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A HIGHLY STEREOSELECTIVE AND PRACTICAL SYNTHESIS OF CYCLOMANNOHEXAOSE, Cyclo{→4)-[α-D-Man*p*-(1→4)-]$_5$-α-D-Man*p*-(1→}, A *manno* ISOMER OF CYCLOMALTOHEXAOSE

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ABSTRACT

Phenylselenyl triflate-promoted cycloglycosylation of methyl *O*-(2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-[*O*-(2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)]$_4$-2,3,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside afforded 64% of cyclo{→4)-[*O*-(2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)]$_5$-*O*-(2,3,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→} which was then hydrogenolysed to give a *manno* isomer of cyclomaltohexaose (α-cyclodextrin). The key mannohexaosyl intermediate for cycloglycosylation was prepared in a stereocontrolled manner from 3,6-di-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl trichloroacetimidate and *p*-methoxyphenyl 3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranoside.

INTRODUCTION

The ability of cyclomalto-oligosaccharides (cyclodextrins, CDs) to form inclusion complexes[1] makes it of interest to synthesize cyclic oligosaccharides composed of monosaccharides other than α-D-glucopyranose. Few papers[2], however, have appeared on the synthesis of cyclo-oligosaccharides. The observation that cycloglycosylation of the benzylated derivatives of glucohexaosyl fluoride (**1**) and glucooctaosyl fluoride (**3**), under the conditions described by Mukaiyama *et al.*[3], led, respectively, to the formation of benzylated cyclomaltohexaose (**2**, 21%)[4] and benzylated cyclomalto-octaose (**4**, 9%)[5] prompted the synthesis of a *manno* isomer of αCD, cyclo-(1→4)-α-D-mannohexaose (**5**), as shown in Scheme 1.

The target structure **5** was disconnected to a properly protected mannohexaosyl derivative **6**, which in turn may be retrosynthesized into a mannotriosyl donor **7** and a mannotriosyl acceptor **8**. The donor **7** was designed as a mannotriosyl trichloroacetimidate derivative **9** according to Schmidt[6], which may be converted into the methyl thioglycoside derivative **10**, which is the acceptor **8**. The key intermediate **9** was also designed to carry *p*-methylbenzoyl groups at O-2 as a stereo-

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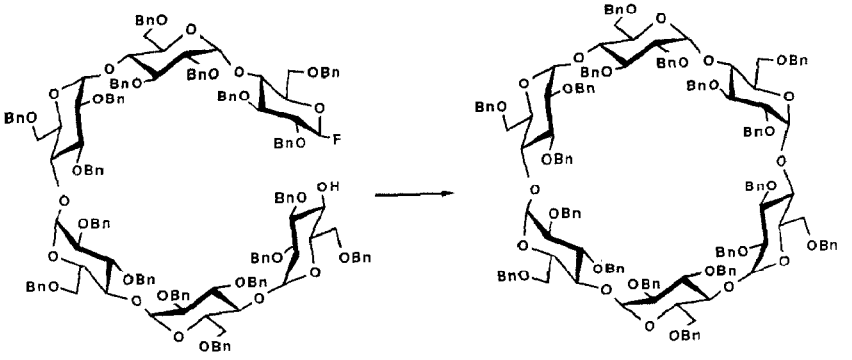

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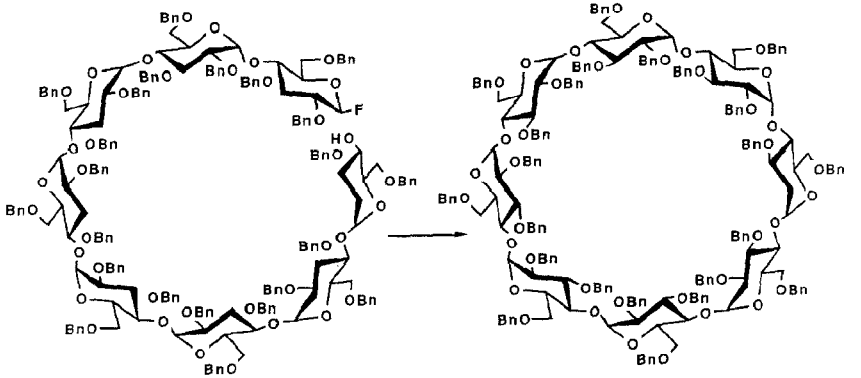

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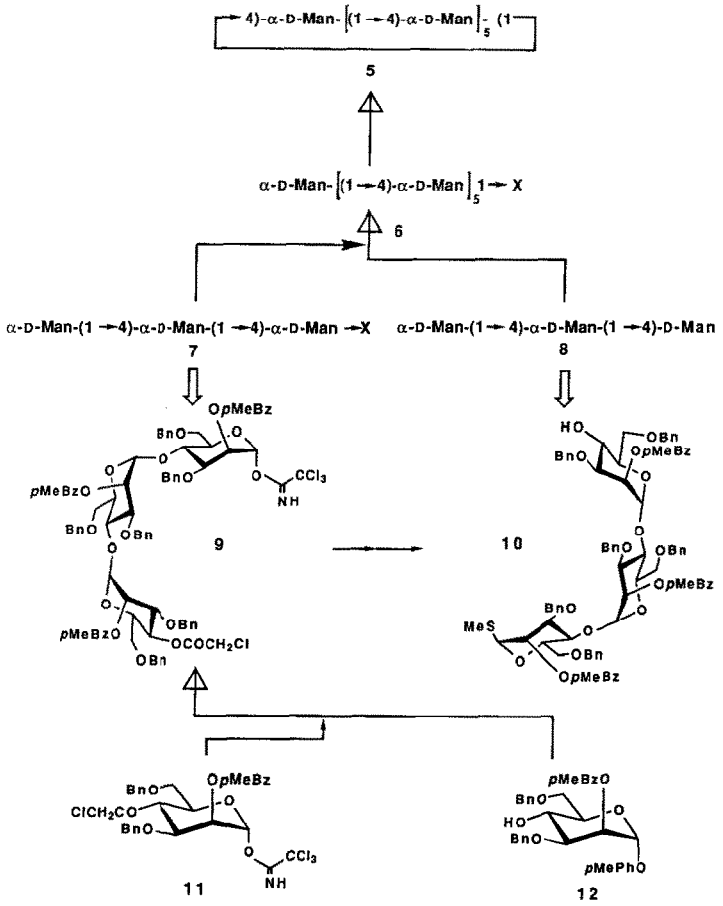
controlling auxiliary[7] for the α-D-*manno* stereoselective glycosylation along with a temporary protecting chloroacetyl group at O-4c. Compound **9** may be prepared from the trichloroacetimidate **11** and the acceptor **12** that carries a temporary protecting group, *p*-methoxyphenyl, at O-1.

RESULTS AND DISCUSSION

Routes to **11** and **12** were studied first. The *p*-methoxyphenyl glycoside **15** was obtained either by boron trifluoride etherate-promoted glycosylation[6] of *p*-methoxyphenol with the trichloroacetimidate **13** in 96% yield or by triflic acid-promoted glycosylation of *p*-methoxyphenol with the penta-acetate **14** in 91% yield. Deacetylation of **15** gave 95% of the tetraol **16**, which was selectively benzylated by the tributylstannylation method[8] to give 3,6-di-*O*-benzyl (**17**) and 2,3,6-tri-

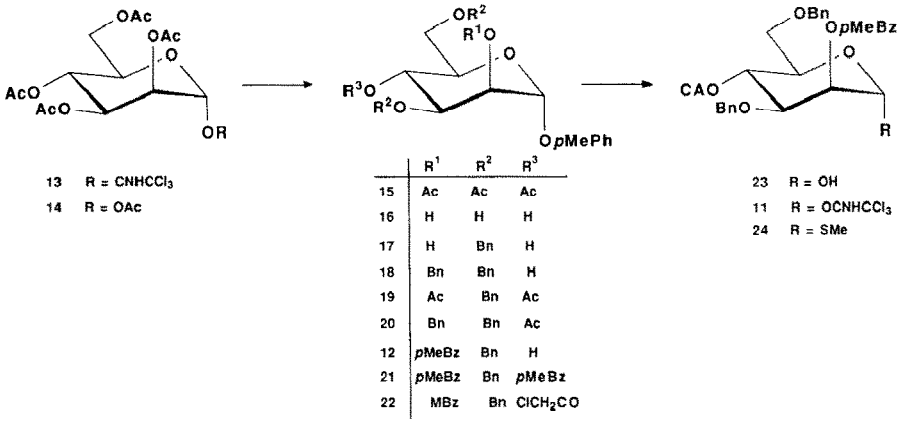


Scheme 1. Retrosynthesis of **5**.

O-benzyl (**18**) derivatives in yields of 75 and 14%, respectively. The structures of **17** and **18** were confirmed by the ^{1}H-n.m.r. data of the acetylated derivatives. Thus, the diacetate **19** (from **17**) gave deshielded signals for H-2 and H-4 at δ 5.523 (dd, $J_{1,2}$ 1.8, $J_{2,3}$ 3.4 Hz) and 5.331 (t, $J_{3,4} = J_{4,5} = 9.8$ Hz), respectively, whereas the acetate **20** gave a deshielded signal for H-4 at δ 5.458 (t, $J_{3,4} = J_{4,5} = 9.8$ Hz). Selective acylation of the diol **17** with *p*-methylbenzoyl chloride in pyridine at −20° gave **12** (81%) and the di-*p*-methylbenzoate **21** (11%).

Chloroacetylation[9] of **12** afforded 81% of chloroacetate **22**. The *p*-methoxyphenyl group of **22** was removed[10] in the presence of ammonium cerium(IV) nitrate in 4:1 acetonitrile–water to give 75% of the hemiacetal **23**, which was converted into **11** (82%) by treatment with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene.

Compounds **11** and **12** were coupled in the presence of trimethylsilyl triflate[11]

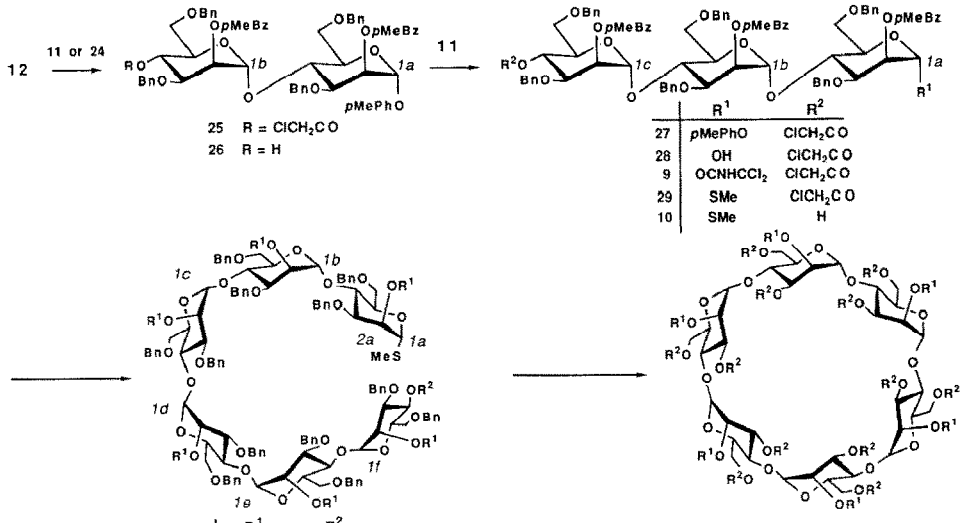


13 R = $CNHCCl_3$
14 R = OAc

	R^1	R^2	R^3
15	Ac	Ac	Ac
16	H	H	H
17	H	Bn	H
18	Bn	Bn	H
19	Ac	Bn	Ac
20	Bn	Bn	Ac
12	*p*MeBz	Bn	H
21	*p*MeBz	Bn	*p*MeBz
22	MBz	Bn	$ClCH_2CO$

23 R = OH
11 R = $OCNHCCl_3$
24 R = SMe

in 1,2-dichloroethane to give 87% of the mannobiosyl derivative **25**. The configurations of the anomeric carbon atoms were assigned from the ^{13}C-n.m.r. data[12], namely, the signals at δ 99.2 and 96.9 each with a $J_{C\text{-}1,H\text{-}1}$ value of 175 Hz. The chloroacetyl group was removed from **25** by treatment with thiourea in ethanol[13] to afford 98% of the mannobiosyl acceptor **26**, which was glycosylated with **11**, as described above, to give the mannotriosyl derivative **27** (84%). The configuration at C-1c of **27**, assigned tentatively as α-D because of the presence of the O-2a stereocontrolling auxiliary in **11**, was confirmed by further transformation into the methyl thioglycoside **10**.



25 R = $ClCH_2CO$
26 R = H

	R^1	R^2
27	*p*MePhO	$ClCH_2CO$
28	OH	$ClCH_2CO$
9	$OCNHCCl_2$	$ClCH_2CO$
29	SMe	$ClCH_2CO$
10	SMe	H

	R^1	R^2
30	*p*MeBz	$ClCH_2CO$
31	*p*MeBz	H
32	*p*MeBz	$EtOCH_2CH_2$
33	H	$EtOCH_2CH_2$
34	Bn	$EtOCH_2CH_2$
35	Bn	H

	R^1	R^2
36	*p*MeBz	Bn
37	Bn	Bn
5	H	H

Conversion of **27** into a mannotriosyl donor **9** was performed first by removal[10] of the *p*-methoxyphenyl group at O-1a to give 72% of the hemiacetal **28**, which was further transformed conventionally into **9** (92%). Treatment of **9** with methyl tributyltin sulfide[14] and boron trifluoride etherate gave 87% of the methyl thioglycoside **29** which, with thiourea[13], afforded the glycosyl acceptor **10** (89%). The anomeric configurations of **10** were confirmed by the ^{13}C-n.m.r. spectrum which contained two signals for three anomeric carbon atoms at δ 99.4 ($J_{C\text{-}1,H\text{-}1}$ 175 Hz) for both C-1b and C-1c, and at 83.8 ($J_{C\text{-}1,H\text{-}1}$ 169 Hz) for C-1a.

Compounds **9** and **10** were coupled in the presence of trimethylsilyl triflate[11] to give 87% of the mannohexaosyl methyl thioglycoside **30**, which was dechloroacetylated to give **31** (81%), the equivalent of **6**. The newly introduced anomeric centres at C-1d in **30** and **31**, assigned tentatively as α-D, were confirmed by transformation into the C_6 symmetrical cyclomannohexaoses **37** and **5**.

Up to this stage, the *p*-methylbenzoyl group was an effective O-2 stereocontrolling auxiliary and resulted in α-D products. However, cycloglycosylation of **31** into **36** could not be achieved using the promoters phenylselenyl triflate[15] or the

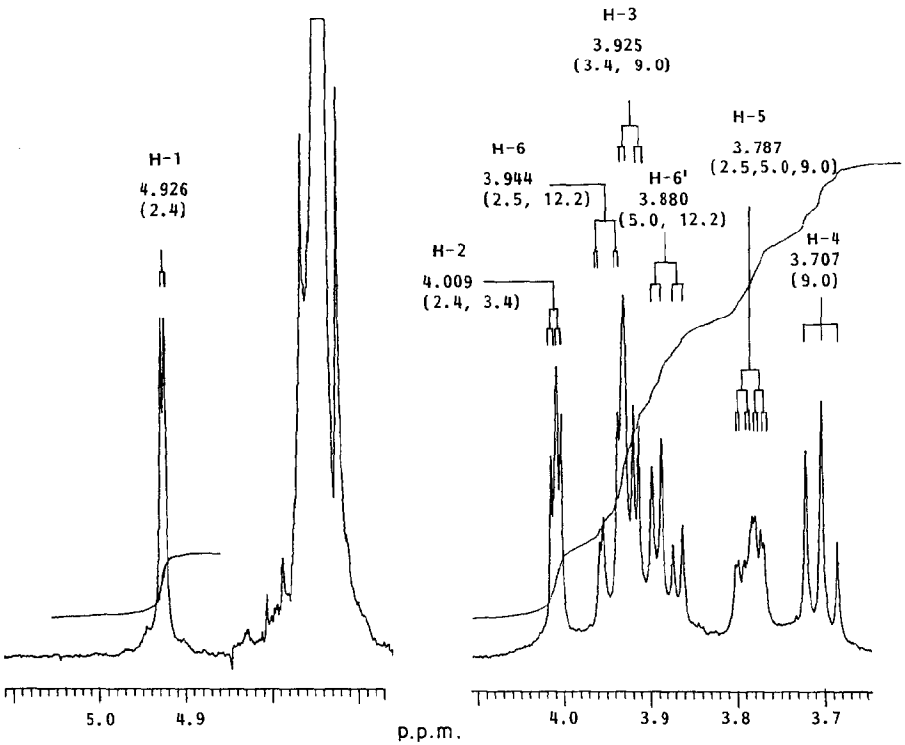


Fig. 1. The 500-MHz ^{1}H-n.m.r. spectrum of cyclo-α-(1→4)-linked mannohexaose **5** recorded for a solution in D_2O at 20° and expressed in p.p.m. downward from Me_4Si by reference to internal Bu^{t}OH (1.230). Values in parentheses are *J* in Hz.

cupric bromide–tetrabutylammonium bromide complex and silver triflate[18]. T.l.c. of the reaction mixture revealed a multitude of products. This result contrasts with the smooth coupling of the methyl thioglycoside **24** and the acceptor **12**, under similar conditions, to afford ~95% of the mannobioside derivative **25**.

Since cycloglycosylations have been observed[4,5] by use of a 2a-*O*-benzyl group, **31** was converted into the 2a-*O*-benzyl derivative **35** (75% overall yield) by treatment in sequence with ethyl vinyl ether and pyridinium *p*-toluenesulfonate in 1,2-dichloroethane (→**32**), methanolic sodium methoxide (→**33**), sodium hydride and benzyl bromide in *N,N*-dimethylformamide (→**34**), and Amberlyst 15 resin in 1:1 chloroform–methanol (→**35**).

Cycloglycosylation of **35** into **37** was achieved in 1,2-dichloroethane at −20° in the presence of phenylselenyl triflate and activated powdered molecular sieves 4A. Chromatography of the mixture of products afforded 92% of **37**, the structure of which was assigned readily on the basis of the ^{1}H- and ^{13}C-n.m.r. data. There was only one signal for H-1 at δ 5.043 (d, $J_{1,2}$ 1.5 Hz) and one signal for C-1 at δ 100.9 ($J_{C\text{-}1,H\text{-}1}$ 165 Hz). Hydrogenolysis (Pd/C) of **37** in methanol gave cyclomannohexaose **5** (93%), the structure of which was confirmed by ^{1}H-n.m.r. data shown in Fig. 1.

The efficiency of the cycloglycosylation of **35** was high compared with that for the *gluco* isomer **1**. Even though both the leaving group and the glycosylation method were different for **35** and **1**, the reducing-end mannoside residue in **35** seems to have played a crucial role in controlling the efficiency of cycloglycosylation.

EXPERIMENTAL

General. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter, for solutions in $CHCl_3$ at 25°, unless noted otherwise. Column chromatography was performed on Silica Gel (Merck 70–230 mesh). Flash chromatography was performed on columns of Wako gel C-300 (200–300 mesh). T.l.c. and high-performance (h.p.) t.l.c. were performed on Silica Gel 60 F_{254} (Merck). Molecular sieves were purchased from Nakarai Chemicals. N.m.r. spectra were recorded with a JEOL GX400 [^{1}H (400 MHz)] or FX90Q [^{13}C (22.50 MHz)] spectrometer. The values of δ_C and δ_H are expressed in p.p.m. downwards from the signal for internal Me_4Si, for solutions in $CDCl_3$, unless noted otherwise. Values of δ_H (D_2O) and δ_C (D_2O) are expressed in p.p.m. downward from the signal for Me_4Si, by reference to internal Me_2CO (2.225) or Me_3COH (1.230), and 1,4-dioxane (67.4) or MeOH (49.8), respectively.

p-*Methoxyphenyl 2,3,4,6-tetra-O-acetyl-α-*D-*mannopyranoside* (**15**). — (*a*) To a stirred mixture of *p*-methoxyphenol (240 mg, 19 mmol) and powdered molecular sieves AW 300 (1 g) in $Cl(CH_2)_2Cl$ (2 mL) were added dropwise successively a solution of **13** (476 mg, 966 μmol) in $Cl(CH_2)_2Cl$ (4.5 mL) and $BF_3 \cdot Et_2O$ (24 μL,

190 μmol) at −20° to −25° (solid CO_2–CCl_4) under Ar. The mixture was stirred for 1 h at −20°, then neutralized with Et_3N (100 μL), diluted with EtOAc, and filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (4:1 toluene–EtOAc) of the residue gave **15** (420 mg, 96%), $[\alpha]_D$ +70° (*c* 3), R_F 0.26. ^{1}H-N.m.r. data: δ 7.020 (d, 2 H, *J* 9.2 Hz, aromatic), 6.826 (d, 2 H, *J* 9.2 Hz, aromatic), 5.547 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 10.1 Hz, H-3), 5.437 (dd, 1 H, $J_{1,2}$ 1.8 Hz, H-2), 5.408 (d, 1 H, H-1), 5.354 (t, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 4.278 (dd, 1 H, $J_{6,6}$ 11.9 Hz, H-6), 4.142 (ddd, 1 H, $J_{5,6}$ 2.1 and 5.2 Hz, H-5), 4.093 (dd, 1 H, H-6), 3.769 (s, 3 H, OMe), 2.189, 2.057, 2.044, and 2.032 (4 s, 12 H, 4 Ac).

Anal. Calc. for $C_{21}H_{26}O_{11}$: C, 55.51; H, 5.77. Found: C, 55.61; H, 5.79.

(*b*) To a mixture of **14** (505 mg, 1.3 mmol) and *p*-methoxyphenol (317 mg, 2.6 mmol) in $Cl(CH_2)_2Cl$ (4 mL) was added CF_3SO_3H (19 μL, 0.21 mmol) at 0° under Ar. After stirring for 6 h at 20°, the mixture was diluted with EtOAc, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatrography (10:7 hexane–EtOAc) of the residue gave **15** (535 mg, 91%).

p-*Methoxyphenyl* α-D-*mannopyranoside* (**16**). — A solution of **15** (300 mg, 66 μmol) in 0.2M NaOMe–MeOH (18 mL) was stirred for 18 h at 20°, neutralized with Amberlyst 15 (H^+) resin, filtered through Celite, and concentrated *in vacuo*. Column chromatography (6:1 CH_2Cl_2–MeOH) of the residue gave **16** (162 mg, 95%), m.p. 152–153° (from MeOH–$CHCl_3$), $[\alpha]_D$ +113° (*c* 1.3, methanol), R_F 0.26 (7:1 $CHCl_3$–MeOH). ^{1}H-N.m.r. data: δ (CD_3OD) 7.035 (d, 2 H, *J* 9.5 Hz, aromatic), 6.831 (d, 2 H, *J* 9.5 Hz, aromatic), 5.339 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 3.994 (dd, $J_{2,3}$ 3.4 Hz, H-2), 3.887 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.778 (dd, 1 H, $J_{6,6}$ 11.9 Hz, H-6), 3.741 (s, 3 H, OMe), and 3.653 (ddd, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 2.8 and 5.2 Hz, H-5).

Anal. Calc. for $C_{13}H_{18}O_7$: C, 54.38; H, 6.36. Found: C, 54.45; H, 6.35.

p-*Methoxyphenyl 3,6-di*-O-*benzyl*-α-D-*mannopyranoside* (**17**) *and* p-*methoxyphenyl 2,3,6-tri*-O-*benzyl*-α-D-*mannopyranoside* (**18**). — A mixture of **16** (4.95 g, 17.4 mmol) and $(Bu_3Sn)_2O$ (25.8 g, 43.5 mmol) in toluene (500 mL) was stirred for 4 h under reflux with continuous azeotropic removal of water, then concentrated *in vacuo*. A mixture of the residual oil, benzyl bromide (44.0 g, 257 mmol), and Bu_4NBr (276 mg, 850 μmol) in toluene (10 mL) was stirred for 8 h at 120° under Ar, then concentrated *in vacuo*, and co-concentrated with tetralin *in vacuo*. To a solution of the residue in EtOAc was added aq. KF. The mixture was stirred for 1 h at 20° to precipitate Bu_3SnF, then filtered through Celite, washed with H_2O and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (5:2 toluene–EtOAc) of the residue gave **17** (6.20 g, 76.4%) and **18** (1.36 g, 14%).

Compound **17** had $[\alpha]_D$ +74° (*c* 1.9), R_F 0.27. ^{1}H-N.m.r. data: δ 5.467 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.763 (d, 1 H, *J* 11.6 Hz, C*H*$_2$Ph), 4.719 (d, 1 H, *J* 11.6 Hz, C*H*$_2$Ph), 4.550 (d, 1 H, *J* 11.9 Hz, C*H*$_2$Ph), 4.490 (d, 1 H, *J* 11.9 Hz, C*H*$_2$Ph), 4.163 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-2), 4.013 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.745 (s, 3 H, OMe).

Anal. Calc. for $C_{27}H_{30}O_7$: C, 69.51; H, 6.48. Found: C, 69.68; H, 6.63.

Diacetate **19** (of **17**). ^{1}H-N.m.r. data: δ 7.35–7.20 (m, 10 H, 2 Ph), 7.021 (d, 2 H, *J* 9.1 Hz, $MeOC_6H_4$), 6.784 (d, 2 H, *J* 9.1 Hz, $MeOC_6H_4$), 5.523 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.4 Hz, H-2), 5.410 (d, 1 H, H-1), 5.331 (t, 1 H, *J* 9.8 Hz, H-4), 4.709 (d, 1 H, *J* 12.0 Hz, CH_2Ph), 4.513 (d, 1 H, *J* 12.4 Hz, CH_2Ph), 4.505 (d, 1 H, *J* 12.0 Hz, CH_2Ph), 4.454 (d, 1 H, *J* 12.4 Hz, CH_2Ph), 3.757 (s, 3 H, OMe), 2.156 and 1.926 (2 s, 6 H, 2 Ac).

Compound **19** had $[\alpha]_D$ +25° (*c* 0.8), R_F 0.65. ^{1}H-N.m.r. data: δ 7.4–7.2 (m, 15 H, 3 Ph), 6.977 (d, 2 H, *J* 9.1 Hz, $MeOC_6H_4$), 6.782 (d, 2 H, *J* 9.1 Hz, $MeOC_6H_4$), 5.457 (d, 1 H, *J* 1.8 Hz, H-1), 4.732 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.703 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.666 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.608 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.578 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.508 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.163 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 3.956 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 3.916 (dd, 1 H, H-3), 3.748 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{36}O_7$: C, 73.36; H, 6.52. Found: C, 73.34; H, 6.61.

Acetate **20** (of **18**). ^{1}H-N.m.r. data: δ 5.458 (t, 1 H, *J* 9.8 Hz, H-4), 5.422 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 4.797 (d, 1 H, *J* 12.5 Hz, CH_2Ph), 4.728 (d, 1 H, *J* 12.5 Hz, CH_2Ph), 4.645 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.559 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.491 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.458 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 3.954 (t, 1 H, $J_{2,3}$ 2.1 Hz, H-2), 3.751 (s, 3 H, OMe), 3.615 (dd, 1 H, $J_{5,6}$ 5.8, $J_{6,6}$ 10.0 Hz, H-6), 3.568 (dd, 1 H, $J_{5,6}$ 3.1 Hz, H-6), and 1.929 (s, 3 H, Ac).

p-*Methoxyphenyl 3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranoside* (**12**) *and* p-*methoxyphenyl 3,6-di*-O-*benzyl-2,4-di*-O-p-*methylbenzoyl*-α-D-*mannopyranoside* (**21**). — A solution of **13** (115 mg, 246 μmol) in pyridine (4 mL) was stirred with *p*-toluoyl chloride (85 μL, 640 μmol) at −20° to −25° (solid CO_2–CCl_4 bath) under Ar for 4 h at −20°. MeOH (0.4 mL) was added, and the mixture was stirred for 20 min at 20°, diluted with EtOAc, washed with H_2O, aq. $NaHCO_3$, and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography on SiO_2 (5:1 hexane–EtOAc) of the residue gave **12** (119 mg, 81%) and **21** (18 mg, 11%).

Compound **12** had $[\alpha]_D$ +11° (*c* 0.8), R_F 0.37 (3:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 7.954 (d, 2 H, *J* 8.1 Hz, MeC_6H_4), 7.4–7.25 (m, 10 H, 2 Ph), 7.185 (d, 2 H, *J* 8.1 Hz, MeC_6H_4), 7.045 (d, 2 H, *J* 9.2 Hz, $MeOC_6H_4$), 6.802 (d, 2 H, *J* 9.2 Hz, $MeOC_6H_4$), 5.747 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 5.565 (d, 1 H, H-1), 4.850 (d, 1 H, *J* 11.0 Hz, CH_2Ph), 4.649 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.568 (d, 1 H, *J* 11.0 Hz, CH_2Ph), 4.545 (d, 1 H, *J* 11.9 Hz, CH_2Ph), 4.292 (dt, 1 H, $J_{4,OH}$ 2.1, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 4.094 (dd, 1 H, H-3), 4.020 (ddd, 1 H, $J_{5,6}$ 3.1 and 4.7 Hz, H-5), 3.857 (dd, 1 H, $J_{5,6}$ 4.7, $J_{6,6}$ 10.7 Hz, H-6), 3.802 (dd, 1 H, $J_{5,6}$ 3.1 Hz, H-6), 3.758 (s, 3 H, OMe), 2.556 (d, 1 H, $J_{OH,4}$ 2.1 Hz, O*H*), and 2.404 (s, 3 H, PH*Me*).

Anal. Calc. for $C_{35}H_{36}O_8$: C, 71.90; H, 6.14. Found: C, 71.98; H, 6.21.

Compound **21** had $[\alpha]_D$ −19° (*c* 0.7), R_F 0.83 (6:1 toluene–EtOAc). ^{1}H-N.m.r. data: δ 5.800 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.777 (dd, $J_{1,2}$ 1.8 Hz, $J_{2,3}$ 3.4 Hz, H-2), 5.580 (d, 1 H, H-1), 4.296 (dd, H-3), 4.239 (td, 1 H, $J_{5,6}$ 4.0 Hz, H-5), 3.759 (s, 3 H, OMe), 2.438 and 2.407 (2 s, 6 H, 2 Ph*Me*).

Anal. Calc. for $C_{43}H_{42}O_9$: C, 73.49; H, 6.02. Found: C, 73.54; H, 6.13.

p-*Methoxyphenyl 3,6-di*-O-*benzyl-4*-O-*chloroacetyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranoside* (**22**). — To a solution of **12** (467 mg, 800 μmol) in *N,N*-dimethylformamide (4 mL) were added successively a solution of $(ClCH_2CO)_2O$ (341 mg, 2.0 mmol) in *N,N*-dimethylformamide (5 mL) and $NaHCO_3$ (168 mg, 2.0 mmol) at 20°. The mixture was stirred for 18 h at 20°, then poured into ice–water, and extracted with EtOAc. The extract was washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (3:1 hexane–EtOAc) of the residue gave **22** (429 mg, 81%) and **12** (67 mg).

Compound **18** had $[\alpha]_D$ −3.0° (*c* 0.5), R_F 0.38. ^{1}H-N.m.r. data: δ 7.954 (d, 2 H, *J* 8.0 Hz, MeC_6H_4), 7.182 (d, 2 H, *J* 8.0 Hz, MeC_6H_4), 7.035 (d, 2 H, *J* 9.2 Hz, $MeOC_6H_4$), 6.801 (d, 2 H, *J* 9.2 Hz, $MeOC_6H_4$), 5.733 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 5.610 (t, 1 H, *J* 9.8 Hz, H-4), 5.559 (d, 1 H, H-1), 4.747 (d, 1 H, *J* 12.2 Hz, CH_2Ph), 4.549 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.520 (d, 1 H, *J* 12.2 Hz, CH_2Ph), 4.461 (d, 1 H, *J* 11.6 Hz, CH_2Ph), 4.200 (dd, 1 H, $J_{3,4}$ 9.8 Hz, H-3), 4.103 (td, 1 H, $J_{4,5}$ 9.8, $J_{5,6}$ 4.0 Hz, H-5), 3.804 (d, 1 H, *J* 14.7 Hz, CH_2Cl), 3.771 (d, 1 H, *J* 14.7 Hz, CH_2Cl), 3.760 (s, 3 H, OMe), 3.645 (dd, 1 H, $J_{5,6}$ 3.4, $J_{6,6}$ 10.7 Hz, H-6), 3.611 (dd, 1 H, $J_{5,6}$ 4.6 Hz, H-6), and 2.462 (s, 3 H, Ph*Me*).

Anal. Calc. for $C_{39}H_{37}ClO_9$: C, 67.22; H, 5.64. Found: C, 67.48; H, 5.89.

3,6-Di-O-*benzyl-4*-O-*chloroacetyl-2*-O-p-*methylbenzoyl*-D-*mannopyranose* (**23**). — A mixture of **22** (150 mg, 230 μmol) and ammonium cerium(IV) nitrate (378 mg, 690 μmol) in CH_3CN (1.2 mL) and H_2O (0.3 mL) was stirred for 3 h at 20°, then diluted with EtOAc. The organic layer was washed with H_2O, aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (4:1 hexane–EtOAc) of the residue gave **23** (96 mg, 75%), R_F 0.22 (3:1 hexane–EtOAc), ^{1}H-N.m.r. data: δ 3.773 (s, 2 H, CH_2Cl) and 2.393 (s, 3 H, Ph*Me*).

Anal. Calc. for $C_{30}H_{31}ClO_8$: C, 64.92; H, 5.63. Found: C, 65.32; H, 5.70.

3,6-Di-O-*benzyl-4*-O-*chloroacetyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl trichloroacetimidate* (**11**). — To a stirred solution of **23** (282 mg, 508 μmol) in $Cl(CH_2)_2Cl$ (2.5 mL) were added successively Cl_3CCN (734 mg, 509 μL, 5.08 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (7.6 μL, 51 μmol) at −20° to −25° (dry ice–CCl_4) under Ar. The mixture was stirred for 2.5 h at −20° and chromatographed directly (5:1 hexane–EtOAc) to give **11** (290 mg, 82%), $[\alpha]_D$ −20° (*c* 1.9), R_F 0.56. N.m.r. data: ^{1}H, δ 8.754 (s, 1 H, C=NH), 7.953 (d, 2 H, *J* 8.2 Hz, $COC_6H_4CH_3$), 6.414 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 5.705 (dd, 1 H, $J_{2,3}$ 3.1 Hz, H-2), 5.652 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 3.799 (s, 2 H, $ClCH_2CO$), and 2.406 (s, 3 H, C_6H_4Me); ^{13}C, δ 95.1 ($J_{C\text{-}1,H\text{-}1}$ 179.4 Hz, C-1), 40.6 ($COCH_2Cl$), and 21.6 ($C_6H_4CH_3$).

Anal. Calc. for $C_{32}H_{31}Cl_4NO_8$; C, 54.95; H, 4.47; N, 2.00. Found: C, 54.77; H, 4.43; N, 1.96.

Conversion of **11** *into the methyl thioglycoside* **24**. — To a stirred mixture of **11** (262 mg, 375 μmol), Bu_3SnSMe (202 mg, 599 μmol), and molecular sieves AW300 (600 mg) in $Cl(CH_2)_2Cl$ (5 mL) was added BF_3–Et_2O (74 μL, 599 μmol) at −22° under Ar. The mixture was stirred for 3 h at −20°, neutralized with Et_3N (500

μL), diluted with EtOAc, stirred with aq. KF, filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (18:1 toluene–EtOAc) of the residue gave methyl 3,6-di-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-*p*-methylbenzoyl-1-thio-α-D-mannopyranoside (**24**; 205 mg, 94%), $[\alpha]_D$ −2.7° (*c* 1.3), R_F 0.49 (15:1 toluene–EtOAc). N.m.r. data: ^1H δ 5.544 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 3.939 (dd, 1 H, $J_{2,3}$ 3.1 Hz), 3.778 (s, 2 H, CH_2Cl), 2.378 (s, 3 H, Ph*Me*), and 2.150 (s, 3 H, SMe); ^{13}C, δ 83.9 ($J_{C\text{-}1,H\text{-}1}$ 172 Hz, C-1), 40.6 (CH_2Cl), 21.6 ($PhCH_3$), and 13.8 (SCH_3).

p-*Methoxyphenyl* O-*(3,6-di-O-benzyl-4-O-chloroacetyl-2-*O-p-*methylbenzoyl-α-*D-*mannopyranosyl)-(1→4)-3,6-di-*O-*benzyl-2-*O-p-*methylbenzoyl-α-*D-*mannopyranoside* (**25**). — (*a*) To a stirred mixture of **12** (135 mg, 230 μmol) and molecular sieves 4A (MS4A, 1.5 g) in $Cl(CH_2)_2Cl$ (4 mL) were added successively a solution of **11** (134 mg, 191 μmol) in $Cl(CH_2)_2Cl$ (4 mL) and a solution of $CF_3SO_2OSiMe_3$ (7.3 μL, 38 μmol) in $Cl(CH_2)_2Cl$ (0.5 mL) at −20° under Ar. After stirring for 30 min at −20°, the mixture was neutralized with Et_3N (120 μL), diluted with EtOAc, filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (5:1 hexane–EtOAc) of the residue gave **25** (186 mg, 87%), $[\alpha]_D$ −3.2° (*c* 1.4), R_F 0.56 (3:1 hexane–EtOAc). N.m.r. data: ^1H δ 5.737 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2a or b), 5.715 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2b or a), 5.632 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1a or b), 5.558 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1b or a), 5.480 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4b), 4.415 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4a), 3.774 (s, 3 H, OMe), 3.734 (d, 1 H, *J* 12.2 Hz, $ClCH_2CO$), 3.765 (d, 1 H, *J* 12.2 Hz, $ClCH_2CO$), and 2.381 (s, 6 H, 2 C_6H_4Me); ^{13}C δ 99.2 ($J_{C\text{-}1,H\text{-}1}$ 175 Hz, C-1), 96.9 ($J_{C\text{-}1,H\text{-}1}$ 175 Hz, C-1), 55.7 (OCH_3), 40.7 ($ClCH_2CO$), and 21.7 (2 $C_6H_4CH_3$).

Anal. Calc. for $C_{65}H_{65}ClO_{15}$: C, 69.60; H, 5.84. Found: C, 69.70; H, 5.82.

(*b*) To a stirred mixture of MS4A (500 mg) and PhSeCl (60 mg, 0.31 mmol) in $Cl(CH_2)_2Cl$ (2.5 mL) was added $AgOSO_2CF_3$ (70 mg, 0.27 mmol) at 0° under Ar. After stirring for 20 min, the mixture was cooled to −23°, and a solution of **24** (52 mg, 90 μmol) and **12** (54 mg, 92 μmol) in $Cl(CH_2)_2Cl$ (3 mL) at −23° was added dropwise under Ar. After stirring for 1 h, the mixture was neutralized with aq. $NaHCO_3$ (0.5 mL), diluted with EtOAc, filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (18:1 toluene–EtOAc) of the residue gave **25** (94 mg, 93%).

(*c*) To a mixture of $AgOSO_2CF_3$ (53 mg, 0.21 mmol), $CuBr_2$ (46 mg, 0.21 mmol), Bu_4NBr (13.0 mg, 41 μmol), and MS4A (600 mg) was added a solution of **24** (40 mg, 69 μmol) and **12** (41 mg, 70 μmol) in $Cl(CH_2)_2Cl$ (4 mL) at 0°. The mixture was stirred for 1 h at 0°, then for 2 h at 20°, diluted with EtOAc, filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (18:1 toluene–EtOAc) of the residue gave **25** (74 mg, 96%).

p-*Methoxyphenyl* O-*(3,6-di-O-benzyl-2-*O-p-*methylbenzoyl-α-*D-*mannopyranosyl)-(1→4)-3,6-di-*O-*benzyl-2-*O-p-*methylbenzoyl-α-*D-*mannopyranoside* (**26**). —

A mixture of **25** (853 mg, 760 μmol) and $(NH_2)_2CS$ (203 mg, 2.66 mmol) in EtOH (45 mL) was stirred for 8 h at 90°, then diluted with EtOAc, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (5:2 hexane–EtOAc) of the residue gave **26** (779 mg, 98%), $[\alpha]_D$ −12° (*c* 1.9), R_F 0.23 (3:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 5.745 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2a or b), 5.726 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2b or a), 5.628 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1a or b), 5.554 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1b or a), 4.429 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4a), 4.110 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4b), 3.769 (s, 3 H, OMe), 2.381 (s, 3 H, C_6H_4Me), and 2.378 (s, 3 H, C_6H_4Me).

Anal. Calc. for $C_{63}H_{64}O_{14}$: C, 72.37; H, 6.18. Found: C, 72.33; H, 6.14.

p-*Methoxyphenyl* O-*(3,6-di*-O-*benzyl-4*-O-*chloroacetyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl)-(1→4)-3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranoside* (**27**). — To a stirred mixture of **26** (96 mg, 91 μmol) and MS4A (800 mg) in $Cl(CH_2)_2Cl$ (3 mL) were added successively a solution of **11** (70 mg, 0.10 mmol) in $Cl(CH_2)_2Cl$ (3 mL) and $CF_3SO_2OSiMe_3$ (4 μL, 0.02 mmol) at −20° under Ar. After stirring for 30 min at −20°, the mixture was neutralized with Et_3N (60 μL), diluted with EtOAc, filtered through Celite, washed with aq. $NaHCO_3$ and NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (3:1 hexane–EtOAc) of the residue gave **27** (122 mg, 84%), $[\alpha]_D$ −26° (*c* 1.1), R_F 0.29. ^{1}H-N.m.r. data: δ 5.753 (m, 2 H, 2 H-2), 5.680 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 5.582 (d, 2 H, $J_{1,2}$ 1.8 Hz, 2 H-1), 5.563 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.468 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4c), 3.785 (s, 3 H, OMe), 3.715 (s, 2 H, $COCH_2Cl$), 2.372, 2.365, and 2.355 (3 s, 9 H, 3 C_6H_4Me).

Anal. Calc. for $C_{93}H_{93}ClO_{21}$: C, 70.60; H, 5.92. Found: C, 70.38; H, 5.97.

Conversion of **27** *into the hemiacetal* **28**. — A mixture of **27** (155 mg, 98 μmol) and ammonium cerium(IV) nitrate (161 mg, 294 μmol) in 4:1 CH_3CN–H_2O (2 mL) was stirred for 2 h at 5–10°, then diluted with EtOAc. The organic layer was washed with H_2O, aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (8:1 toluene–EtOAc) of the residue gave *O*-(3,6-di-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-D-mannopyranose (**28**; 104 mg, 72%), R_F 0.31 (2:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 5.722 (bt, 1 H, H-2), 5.696 (bt, 1 H, H-2), 5.583 (bt, 1 H, H-2), 5.556 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.506 (bs, 1 H, H-1), 5.480 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4c), 5.382 (bs, 1 H, H-1a), 3.737 (s, 2 H, $COCH_2Cl$), 2.374 (s, 6 H, 2 C_6H_4Me), and 2.353 (s, 3 H, C_6H_4Me).

Conversion of **28** *into the trichloroacetimidate* **9**. — To a stirred solution of **28** (110 mg, 75 μmol) in $Cl(CH_2)_2Cl$ (1.6 mL) was added successively CCl_3CN (75 μL, 0.75 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.1 mg, 7.5 μmol) at −20° to −25° (dry ice–CCl_4 bath) under Ar. After stirring for 2.5 h at −20°, the mixture was chromatographed (3:1 hexane–EtOAc) to give *O*-(3,6-di-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-ben-

zyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl trichloroacetimidate (**9**; 112 mg, 92%), $[\alpha]_D$ −21° (*c* 0.7), R_F 0.32. ^{1}H-N.m.r. data: δ 8.768 (s, 1 H, C=NH), 7.9–7.8 (m, 6 H, COC_6H_4), 7.5–7.0 (m, 36 H, aromatic), 6.420 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1a), 5.745 (bs, 2 H, 2 H-2), 5.688 (dd, 1 H, $J_{1,2}$ 2.1, $J_{2,3}$ 2.8 Hz, H-2), 5.571 (d, 2 H, $J_{1,2}$ 1.8 Hz, H-1bc), 5.484 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4c), 3.723 (s, 2 H, $COCH_2Cl$), 2.377, 2.369, and 2.353 (3 s, 9 H, 3 C_6H_4Me).

Methyl O-(3,6-di-O-benzyl-4-O-chloroacetyl-2-O-p-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-O-(3,6-di-O-benzyl-2-O-p-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-3,6-di-O-benzyl-2-O-p-methylbenzoyl-1-thio-α-D-mannopyranoside (**29**). — To a stirred mixture of **9** (74 mg, 46 μmol), Bu_3SnSMe (23 mg, 68 μmol), and MS AW300 (950 mg) in $Cl(CH_2)_2Cl$ (2.5 mL) was added $BF_3 \cdot Et_2O$ (8.4 μL, 68 μmol) at −20° under Ar. After stirring for 2 h, the mixture was neutralized with Et_3N (50 μL), diluted with EtOAc, filtered through Celite, washed with aq. KF, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (18:1 toluene–EtOAc) of the residue gave **29** (60 mg, 87%), $[\alpha]_D$ −18° (*c* 0.6), R_F 0.44 (5:1 toluene–EtOAc). ^{1}H-N.m.r. data: δ 5.712 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.3 Hz, H-2), 5.692 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.4 Hz, H-2), 5.662 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 5.564 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 5.514 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.476 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4c), 5.326 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1a), 3.727 (s, 2 H, $COCH_2Cl$), 2.372 (s, 6 H, 2 C_6H_5Me), 2.353 (s, 3 H, C_6H_5Me), and 2.216 (s, 3 H, SMe).

Anal. Calc. for $C_{87}H_{89}ClO_{19}S$: C, 69.38; H, 5.96. Found: C, 69.48; H, 6.07.

Methyl O-(3,6-di-O-benzyl-2-O-p-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-O-(3,6-di-O-benzyl-2-O-p-methylbenzoyl-α-D-mannopyranosyl)-(1→4)-3,6-di-O-benzyl-2-O-p-methylbenzoyl-1-thio-α-D-mannopyranoside (**10**). — A mixture of **29** (48 mg, 32 μmol) and $(NH_2)_2CS$ (8.4 mg, 0.11 mmol) in EtOH (4.5 mL) was stirred for 3 h at 87°, then cooled to 20°, diluted with EtOAc, washed with H_2O, aq. $NaHCO_3$, and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (3:1 hexane–EtOAc) of the residue gave **10** (41 mg, 89%), $[\alpha]_D$ −26° (*c* 0.4), R_F 0.23. N.m.r. data: ^{1}H, δ 5.713 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.1 Hz, H-2), 5.693 (dd, 1 H, $J_{1,2}$ 1.5, $J_{2,3}$ 3.1 Hz, H-2), 5.654 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2), 5.545 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 5.510 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.324 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1a), 2.374 (s, 6 H, 2 C_6H_4Me), 2.349 (s, 3 H, C_6H_4Me), and 2.208 (s, 3 H, SMe); ^{13}C, δ 99.4 ($J_{C\text{-}1,H\text{-}1}$ 175 Hz, C-1bc) and 83.8 ($J_{C\text{-}1,H\text{-}1}$ 169 Hz, C-1a).

Anal. Calc. for $C_{85}H_{88}O_{18}S$: C, 71.41; H, 6.20. Found: C, 71.52; H, 6.17.

Conversion of **10** *into the thioglycoside* **30**. — To a stirred mixture of **10** (30 mg, 21 μmol) and MS4A (600 mg) in $Cl(CH_2)_2Cl$ (2.5 mL) were added successively a solution of **9** (33 mg, 20 μmol) in $Cl(CH_2)_2Cl$ (2.0 mL) and a 0.26M solution of $CF_3SO_2OSiMe_3$ in CH_2Cl_2 (15.4 μL, 4 μmol) at −20° under Ar. After stirring for 30 min at −20°, the mixture was neutralized with Et_3N (12 μL), diluted with EtOAc, filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (3:1 hexane–EtOAc) of the residue gave methyl *O*-(3,6-di-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-*p*-methylben-

zoyl-α-D-mannopyranosyl)-(1→4)-[*O*-(3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-α-D-mannopyranosyl)-(1→4)]$_4$-3,6-di-*O*-benzyl-2-*O*-*p*-methylbenzoyl-1-thio-α-D-mannopyranoside (**30**; 50 mg, 87%), $[\alpha]_D$ −43° (*c* 0.9), R_F 0.42 (2:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 5.779 (bs, 2 H, 2 H-2), 5.762 (bt, 1 H, *J* 2.0 Hz, H-2), 5.739 (bt, 1 H, *J* 2.0 Hz, H-2), 5.690 (bt, *J* 2.0 Hz, 2 H-2), 5.587 (s, 2 H, 2 H-1), 5.565 (s, 2 H, 2 H-1), 5.548 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.476 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.8 Hz, H-4f), 5.336 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1a), 3.687 (s, 2 H, $COCH_2Cl$), 2.363 (6 H), 2.355, 2.339, 2.335, 2.329 (5 s, 18 H, 6 C_6H_4*Me*), and 2.222 (s, 3 H, SMe).

Methyl O-*(3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl)-(1→4)-[*O-*(3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl-(1→4)]$_4$-3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl-1-thio*-α-D-*mannopyranoside* (**31**). — A mixture of **30** (606 mg, 210 μmol) and $(NH_2)_2CS$ (56 mg, 0.73 mmol) in EtOH (45 mL) was stirred for 7 h at 85°, then cooled to 20°, diluted with EtOAc, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (5:2 hexane–EtOAc) of the residue gave **31** (479 mg, 81%) and **30** (50 mg).

Compound **31** had $[\alpha]_D$ −53° (*c* 0.9), R_F 0.34 (2:1 hexane–EtOAc). N.m.r. data: ^{1}H, δ 5.770 (bs, 2 H, 2 H-2), 5.756 (bt, 1 H, *J* 2.0 Hz, H-2), 5.737 (bt, 1 H, *J* 2.0 Hz, H-2), 5.695 (bt, 1 H, *J* 2.0 Hz, H-2), 5.683 (bt, 1 H, *J* 2.0 Hz, H-2), 5.572 (s, 1 H, H-1), 5.562 (s, 2 H, 2 H-1), 5.540 (s, 2 H, 2 H-1), 5.331 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1a), 2.367, 2.361, 2.354, 2.331 (4 s, ratios 1:1:2:2, 18 H, 6 C_6H_4*Me*), and 2.220 (s, 3 H, SMe); ^{13}C, δ 99.4, 99.1, 99.0, 98.9, 98.8 (C-1bcdef), and 83.9 ($J_{C\text{-}1,H\text{-}1}$ 164 Hz, C-1a).

Anal. Calc. for $C_{169}H_{172}O_{36}S$: C, 72.21; H, 6.17. Found: C, 72.16; H, 6.24.

Methyl O-*(3,6-di*-O-*benzyl-4*-O-*ethoxyethyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl-(1→4)-[*O-*(3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl*-α-D-*mannopyranosyl)-(1→4)]$_4$-3,6-di*-O-*benzyl-2*-O-p-*methylbenzoyl-1-thio*-α-D-*mannopyranoside* (**32**). — A mixture of **31** (141 mg, 50 μmol), ethyl vinyl ether (24 μL, 0.25 mmol), pyridinium *p*-toluenesulfonate (13 mg, 50 μmol) in $Cl(CH_2)_2Cl$ (3 mL) was stirred for 4 h at 20°, then poured into aq. $NaHCO_3$, and extracted with EtOAc. The extract was washed with H_2O, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (40:20:3 hexane–EtOAc–Et_3N) of the residue gave **32** (142 mg, 98%), R_F 0.39 (2:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 5.77–5.73 (bs, 5 H, 5 H-2), 5.678 (bs, 1 H, H-2), 5.570, 5.555, 5.538 (2.5 H), and 5.523 (0.5 H) (4 s, 5 H, 5 H-1), 5.330 (s, 1 H, H-1a), 2.360 and 2.333 (2 s, ratio 1:2, 18 H, 6 C_6H_4*Me*), 2.219 (s, 3 H, SMe), 1.194 and 1.125 (2 d, ratio 1:1, 3 H, *J* 5.2 Hz, CH_3CH), 0.992 and 0.917 (2 t, ratio 1:1, 3 H, *J* 7.0 Hz, CH_3CH_2).

Anal. Calc. for $C_{173}H_{180}O_{37}S \cdot C_2H_5O_2CCH_3$: C, 71.55; H, 6.38. Found: C, 71.44; H, 6.18.

Methyl O-*(3,6-di*-O-*benzyl-4*-O-*ethoxyethyl*-α-D-*mannopyranosyl)-(1→4)-[*O-*(3,6-di*-O-*benzyl*-α-D-*mannopyranosyl)-(1→4)]$_4$-3,6-di*-O-*benzyl-1-thio*-α-D-*mannopyranoside* (**33**). — A solution of **32** (142 mg, 49 μmol) in tetrahydrofuran (4 mL) and 0.1M NaOMe–MeOH (9 mL) was stirred for 19 h at 20°, then for 2 h at 50°, diluted with aq. NaCl, and extracted with EtOAc. The extract was washed

with aq. NaCl, dried (Na_2SO_4), and concentrated *in vacuo*. Chromatography (20:5:1 EtOAc–hexane–Et_3N) of the residue gave **33** (95 mg, 89%), R_F 0.51 (10:3 EtOAc–hexane). ^{1}H-N.m.r. data: δ 5.298 (d, 0.5 H, $J_{1,2}$ 2.1 Hz, 0.5 H-1), 5.284 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 5.269 (bd, 3.5 H, $J_{1,2}$ 2 Hz, 3.5 H-1), 5.244 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1a), 4.873 (q, 0.5 H, *J* 5.2 Hz, 0.5 CH_3CH), 4.739 (q, 0.5 H, *J* 5.2 Hz, 0.5 CH_3CH), 2.151 (s, 3 H, SMe), 1.251 and 1.150 (2 d, ratio 1:1, 3 H, *J* 5.2 Hz, CH_3CH), 1.079 and 1.042 (2 t, ratio 1:1, 3 H, *J* 7.0 Hz, CH_3CH_2).

Anal. Calc. for $C_{125}H_{144}O_{31}S \cdot C_6H_5CH_3$: C, 69.95; H, 6.76. Found: C, 69.78; H, 6.80.

Methyl O-*(2,3,6-tri-*O*-benzyl-4-*O*-ethoxyethyl-α-*D*-mannopyranosyl)-(1→4)-[*O*-(2,3,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-(1→4)]$_4$-2,3,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**34**). — To a stirred solution of **33** (31.4 mg, 14.4 μmol) and benzyl bromide (15.5 μL, 130 mmol) in *N,N*-dimethylformamide (3.0 mL) was added NaH (58%; 5.4 mg, 0.13 mmol) at 0° under Ar. The mixture was stirred for 1.5 h at 0°, then for 3 h at 20°. The excess of NaH was decomposed with MeOH (200 μL), the mixture was poured into water–ice, and extracted with EtOAc. The extract was washed with H_2O and aq. NaCl, dried (Na_2SO_4), and concentrated *in vacuo*. Chromatography (15:5:1 hexane–EtOAc–Et_3N) of the residue gave **34** (33.7 mg, 86%), R_F 0.38 (2:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 7.5–7.0 (m, 90 H, 18 Ph) and 2.170 (s, 3 H, SMe).

Anal. Calc. for $C_{167}H_{180}O_{31}S$: C, 73.87; H, 6.68. Found: C, 74.19; H, 7.14.

Methyl O-*(2,3,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-(1→4)-[*O*-(2,3,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-(1→4)]$_4$-2,3,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**35**). — A mixture of **34** (33 mg, 12 μmol) and Amberlyst 15 (H^+) resin (380 mg) in 1:1 $CHCl_3$–MeOH (3 mL) was stirred for 2.5 h at 20°, then filtered through Celite, and concentrated *in vacuo*. Chromatography (2:1 hexane–EtOAc) of the residue gave **35** (31 mg, 99%), $[\alpha]_D$ −2.1° (*c* 0.8), R_F 0.27. ^{1}H-N.m.r. data: δ 7.4–7.0 (m, 90 H, 18 Ph), 5.333 (s, 2 H, 2 H-1), 5.290 (s, 4 H, 4 H-1), 2.172 (s, 3 H, SMe).

Anal. Calc. for $C_{163}H_{172}O_{30}S$: C, 74.06; H, 6.56; S, 1.21. Found: C, 73.94; H, 6.57; S, 1.24.

*Cyclo{→4)-[O-(2,3,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-(1→4)]$_5$-*O*-(2,3,6-tri-*O*-benzyl-α-*D*-mannopyranosyl)-(1→}* (**37**). — To a stirred mixture of C_6H_5SeCl (5.6 mg, 29 μmol) and MS4A (500 mg) in $Cl(CH_2)_2Cl$ (2.5 mL) was added $AgOSO_2CF_3$ (7.8 mg, 30 μmol) at 0° under Ar. The mixture was stirred for 30 min at 0°, then cooled to −22°, and a solution of **35** (16 mg, 6 μmol) in $Cl(CH_2)_2Cl$ (5.0 mL) was added dropwise during 40 min at −20° under Ar. The mixture was stirred for 3 h at −22°, diluted with EtOAc, and filtered through Celite, washed with aq. $NaHCO_3$ and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography (10:1 toluene–EtOAc) of the residue gave **37** (14.5 mg, 92%), m.p. 136–137° (from EtOAc–toluene), $[\alpha]_D$ −2.8° (*c* 0.3), R_F 0.45 (8:1 toluene–EtOAc). N.m.r. data: ^{1}H, δ 7.3–7.1 (m, 90 H, 18 Ph), 5.043 (d, 6 H, $J_{1,2}$ 1.5 Hz, H-1), 4.528 (s, 12 H, OCH_2Ph), 4.490 (d, 6 H, *J* 12.2 Hz, OCH_2Ph), 4.405 (d, 6 H, *J* 12.2 Hz,

OCH_2Ph), 4.289 (d, 6 H, *J* 11.6 Hz, OCH_2Ph), 4.202 (d, 6 H, *J* 11.6 Hz, OCH_2Ph), 4.071 (t, 6 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.979 (dd, 6 H, $J_{5,6}$ 4.3, $J_{6,6}$ 10.7 Hz, H-6), 3.882 (dd, 1 H, $J_{5,6}$ 4.0 Hz, H-5), 3.87–3.83 (m, 12 H, H-2,3), 3.753 (bd, 6 H, $J_{6,6}$ 10.1 Hz, H-6); ^{13}C, δ 100.9 ($J_{C\text{-}1,H\text{-}1}$ 165 Hz, C-1).

Anal. Calc. for $C_{162}H_{168}O_{30} \cdot 0.5\ C_6H_5CH_3$: C, 75.26; H, 6.56. Found: C, 75.44; H, 6.69.

Cyclo{→4)-[O-α-D-mannopyranosyl-(1→4)]$_5$-O-α-D-mannopyranosyl-(1→} (**5**). — A mixture of **37** (15 mg, 5.7 μmol) and 10% Pd/C (34 mg) in MeOH (3 mL) was stirred for 15 h at 50° under H_2. More Pd/C (34 mg) was added, the mixture was stirred for a further 8 h at 50° under H_2, then diluted with MeOH, filtered through Celite, and concentrated *in vacuo*. Chromatography (Sephadex G-25, H_2O) of the residue gave **5** (5.4 mg, 93%), $[\alpha]_D$ +27° (*c* 0.2, water), R_F 0.23 (2:2:1 n-BuOH–MeOH–H_2O). ^1H-N.m.r. data (D_2O, Bu^{t}OH): δ 4.926 (d, 6 H, $J_{1,2}$ 2.4 Hz, H-1), 4.009 (dd, 6 H, $J_{1,2}$ 2.4, $J_{2,3}$ 3.4 Hz, H-2), 3.944 (dd, 6 H, $J_{5,6}$ 2.5, $J_{6,6}$ 12.2 Hz, H-6), 3.925 (dd, 6 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.0 Hz, H-3), 3.880 (dd, 6 H, $J_{5,6}$ 5.2, $J_{6,6}$ 12.2 Hz, H-6), 3.787 (ddd, 6 H, $J_{4,5}$ 9.0, $J_{5,6}$ 2.5, 5.0 Hz, H-5), and 3.703 (t, 6 H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4).

Anal. Calc. for $C_{36}H_{60}O_{30} \cdot 0.5\ H_2O$: C, 44.04; H, 6.26. Found: C, 44.01; H, 6.28.

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