit,[6d] m.p. 79–80°]; R_F 0.19 (3:1 hexane acetone); $[\alpha]_D$ +89.9° (*c* 0.75, EtOH) [lit,[6d], $[\alpha]_D$ −82° (EtOH) for the D enantiomer]; ^{1}H-n.m.r. (270 MHz): δ 1.25 (3 H, s, C-3-Me), 1.35 (3 H, d, *J* 6.2 Hz, H-6), 1.63 (1 H, dd, *J* 12.4 and 10.0 Hz, H-2), 2.05 (1 H, dd, *J* 12.4 and 2.1 Hz, H-2′), 2.08 (1 H, d, *J* 2.0 Hz, OH), 3.22 (3 H, s, OMe), 3.31 (1 H, dd, *J* 9.6 and 2.0 Hz, H-4), 3.43 (1 H, dd, *J* 9.6 and 6.2 Hz, H-5), 3.49 (1 H, s, OMe), and 4.41 (1 H, d, *J* 10.0 and 2.1 Hz, H-1).

Anal. Calc. for $C_9H_{18}O_4$: C, 56.82; H, 9.54. Found: C, 56.54; H, 9.32.

Methyl 2,6-dideoxy-3-O-*methyl-α*-L-ribo-*hexopyranoside* (**24**): Compound **20** (0.572 g, 1.93 mmol) gave **24** (0.278 g, 82%) as colorless crystals, m.p. 40–41° [lit,[9e], m.p. 40–43°]; R_F 0.33 (1:1 toluene–EtOAc); $[\alpha]_D$ −219° (*c* 0.29, MeOH) [lit,[9e], +214° (*c* 0.7, MeOH) for the D enantiomer]; ^{1}H-n.m.r. (270 MHz): δ 1.28 (3 H, d, *J* 6.2 Hz, H-6), 1.74 (1 H, ddd, *J* 15.0, 4.4, and 4.0 Hz, H-2), 2.27 (1 H, ddd, *J* 15.0, 3.9, and 1.0 Hz, H-2′), 2.51 (1 H, d, *J* 10.0 Hz, OH), 3.24 (1 H, ddd, *J* 10.0, 10.0, and 4.0 Hz, H-4), 3.34 (3 H, s. OMe), 3.43 (3 H, s. OMe), 3.59 (1 H, ddd, *J* 4.0, 4.0 and 3.9 Hz, H-3), 3.85 (1 H, dq, *J* 10.0 and 6.0 Hz, H-5), and 4.64 (1 H, dd, *J* 4.4 and 1.0 Hz, H-1).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.62; H, 9.29.

Methyl 2,6-dideoxy-3-O-*methyl-β*-L-arabino-*hexopyranoside* (**25**): Compound **21** (1.45 g, 4.67 mmol) gave **25** (0.693 g, 78%) as a colorless syrup, $[\alpha]_D$ +46.8° (*c* 0.57, EtOH); R_F 0.21 (2:1 hexane–acetone); ^{1}-H-n.m.r. (270 MHz): δ 1.36 (3 H, d, *J* 5.9 Hz, H-6), 1.41 (1 H, ddd, *J* 10.4, 10.4 and 10.0 Hz, H-2), 2.34 (1 H, ddd, *J* 10.4, 4.0 and 2.0 Hz, H-2′), 2.49 (1 H, d, *J* 1.6 Hz, OH), 3.1–3.4 (3 H, H-3, 4 and 5), 3.39 (3 Hz, s, OMe), 3.50 (3 H, s, OMe), and 4.38 (1 H, dd, *J* 10.0 and 2.0 Hz, H-1).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.55; H, 8.84.

Methyl 2,6-dideoxy-3-C-*methyl-α*-L-ribo-*hexopyranoside* (**28**): Compound **13** (75.5 mg, 0.255 mmol) gave **28** (36.3 mg, 81%) as colorless crystals, m.p. 60.5–61.0° (needles) [lit,[5a], m.p. 60.5–61°]; $[\alpha]_D$ −134° (*c* 0.39) [lit,[5a], $[\alpha]_D$ −141° (*c* $CHCl_3$]; R_F 0.25 (3:2 hexane–EtOAc); ^{1}H-n.m.r. (270 MHz): δ 1.23 (3 H, s, Me), 1.33 (3 H, d, *J* 6.0 Hz, H-6), 1.81 (1 H, dd, *J*14.4 and 4.0 Hz, H-2), 2.04 (1 H, dd, *J* 14.4 and 0.8 Hz, H-2′), 2.21 (1 H, d, *J* 11.0 Hz, OH), 2.97 (1 H, dd, *J*11.0 and 10.0 Hz, H-4), 3.37 (3 H, s, OMe), 3.59 (1 H, dq, *J* 10.0 and 6.0 Hz, H-5), 3.84 (1 H, s, OH), and 4.76 (1 H, dd, *J* 4.0 and 0.8 Hz, H-1).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53: H, 9.15. Found: C, 54.32; H, 9.17.

Methyl 2,6-dideoxy-3-C-*methyl-β*-L-arabino-*hexopyranoside* (**29**): Compound **15** (92.0 mg, 0.31 mmol) gave **29** (43.1 mg, 78%) as colorless stystals, m.p. 99.5–100.0° (ether–hexane, needles); $[\alpha]_D$ +45.6° (*c* 1.00, EtOH); R_F 0.32 (1:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.30 (3 H, s, Me), 1.34 (3 H, d, *J* 6.0 Hz, H-6), 1.55–1.65 (1 H, br.

OH), 1.71 (1 H, dd, *J* 12.4 and 9.8 Hz, H-2), 1.8–1.9 (1 H, br, OH), 2.02 (1 H, dd, *J* 12.4 and 2.1 Hz, H-2'), 3.25 (1 H, d, *J* 9.6 Hz, H-4), 3.37 (1 H, dq, *J* 9.6 and 6.0 Hz, H-5), and 4.44 (1 H, dd, *J* 9.8 and 2.1 Hz, H-1).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.51; H, 8.91.

*Methyl 2,6-dideoxy-α-*L*-ribo-hexopyranoside* (**30**): Compound **9** (19.6 mg, 0.069 mmol) gave **30** (9.04 mg, 80%) as a colorless syrup; $[\alpha]_D$ −173° (*c* 1.06) [lit.[10h], $[\alpha]_D$ −174° (*c* 1.0, $CHCl_3$)]; R_F 0.25 (3:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.34 (3 H, d, *J* 6.0 Hz, H-6), 1.92 (1 H, ddd, *J* 14.8, 3.2, and 3.1 Hz, H-2), 2.18 (1 H, ddd, *J* 14.8, 3.2, and 1.2 Hz, H-2'), 2.52 (1 H, d, *J* 10.0 Hz, OH), 3.14 (1 H, ddd, *J* 10.0, 10.0, and 3.2 Hz, H-4), 3.38 (3 H, s, OMe), 3.41 (1 H, d, *J* 10.0 Hz, OH), 3.71 (1 H, dq, *J* 10.0 and 6.0 Hz, H-5), 3.94 (1 H, dddd, *J* 10.0, 3.2, 3.2, and 3.1 Hz, H-3), and 4.79 (1 H, dd, *J* 3.2 and 1.2 Hz, H-1).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.88; H, 8.67.

*Methyl 2,6-dedeoxy-β-*L*-arabino-hexopyranoside* (**31**): Compound **17** (43.1 mg, 0.153 mmol) gave **31** (21.7 mg, 88%) as colorless crystals; m.p. 87.0–87.5° (EtOAc–hexane, needles) [lit,[7d], m.p. 84° EtOAc–hexane, needles)]; $[\alpha]_D$ +73.2° (*c* 1.03, EtOH) [lit,[7d], −85° (*c* EtOH) for the D enantiomer]; R_F 0.25 (1:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz): δ 1.36 (3 H, d, *J* 6.0 Hz, H-6), 1.60 (1 H, ddd, *J* 12.4, 12.4, and 10.0 Hz, H-2), 2.23 (1 H, ddd, *J* 12.4, 5.4 and 2.0 Hz, H-2'), 2.35–2.6 (2 H, br. OH × 2), 3.10 (1 H, dd, *J* 9.2 Hz, H-4), 3.29 (1 H, dq, *J* 9.2 and 6.0 Hz, H-5), 3.50 (3 H, s, OMe), 3.61 (1 H, ddd, *J* 12.4, 9.2 and 5.4 Hz, H-3), 4.42 (1 H, dd, *J* 10.0 and 2.0 Hz, H-1).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.80; H, 8.70. Found: C, 52.04; H, 8.39.

Hydrolysis of methyl 2,6-dideoxyglycosides, **22**, **23**, **24**, **25**, **28**, **29**, **30**, *and* **31**: *General procedure.* — The methyl 2,6-dideoxyglycoside (0.1 mmol) was dissolved in 0.6M HCl (1 mL) and kept for 24 h at 26°. The mixture was made neutral with Amberlite IRA-400 (OH^-) resin and filtered. The filtrate was concentrated to give the crude products, which were purified by column chromatography or/and distilation under diminished pressure. The following free sugars were prepared according to this method.

*2,6-Dideoxy-3-*C*-methyl-3-*O*-methyl-*L*-ribo-hexopyranose (*L*-cladinose)* (**1**): Compound **22** (100 mg, 0.568 mmol) gave **1** (82.1 mg, 89%) as a colorless syrup; $[\alpha]_D$-22.8° (*c* 2.49, H_2O, equil.) [lit.[4a], $[\alpha]_D$ −23° (*c* 2.6, H_2O)]; R_F 0.67 and 0.56 (1:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz): α anomer of **1**: δ 1.30 (3 H, s, C-3-Me), 1.31 (3 H, d, *J* 6.0 Hz, H-6), 1.60 (1 H, dd, *J* 14.8 and 4.0 Hz, H-2), 2.05 (1 H, d, *J* 11.0 Hz, OH), 2.24 (1 H, dd, *J* 14.8 and 1.6 Hz, H-2'), 3.04 (1 H, dd, *J* 11.0 and 10.8 Hz, H-4), 3.37 (3 H, s, OMe), 3.92 (1 H, dq, *J* 10.8 and 6.0 Hz, H-5), 4.83 (1 H, d, *J* 10.8 Hz, OH), and 5.07 (1 H, ddd, *J* 10.8, 4.0 and 1.6 Hz, H-1); β anomer of **1**: δ 1.25 (3 H, s, C-3-Me), 1.30 (3 H, d, *J* 6.0 Hz, H-6), 1.34 (1 H, dd, *J* 14.2 and 9.8 Hz, H-2), 2.11 (1 H, d, *J* 11.0 Hz, OH), 2.33 (1 H, dd, *J* 14.2 and 1.9 Hz, H-2'), 2.98 (1 H, dd, *J* 11.0 and 9.0 Hz, H-4), 3.25 (3 H, s, OMe), 3.32 (1 H, d, *J* 6.0 Hz, OH), 3.67 (1 H, dq, *J* 9.0 and 6.0 Hz, H-5), and 4.92 (1 H, ddd, *J* 9.8, 1.9 and 6.0 Hz, H-1).

*2,6-Dideoxy-3-*C*-methyl-3-*O*-methyl-*L*-arabino-hexopyranose* (**26**): Compound **23** (45.0 mg, 0.237 mmol) gave **26** (40.8 mg, 98%) as a colorless syrup; $[\alpha]_D$ −9.5° (*c* 0.40, H_2O, equil.); R_F 0.28 and 0.20 (1:10 benzene–ether); ^{1}H-n.m.r. (270 MHz, $CDCl_3$ +

D_2O, mixture of the pyranose anomers and the furanose anomers): δ 3.23 (s, OMe), 3.24 (s, OMe), 3.29 (s, OMe), 3.37 (s, OMe), 4.86 (dd, *J* 8.0 and 2.0 Hz), 4.90 (dd, *J* 6.6 and 1.9 Hz), 5.35 (dd, *J* 4.4 and 0.4 Hz), and 5.58 (dd, *J* 7.6 and 2.0 Hz), (other peaks were very complicated).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.46; H, 8.81.

*2,6-Dideoxy-3-*C*-methyl-*L*-*ribo*-hexopyranose (*L*-mycarose)* (**2**): Compound **28** (100 mg, 0.569 mmol) gave **2** (92.3 mg, 100%) as colorless crystals; m.p. 128.0–132.5° ($CHCl_3$, needles) [lit.[5a], m.p. 128–129°]; $[\alpha]_D$ −28.8° (*c* 0.95, H_2O, equilibrated) [lit.[5a], $[\alpha]_D$ −31.1° (*c* 4, H_2O)]; R_F 0.24 and 0.16 (1:4 benzene–EtOAc); ^{1}H-n.m.r. (270 MHz, CD_3OD, β anomer): δ 1.22 (3 H, s, Me), 1.23 (3 H, d, *J* 6.2 Hz, H-6), 1.48 (1 H, dd, *J* 13.8 and 10.0 Hz, H-2), 1.90 (1 H, dd, *J* 13.8 and 2.2 Hz, H-2′), 2.90 (1 H, s, *J* 9.8 Hz, H-4), 3.67 (1 H, dq, *J* 9.8 and 6.2 Hz, H-5), and 5.01 (1 H, dd, *J* 10.0 and 2.2 Hz, H-1).

*2,6-Dideoxy-3-*C*-methyl-*L*-*arabino*-hexopyranose (*L*-olivomycose)* (**27**): Compound **29** (103 mg, 0.582 mmol) gave **27** (71.6 mg, 76%) as colorless crystals; m.p. 109–111.5° (acetone, needles) [lit.[8a], m.p. 108–112° (acetone, needles)]; $[\alpha]_D$-21.5° (*c* 0.80, H_2O, equilibrated) [lit.[8a], $[\alpha]_D$ +20.7° (H_2O) for the D enantiomer]; R_F 0.24 (6:1 $CHCl_3$–MeOH); ^{1}H-n.m.r. (270 MHz, CD_3OD, β anomer): δ 1.22 (3 H, s, Me), 1.25 (3 H, d, *J* 6.0 Hz, H-6), 1.60 (1 H, dd, *J* 12.2 and 9.8 Hz, H-2), 1.92 (1 H, dd, *J* 12.2 and 2.2 Hz, H-2′), 3.08 (1 H, d, *J* 9.6 and 6.0 Hz, H-5), and 4.77 (1 H, dd, *J* 9.8 and 2.2 Hz, H-1).

*2,6-Dideoxy-3-*O*-methyl-*L*-*arabino*-hexopyranose (*L*-oleandrose)* (**3**): Compound **25** (200 mg, 1.14 mmol) gave **3** (134 mg, 73%) as colorless crystals; m.p. 58.0–59.5° (ether–hexane, needles) [lit.[6c], m.p. 59–60° (ether–hexane, needles)]; $[\alpha]_D$ +11.8° (*c* 0.88, H_2O, equilibrated) [lit.[6c], $[\alpha]_D$ +11.7° (*c* 1.5, H_2O)]; R_F 0.43 (1:1 hexane–acetone); ^{1}H-n.m.r. (270 MHz, $CDCl_3$, 2:1 mixture of α and β anomers): δ 1.29 (2/3 × 3H, d, *J* 6.2 Hz, H-6-α), 1.35 (1/3 × 3H, *J* 6.2 Hz, H-6-β), 1.4–1.6 (1 H, m, H-2α and β), 2.31 (2/3 H, ddd, *J* 13.0, 4.8 and 1.8 Hz, H-2′α), 2.43 (1/3 H, ddd, *J* 12.2, 4.4 and 2.0 Hz, H-2′β), 2.6–2.65 (1 H, m, OH), 2.75–2.8 (2/3 H, m, OH), 3.1–3.65 (11/3 H, m, H-3, 4, OH and H-5β), 3.41 (3 H, OMe), 3.93 (2/3 H, dq, *J* 9.6 and 6.2 Hz, H-5α), 4.82 (1/3 H, ddd, *J* 10.0, 6.2 and 2.0 Hz, H-1β), and 5.36 (2/3 H, br dd, H-1α).

*2,6-Dideoxy-3-*O*-ethyl-*L*-*ribo*-hexopyranose (*L*-cymarose)* (**32**): Compound **24** (109 mg, 0.62 ol) gave **32** (81.0 ,g, 81%) as colorless crystals; m.p. 83–84° (ether–hexane, needles) [lit.[9k], m.p. 84–85° (ether–hexane, needles)]; $[\alpha]_D$ −51.5° (*c* 0.33, H_2O, equilibrated) [lit.[9k], $[\alpha]_D$ −51.2° (*c* 2.1, H_2O)]; R_F 0.53 (1:9 EtOH–CH_2Cl_2); ^{1}H-n.m.r. (270 Hz, D_2O, 1:1 ixture of α and β anomers and smaller amounts of furanoses): δ 1.20 (1/2 × 3 H, d, *J* 6.2 Hz, H-6α or β), 1.25 (1/2 × 3 H, d, *J* 6.2 Hz, H-6α or β), 1.59 (1/2 H, ddd, *J* 14.2, 10.0, and 2.4 Hz, H-2β), 1.55–2.4 (3/2 H, m, H-2, 2′α and H-2′β), 3.36 (1/2 × 3 H, s, α or β-OMe), 3.44 (1/2 × 3 H, s, α or β-OMe), 3.35–4.2 (3 H, m, H-3, 4, and 5), 5.05 (1/2 H, dd, *J* 10.0 and 2.0 Hz, H-1β), 5.60 (1/2 H, br d, *J* 5.2 Hz. H-1α).

*2,6-Dideoxy-*L*-arabino-hexopyranose (*L*-olivose)* (**4**): Compound **31** (184 mg, 1.14 mmol) gave **4** (154 mg, 92%) as a colorless syrup; $[\alpha]_D$ −21.5° (*c* 0.82, H_2O, equilibrated) [lit.[7a], $[\alpha]_D$ −18.2° (*c* 1, H_2O)]; R_F 0.19 (1:3 toluene–acetone); ^{1}H-n.m.r. (270 MHz, D_2O, 2:3 mixture of α and β anomers): δ 1.27 (2/5 H × 3, d, *J* 6.4 Hz, H-6α), 1.30 (3/5 H × 3, d, *J* 6.4 Hz, H-6β), 1.52 (3/5 H, ddd, *J* 12.2, 12.2 and 10.0 Hz, H-2β),

1.72 (2/5 H, ddd, *J* 13.8, 12.0, and 4.0 Hz, H-2α), 2.14 (2/5 H, ddd, *J* 13.8, 4.8 and 1.2 Hz, H-2'α), 2.28 (3/5 H, ddd, *J* 12.2, 5.0, and 2.0 Hz, H-2'β), 3.06 (3/5 H, dd, *J* 9.6 and 9.6 Hz, H-4β), 3.11 (2/5 H, dd, *J* 9.6 and 9.6 Hz, H-4α), 3.42 (3/5 H, dq, *J* 9.6 and 6.4 Hz, H-5β), 3.68 (3/5 H, ddd, *J* 12.2, 9.6, and 5.0 Hz, H-3β), 3.89 (2/5 H × 2, m, H-5α and H-3α), 4.92 (3/5 H, dd, *J* 10.0 and 2.0 Hz, H-1β), and 5.33 (2/5 H, br d, *J* 4.0 Hz, H-1α).

2,6-Dideoxy-L-ribo-*hexopyranose (*L-*digitoxose)* (**33**): Compound **30** (75.3 mg, 0.464 mmol) gave **33** (50.8 mg, 74%) as colorless crystals; m.p. 105–106° (acetone–ether) [lit.[101], m.p. 105–107° (acetone)]; $[\alpha]_D$ −48.1° (*c* 0.79, H_2O, equilibrated) [lit.[101], $[\alpha]_D$ −47° (*c* 1.00, H_2O)]; R_F 0.19 (1:1 toluene–acetone); ^{1}H-n.m.r. (270 MHz, Me_2SO, β anomer): δ 1.10 (3 H, d, *J* 6.2 Hz, H-6), 1.46 (1 H, ddd, *J* 13.4, 9.6, and 2.7 Hz, H-2), 1.79 (1 H, ddd, *J* 13.4, 3.5, and 2.1 Hz, H-2'), 2.96 (1 H, m, H-4), 3.59 (1 H, dq, *J* 9.6 and 6.2 Hz, H-5), 3.82 (1 H, m, H-3), 4.46 (2 H, m, OH × 2), 4.88 (1 H, ddd, *J* 9.6, 6.0, and 2.1 Hz, H-1), and 6.21 (1 H, d, *J* 6.0 Hz, OH).

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REFERENCES

1 P. M. Collins, *Carbohydrates*, Chapman and Hall, London, 1987.
2 (a) K. Toshima, S. Mukaiyama, T. Ishiyama, and K. Tatsuta, *Tetrahedron Lett.*, 31 (1990) 3339–3342; (b) K. Toshima, S. Mukaiyama, T. Ishiyama, and K. Tatsuta, *Tetrahedron Lett.*, 31 (1990) 6361–6362.
3 K. Toshima, T. Yoshida, S. Mukaiyama, and K. Tatsuta, *Tetrahedron Lett.*, 32 (1991) 4139–4142.
4 (a) E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley, and K. Gerzon, *J. Am. Chem. Soc.*, 76 (1954) 3121–3131; (b) D. M. Lemal, P. D. Pacht, and R. B. Woodward, *Tetrahedron*, 18 (1962) 1275–1293; (c) G. B. Howarth and J. K. N. Jones, *Can. J. Chem.*, 45 (1967) 2253–2256; (d) B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, (*C*), (1966) 398–403; (e) J. Yoshimura, *Adv. Carbohydr. Chem. Biochem.*, 42 (1984) 69–134; (f) A. K. Mallams and R. R. Rossman, *J. Chem. Soc. Perkin Trans. I*, (1989) 799–805; (g) E. R. Koft, P. Dorff, and R. Kullnig, *J. Org. Chem.*, 54 (1989) 2936–2940; (h) C. H. Heathcock and S. H. Montgomery, *Tetrahedron Lett.*, 26 (1985) 1001–1004; (i) S. H. Montgomery, M. C. Pirrung, and C. H. Heathcock, *Carbohydr. Res.*, 202 (1990) 13–32.
5 (a) P. P. Regna, F. A. Hochstein, R. L. Wagner, Jr., and R. B. Woodward, *J. Am. Chem. Soc.*, 75 (1953) 4625–4626; (b) R. Paul and S. Tchelitcheff, *Bull. Soc. Chim. Fr.*, 5 (1957) 443–447; (c) F. Korte, U. Claussen, and K. Gohring, *Tetrahedron*, 18 (1962) 1257–1264; (d) S. Yasuda and T. Matsumoto, *Tetrahedron Lett*, 10 (1969) 4393–4396; (e) 4b–e and 4g.
6 (a) E. Vischer, and T. Reichstein, *Helv. Chim. Acta*, 27 (1944) 1332–1345; (b) F. Blindenbacher and T. Reichstein, *Helv. Chim. Acta*, 31 (1948) 2061–2064; (c) H. Els, W. D. Celmer, and K. Murai, *J. Am. Chem. Soc.*, 80 (1958) 3777–3782; (d) H. Reimann, R. S. Jaret, and O. Z. Sarre, *J. Antibiot.*, 22 (1969) 131–132; (e) 5d; (f) K. Koga, S. Yamada, M. Yoh, and T. Mizoguchi, *Carbohydr. Res.*, 36 (1974) C9-C11; (g) M. Ohzeki, T. Mizoguchi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.*, 25 (1977) 2676–2680; (h) C. Monneret, C. Conreur, and Q. Khuong-Huu, *Carbohydr. Res.*, 65 (1978) 35–45; (i) D. Horton, T-M. Cheung, and W. Weckerle, *Methods Carbohydr. Chem.*, 8 (1980) 195–199; (j) G. Berti, G. Catelani, F. Colonna, and L. Monti, *Tetrahedron*, 38 (1982) 3067–3072; (k) J. Dornhagen, A. Klausener, J. Runsink, and H.-D. Scharf, *Liebigs Ann. Chem.*, (1985) 1838–1846; (l) S. Hatakeyama, K. Sakurai, and S. Takano, *Tetrahedron Lett.*, 27 (1986) 4485–4488; (m) R. L. Tolman and L. H. Peterson, *Carbohydr. Res.*, 189 (1989) 113–122; (n) S. J. Danishefsky, D. M. Armistead, F. E. Wincott, H. G. Selnik, and R. Hungate, *J. Am. Chem. Soc.*, 111 (1989) 2967–2980.

7 (a) B. Iselin and T. Reichstein, *Helv. Chim. Acta.*, 27 (1944) 1146–1149; (b) 6a; (c) 6b; (d) Y. A. Berlin, S. E. Esipov, M. N. Kolosov, M. M. Shemyakin, and M. G. Brazhnikova, *Tetrahedron Lett.*, (1964) 3513–3516; (e) M. Miyamoto, Y. Kawamotsu, and M. Shinohara, *Tetrahedron*, 22 (1966) 2785–2799; (f) 5d; (g) M. Haga, M. Chonan, and S. Tejima, *J. Carbohydr. Res.*, 16 (1971) 486–491; (h) F. Sztaricskai, I. Pelyvás, and R. Bognár, *Tetrahedron Lett.*, 16 (1975) 1111–1114; (i) J. Staněk, Jr., M. Marek, and J. Jarý, *J. Carbohydr. Res.*, 64 (1978) 315–317; (j) M. Chmielewski, *Tetrahedron*, 35 (1979) 2067–2070; (k) P. L. Durette, *Synthesis*, (1980) 1037–1038; (l) G. Fronza, C. Fuganti, P. Grasselli, G. Pedrocchi-Fantoni, and C. Zirotti, *Tetrahedron Lett.*, 23 (1982) 4143–4146; (m) A. Martin, M. Païs, and C. Monneret, *Carbohydr. Res.*, 113 (1983) 189–201; (n) W. R. Roush and R. J. Brown, *J. Org. Chem.*, 48 (1983) 5093–5101.

8 (a) A. K. Ganguly and O. Z. Sarre, *J. Chem. Soc., Commun.*, (1969) 1149–1150; (b) I. Dyong and D. Glittenberg, *Chem. Ber.*, 110 (1977) 2721–2728; (c) J. Thiem and J. Elvers, *Chem. Ber.*, 112 (1979) 818–822.

9 (a) D. A. Prins, *Helv. Chim. Acta*, 29 (1946) 378–382; (b) O. Schinder and T. Reichstein, *Helv. Chim. Acta*, 35 (1952) 730–745; (c) H. R. Bolliger and P. Ulrich, *Helv. Chim. Acta*, 35 (1952) 93–98; (d) A. F. Krasso, E. Weiss, and T. Reichstein, *Helv. Chim. Acta*, 46 (1963) 1691–1696. (e) M. Marek, K. Kefurt, J. Staněk, Jr., and J. Jarý, *Collect. Czech. Chem. Commun.*, 41 (1976) 2596–2606; (f) H. Paulsen and V. Sinnwell, *Chem. Ber.*, 111 (1978) 879–889; (g) 6h; (h) J. S. Brimacombe, R. Hanna, M. S. Saeed, and L. C. N. Tucker, L. *J. Chem. Soc, Perkin Trans. I*, (1982) 2583–2587; (i) T. Nakagawa, K. Hayashi, K. Wada, and H. Mitsuhisa, *Tetrahedron*, 39 (1983) 607–612; (j) 7n; (k) 61; (l) S. Tsukamoto, K. Hayashi, K. Kaneko, and H. Mitsuhisa, *Chem. Pharm. Bull.*, 34 (1986) 3130–3134.

10 (a) F. Micheel, *Ber.*, 63 (1930) 347–359; (b) B. Iselin and T. Reichstein, *Helv. Chim. Acta*, 27 (1944) 1203–1209; (c) M. Gut and D. A. Prins, *Helv. Chim. Acta*, 30 (1947) 1223–1232; (d) 9b; (e) 9c; (f) F. Micheel, *Methods Carbohydr. Chem*, 1 (1962) 204–205; (g) M. Haga, M. Chonan, and S. Tejima, *Carbohydr. Res.*, 16 (1971) 486–491; (h) A. Zeek, *Liebigs Ann. Chem.*, 11 (1975) 2079–2088; (i) T. M. Cheung, D. Horton, and W. Weckerle, *Carbohydr. Res.*, 58 (1977) 139–151; (j) J. Zielinski, J. P. Sowinski, L. Falkowski, A. Rudowski, and E. Borowski, *J, Antibiot.*, 32 (1979) 565–568; (k) 6i; (l) 9h; (m) 9i; (n) 7n; (o) K. Bock, I. Lundt, and C. Pedersen, *Acta. Chem. Scand., Ser. B*, 38 (1984) 555–561; (p) B. Coxon, *J. Carbohydr. Chem.*, 3 (1984) 525–543; (q) 61; (r) S. Köpper and J. Thiem, *J. Carbohydr. Chem.*, 6 (1987) 57–85.

11 L. Kocourek, *Carbohydr. Res.*, 3 (1967) 502–505.

12 A. B. Foster, J. M. Duxbury, T. D. Inch, and J. M. Webber, *Chem. Commun.*, (1967) 881–883.

13 D. B. Dess and J. C. Martin, *J. Org. Chem.*, 48 (1983) 4155–4156.