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TOTAL SYNTHESIS OF CYCLOMALTOOCTAOSE AND AN ISOMER OF CYCLOMALTOHEXAOSE, CYCLO{→6)-[α-D-Glc*p*-(1→4)]$_5$-α-D-Glc*p*-(1-}*,†

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ABSTRACT

The first total synthesis of cyclomaltooctaose (gamma-cyclodextrin) is described, in 21 steps starting from maltose, with 0.02% overall yield. A crucial intramolecular cyclization was executed by using a properly protected glucooctaosyl fluoride as a key intermediate. A similar strategy was also applied to the synthesis of an isomer of cyclomaltohexaose (alpha-cyclodextrin), namely cyclo-{→6)-[α-D-Glc*p*-(1→4)]$_5$-α-D-Glc*p*-(1-}. Regiospecific introduction of an azide function at one of the primary hydroxyl groups of a key glucohexaosyl derivative, for the synthesis of cyclomaltooctaose, was also performed.

INTRODUCTION

In the previous paper[1], we reported a total synthesis of cyclomaltohexaose from maltose in 21 steps in 0.3% overall yield. A crucial intramolecular cyclization in α-(1→4) fashion of a linear glucohexaose derivative was achieved in 21% yield. As part of the project on cyclomaltooligose synthesis, we now describe a first total synthesis of both cyclomaltooctaose (**1**) and an isomer (**11**) of cyclomaltohexaose, starting from maltose.

Based on retrosynthetic analysis of cyclomaltooctaose (**1**), a key intermediate **3** was designed, which may be derived from a properly protected glucooctaose derivative **4**. Compound **4** may in turn be prepared from one molecule of a glycosyl acceptor **5** and three molecules of a glycosyl donor **6**, as shown in Scheme 1. For the synthesis of an isomer (**11**) of alpha-cyclodextrin, a key intermediate diol **12** was designed, which in turn could be prepared from maltose derivatives **5** and **13**, as shown in Scheme 2.

*Part 7 in the series "Glucan Synthesis", For Part 6 see ref. 1.
†Dedicated to Dr. R. Stuart Tipson.
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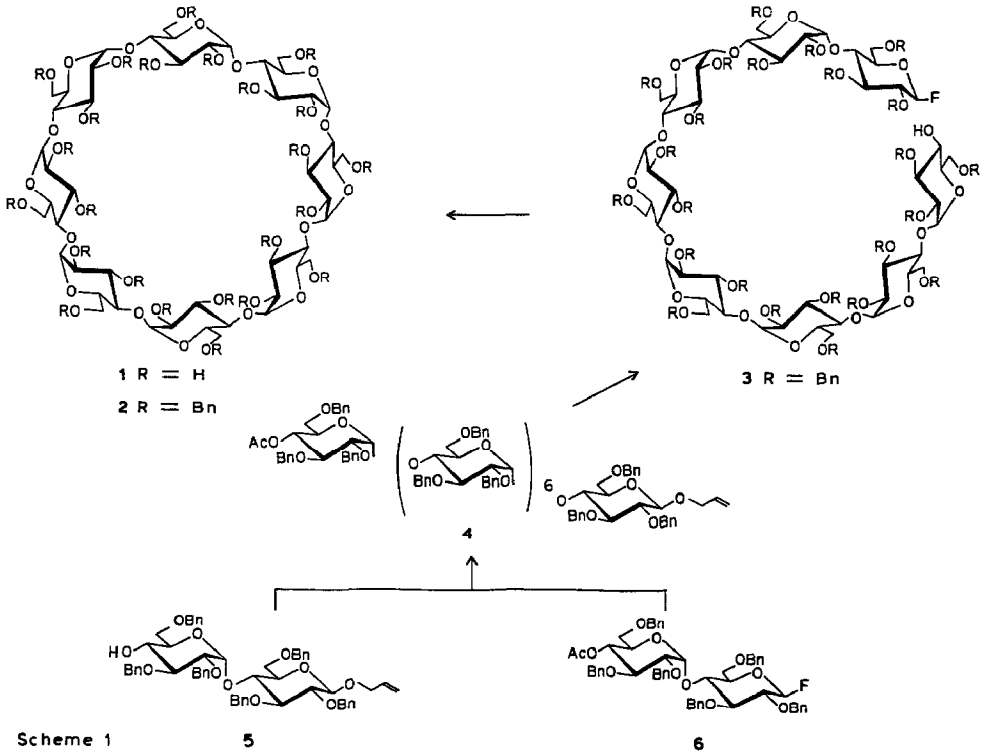
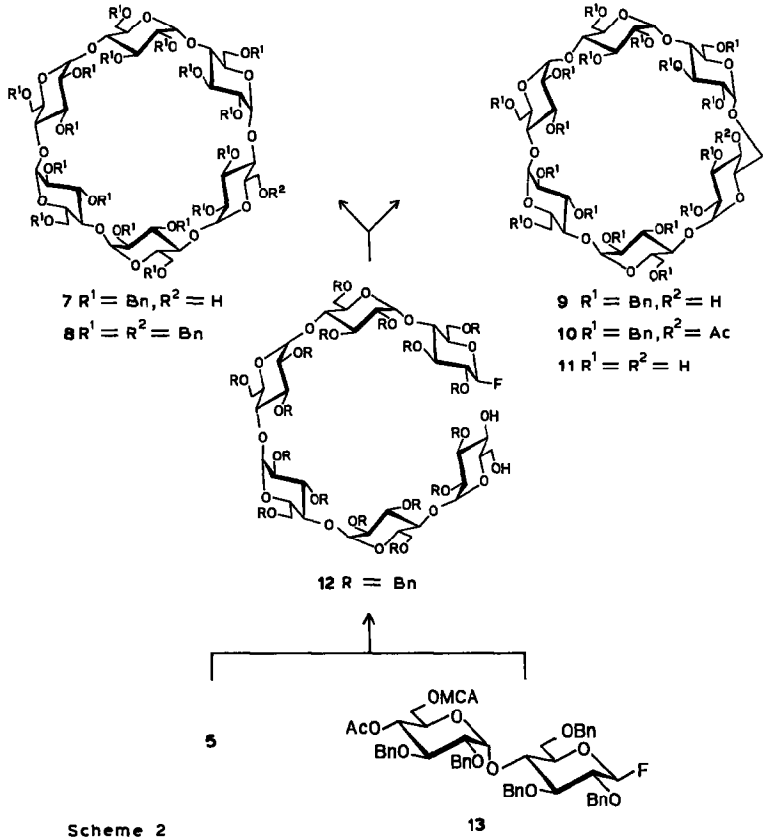


Scheme 1

RESULTS AND DISCUSSION

Synthesis of a key glucooctaose derivative **4** was studied by two approaches. First, reaction of the known[1] glucohexaose derivative **14** with 2.7 equivs. of the glycosyl donor **6** under Mukaiyama's conditions[2] afforded a 21% yield of the desired product **4** and a 5.3% yield of the β anomer **17**. The 1,6-anhydro derivative **20** and a glycal **21** were isolated in 41 and 23% yields, respectively, as the major byproducts arising from the excess of glycosyl donor **6**. The structures of compounds **4** and **17** were assigned by ^{13}C-n.m.r. data, which showed one signal for a β-D-anomeric carbon near δ 102 for compound **4** but two signals for compound **17**. These assignments were confirmed by ^{1}H-n.m.r. data of the deblocked products **16** and **19** (Fig. 1).

An alternative approach to the glucooctaose derivative **4** was examined that employs both a glucotetraosyl glycosyl acceptor **22** and the previously reported[1] glucotetraosyl glycosyl donor **23**. Equivalent amounts of compounds **22** and **23** were reacted under Mukaiyama's conditions[2], to give a mixture of glucooctaose derivatives **4** and **24** in 27% yield, which could not be separated even by repeated chromatography on SiO_2. Examination of this mixture by high-performance t.l.c. indicated the ratio of **4** and **24** to be ~3:1. From these experimental results, the



Scheme 2

former approach *via* the glycosyl donor **6** and glycosyl acceptor **14** was found more efficient and practical for the preparation of compound **4**.

The conversion of compound **4** into a key glycosyl donor **3** was performed in 4 steps. Deallylation[3] of compound **4** with $PdCl_2$ and NaOAc gave a 71% yield of the hemiacetal **26**, which was treated with thionyl chloride[4] in the presence of a catalytic amount of *N,N*-dimethylformamide (DMF), and then with silver fluoride in acetonitrile[5] to give the fluoride **27** in 66% yield. The β-D-configuration at C-1a of compound **27** was assigned from ^{1}H-n.m.r. data[6], which included a signal for H-1a at δ 5.353 having $^3J_{H,H}$ 5.8 and $^2J_{H,F}$ 54.4 Hz (Fig. 2). Deacetylation of compound **27** with NaOMe in methanol gave a 92% yield of the desired intermediate **3**. ^{1}H-N.m.r. spectroscopy of compound **3** showed disappearance of a singlet for acetate methyl at δ 1.782 and a deshielded triplet for H-4h at δ 5.089, both of which were present in the spectrum of compound **27**.

Crucial intramolecular glycosylation of compound **3** in the presence of silver triflate, stannous chloride[2], and powdered 4A molecular sieves in ether, and purification of the products by chromatography on silica gel, afforded the desired perbenzylated cyclomaltooctaose **2** in 8.4% yield. The major byproducts of the reac-

14
6
4
5
20
21
4 OCH2CH=CH2 Bn Ac
15 OCH2CH=CH2 Bn H
16 Pr H H
17 OCH2CH=CH2 Bn Ac
18 OCH2CH=CH2 Bn H
19 Pr H H

Scheme 3

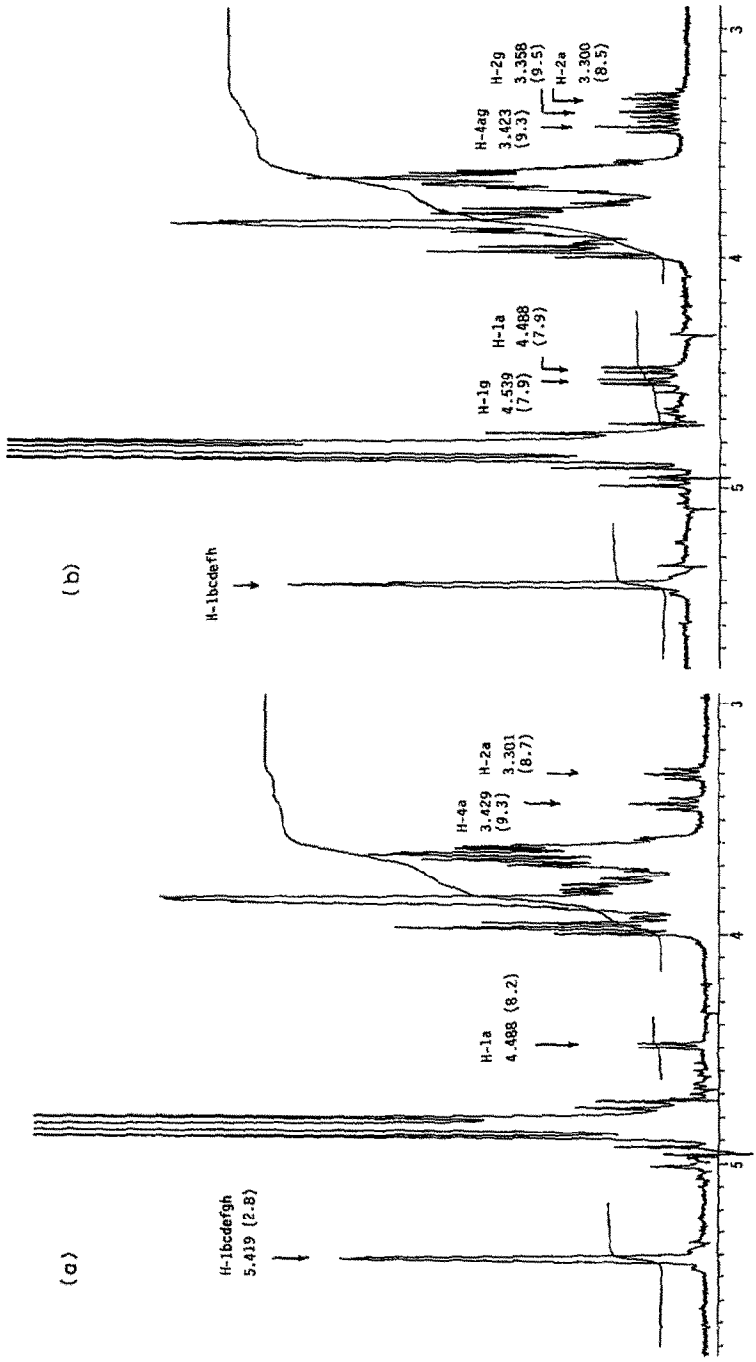
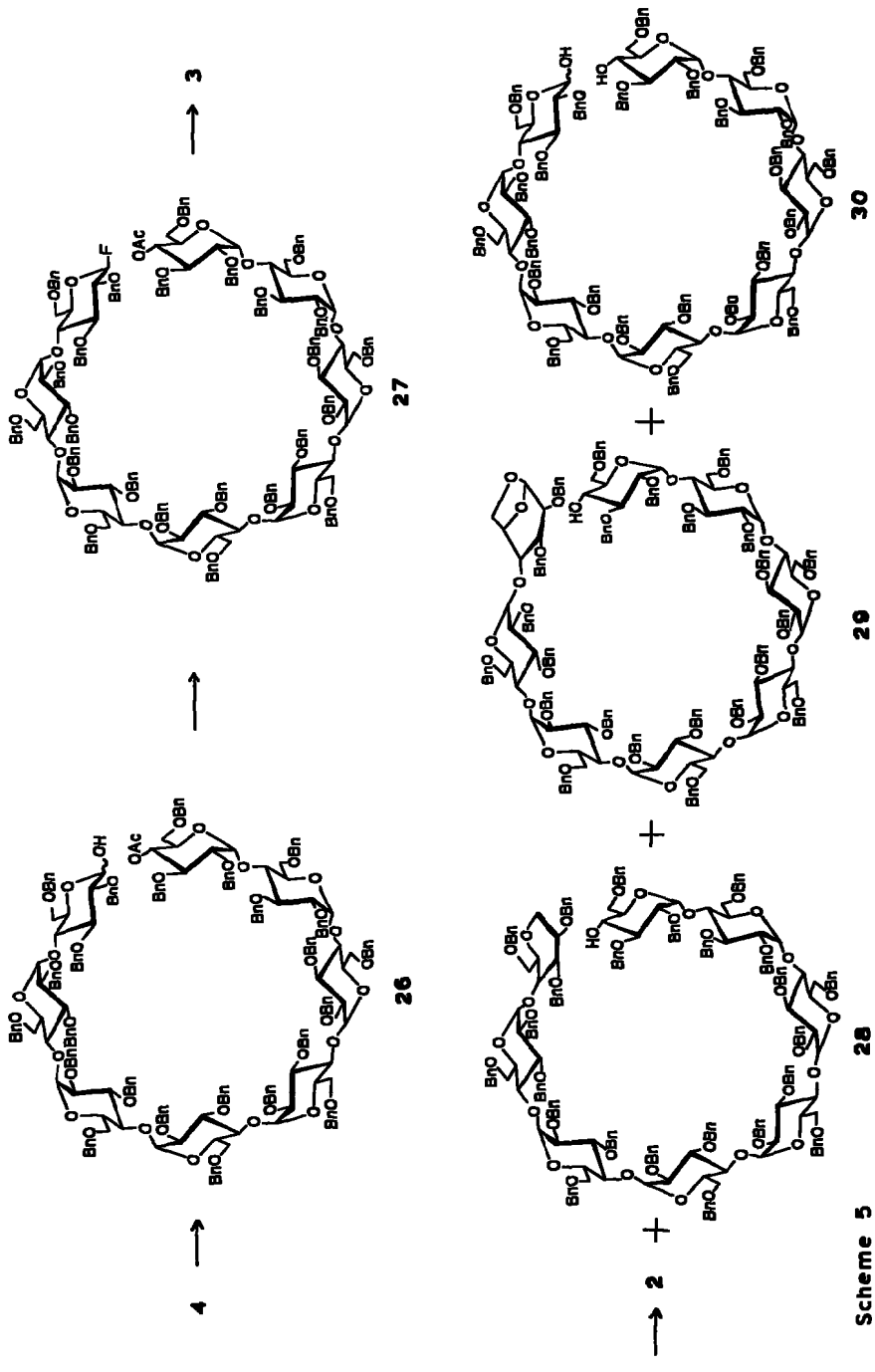


Fig. 1. The 400-MHz ^{1}H-n.m.r. spectra of synthetic propyl glycosides recorded in D_2O at 20°. Values in parentheses are J in Hz: (*a*) α-Glc*p*-[(1→4)-α-Glc*p*]$_5$-1→Pr (**16**); (*b*) α-Glc*p*-(1→4)-β-Glc*p*-(1→4)-[α-Glc*p*-(1→4)]$_5$-β-Glc*p*-1→Pr (**19**).

Scheme 4



Scheme 5

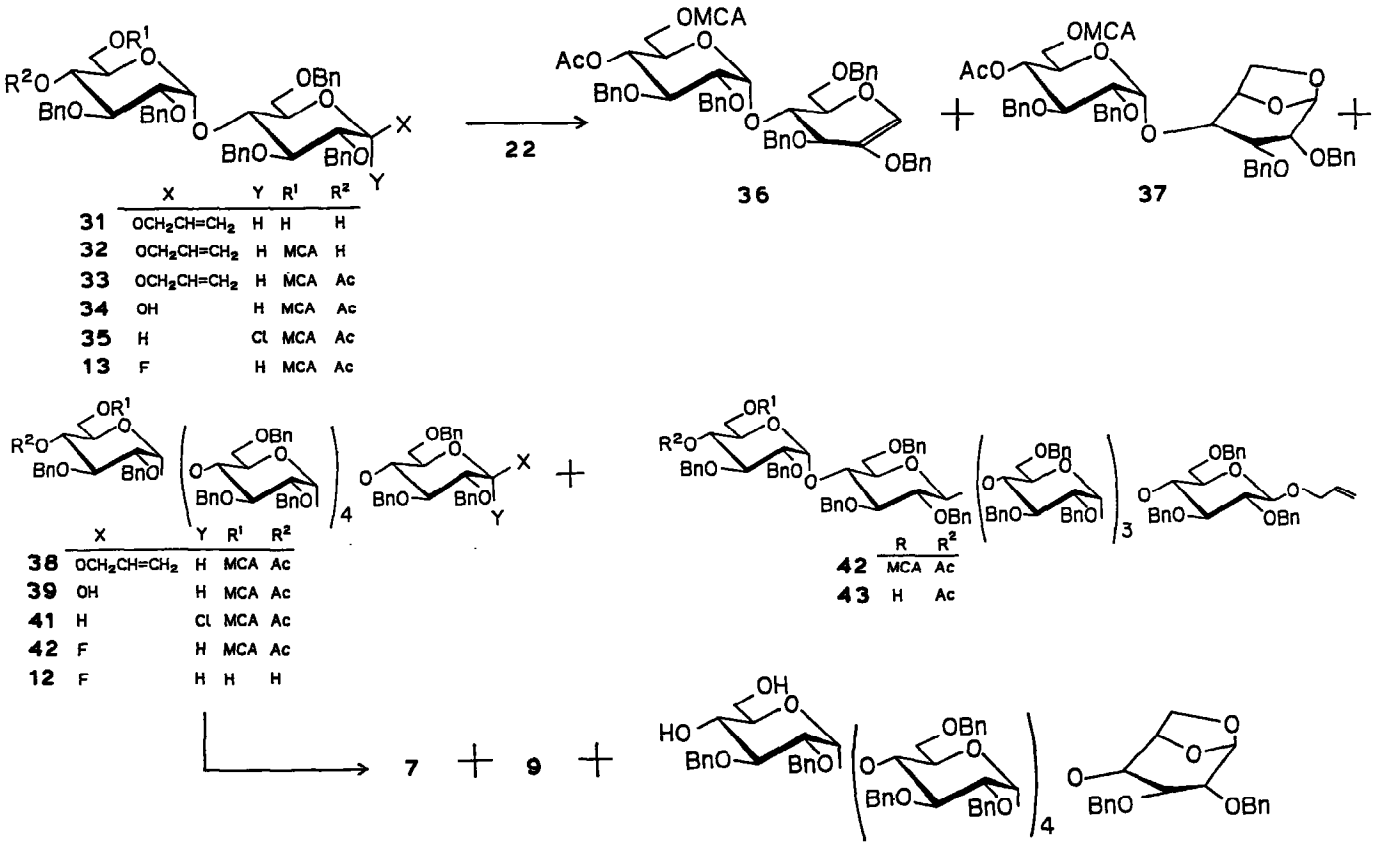
tion, the glycal **28**, the 1,6-anhydro derivative **29**, and a hydrolysis product **30** were isolated in 17.5, 10, and 24% yields, respectively, and their structures were assigned from ^{1}H-n.m.r. data. The perbenzylated cyclomaltooctaose **2** was also prepared conventionally from commercially available cyclomaltooctaose. The product **2** obtained by the totally synthetic route was identical with that obtained from natural cyclomaltooctaose, based on ^{1}H-n.m.r. spectral comparison. The perbenzylated cyclomaltooctaose was submitted to catalytic hydrogen-transfer conditions[7] to afford cyclomaltooctaose in 63% yield, thus completing the first total synthesis of cyclomaltooctaose, starting from maltose, in 21 steps in 0.02% overall yield.

It may be noted that the key intramolecular glycosylation was found more efficient for the synthesis of cyclomaltohexaose[1] (21%) than for the synthesis of cyclomaltooctaose (8%).

Next, regioselective intramolecular glycosylation to afford the cyclo-glucohexaose **9** by use of a key intermediate diol **12** was studied (Scheme 2). Compound **12** was prepared by glycosylation of a glucotetraosyl acceptor **22** with a glucobiosyl donor **13**. The latter could be prepared from the already reported[1] allyl penta-*O*-benzyl-*β*-maltoside **31** in 5 steps as follows. Treatment of diol **31** with $(ClCH_2CO)_2O$ and pyridine in 1,2-dichloroethane at $-5°$ afforded a 56% yield of monoester **32** and a 19% yield of the diester. Acetylation of compound **32** gave a 90% yield of a properly protected product **33**, which was deallylated to give hemiacetal **34** in 86% yield. Transformation of compound **34** into fluoride **13** was achieved as described previously in 81% overall yield. Glycosylation of the glucotetraosyl glycosyl acceptor **22** with four equivs. of a maltosyl donor **13**, followed by chromatographic purification afforded an 18% yield of the desired product **38**, a 28% yield of glycal **36**, a 48% yield of 1,6-anhydro derivative **37**, and a mixture of compound **42** and unreacted glycosyl acceptor **22**. The structure of compound **38** was assigned from ^{13}C-n.m.r. data, which showed a signal for a *β*-D anomeric carbon at δ 102.6 for C-1a and three signals for five *α*-D anomeric carbon atoms (C-1bcdef) at δ 96.4, 96.3, and 96.1 in the ratio of 2:1:2. The mixture of compounds **42** and **22** was treated with thiourea[8] and pyridine to remove the monochloroacetyl group selectively, giving an alcohol **43** in 8.2% yield (based on glycosyl acceptor **22**). The structure of compound **43** was assigned from ^{13}C-n.m.r. data, which showed signals for two *β*-D anomeric carbon atoms (at δ 102.6 and 102.1 for C-1a and C-1e, respectively), as well as signals for four *α*-D anomeric carbon atoms (C-1bcdf) at δ 96.7, 96.5, 96.4, and 96.2.

Deallylation of compound **38** with $PdCl_2$–NaOAc gave a 66% yield of hemiacetal **39**, which was further transformed into the *β*-fluoride **41** *via* the *α*-chloride **40** in 84% yield. The configuration at C-1a was assigned as *β*-D from ^{1}H-n.m.r. data, which showed a signal for H-1a at δ 5.357 as a double doublet having $^3J_{H,H}$ 6.0 and $^2J_{H,F}$ 54.0 Hz (ref. 6, Fig. 2).

Deacetylation[9] of compound **41** with NaOMe gave a quantitative yield of a key intermediate **12**, which was treated under Mukaiyama's conditions to give a mixture of products. Separation by chromatography on SiO_2 afforded a 19% yield



	X	Y	R^1	R^2
31	$OCH_2CH=CH_2$	H	H	H
32	$OCH_2CH=CH_2$	H	MCA	H
33	$OCH_2CH=CH_2$	H	MCA	Ac
34	OH	H	MCA	Ac
35	H	Cl	MCA	Ac
13	F	H	MCA	Ac

	X	Y	R^1	R^2
38	$OCH_2CH=CH_2$	H	MCA	Ac
39	OH	H	MCA	Ac
41	H	Cl	MCA	Ac
42	F	H	MCA	Ac
12	F	H	H	H

	R	R^2
42	MCA	Ac
43	H	Ac

Scheme 6

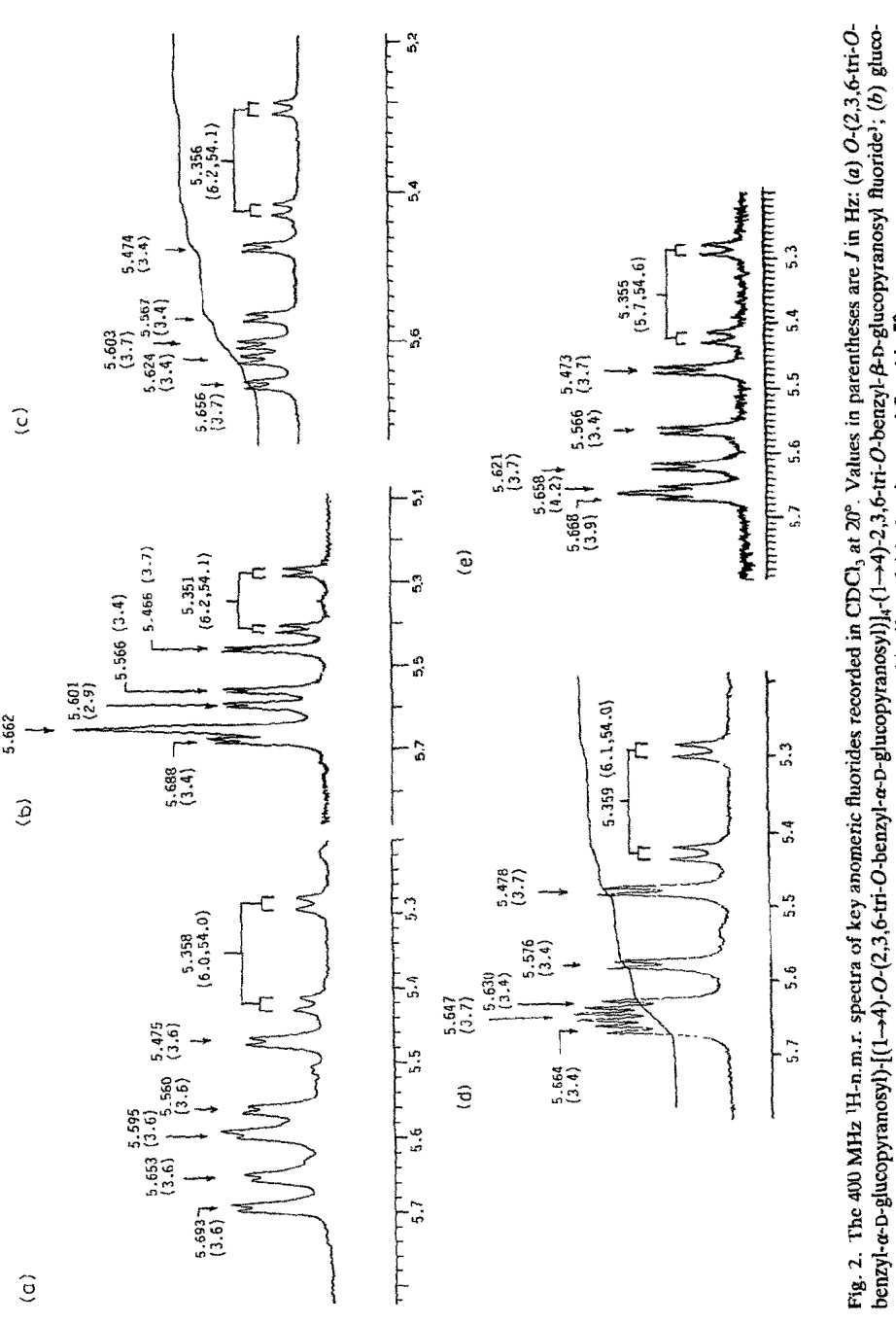


Fig. 2. The 400 MHz ^{1}H-n.m.r. spectra of key anomeric fluorides recorded in $CDCl_3$ at 20°. Values in parentheses are J in Hz: (*a*) *O*-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-[(1→4)-*O*-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)]$_4$-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranosyl fluoride[3]; (*b*) glucooctaosyl fluoride **3**; (*c*) glucohexaosyl fluoride **12**; (*d*) glucohexaosyl fluoride **49**, and (*e*) glucohexaosyl fluoride **50**.

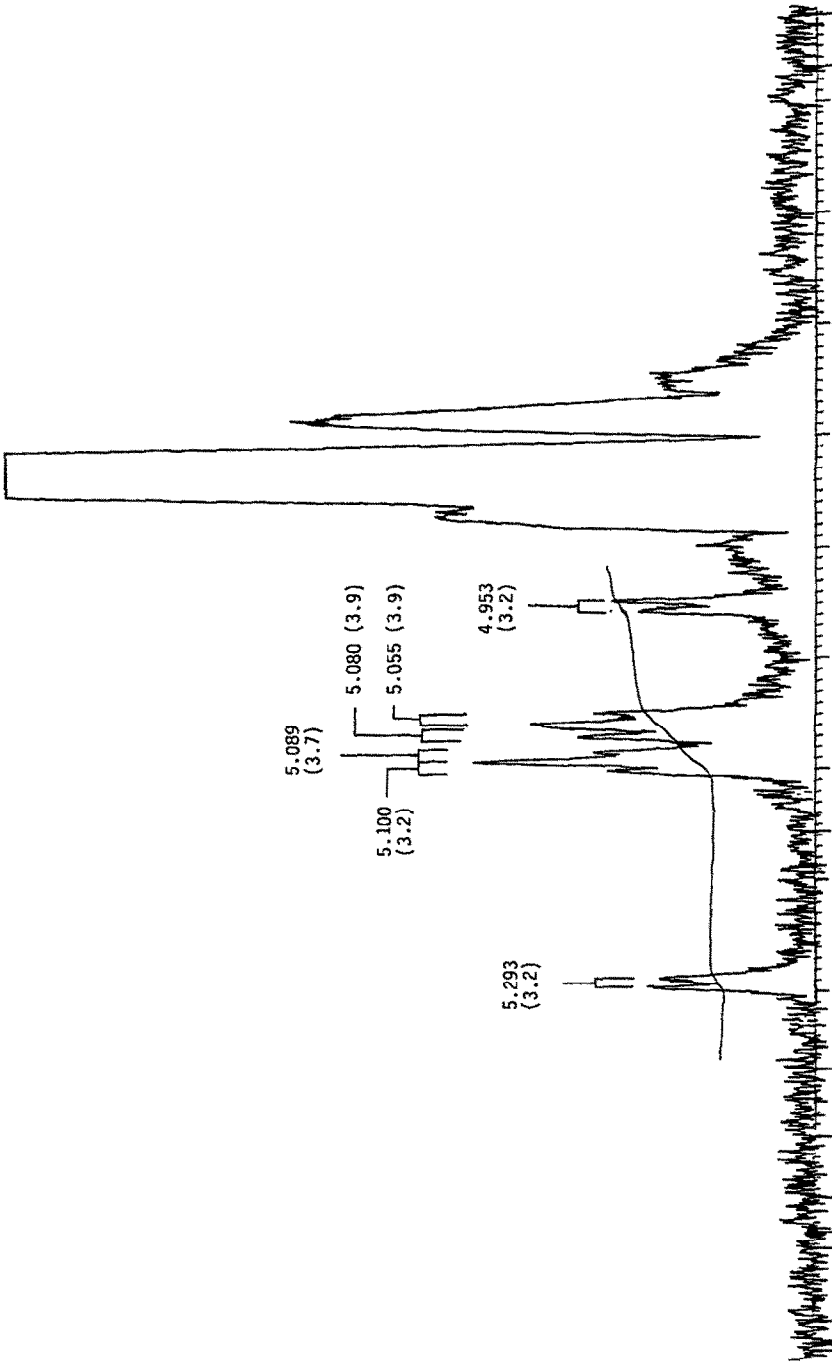
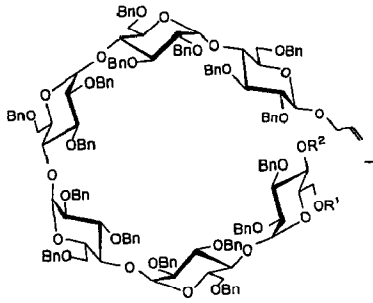


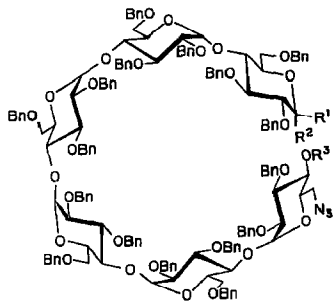
Fig. 3. The 400-MHz ^{1}H-n.m.r. spectrum of alpha-isocyclodextrin **11** recorded in D_2O at 20°. Values in parentheses are *J* in Hz.

of α-(1→4)-linked product **7** and a 47% yield of α-(1→6)-linked product **9**, together with a 14% yield of the 1,6-anhydro derivative **44**. The structure of compound **7** was confirmed by transformation into the perbenzyl derivative **8**, which was then shown to be identical to an authentic sample[1] through comparison of ^{1}H-n.m.r. data. The structure of the major product **9** was expected to be that of an α-(1→6) isomer of compound **7**. The assigned structure of compound **9** was confirmed by its conversion into the deprotected compound **11**. The ^{1}H-n.m.r. spectrum of compound **11** showed six doublets having $^3J_{H,H}$ ~3.5 Hz at δ 5.293, 5.100, 5.089, 5.066, 5.055, and 4.953, as shown in Fig. 3.

Having developed these synthetic routes to cyclomaltohexaose, cyclomaltooctaose, and an isomeric cyclomaltohexaose by intramolecular glycosylation, we now turned our efforts to developing an approach to such specifically substituted cyclooligoses as the azido-substituted cyclomaltohexaose **51**.

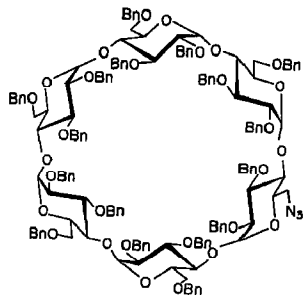
As the regioselectively protected glucohexaose derivative **38** had been prepared, conversion of compound **38** into a key intermediate **50** was quite straightforward. Treatment of compound **38** with thiourea[8] selectively removed the monochloroacetyl group to give the monoacetate **45** in 86% yield. Tosylation of compound **45** gave sulfonate **46** and a subsequent displacement reaction with sodium azide afforded the azido acetate **47** in 69% overall yield. Compound **47** was





45 $R^1 = H, R^2 = Ac$
46 $R^1 = Ts, R^2 = Ac$
47 $R^1 = N_3, R^2 = Ac$

	R^1	R^2	R^3
48	H	OH	Ac
49	F	H	Ac
50	F	H	H



Scheme 7 **51**

converted into the anomeric fluoride **49** in three steps as described previously in 48% overall yield: (*i*) $PdCl_2$–NaOAc, (*ii*) $SOCl_2$–DMF, and (*iii*) AgF–CH_3CN. The configuration at C-1a of compound **49** was assigned from ^{1}H-n.m.r. data (Fig. 2). Deacetylation of compound **49** afforded the key intermediate **50**. However, because of the scarcity of compound **50**, a preliminary experiment for the intramolecular glycosylation under Mukaiyama's conditions afforded only traces of products, and their structures await characterization.

In conclusion, a total synthesis of cyclomaltooctaose has been executed through intramolecular glycosylation of a key intermediate, the glucooctaosyl fluoride **3**. This intramolecular cyclization strategy was also shown to be applicable to the synthesis of an isomer (**11**) of cyclomaltohexaose.

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. Evaporations were conducted *in vacuo*. Column chromatography was performed on columns of 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 t.l.c. were performed on Silica Gel 60 F_{254} (Merck, Darmstadt); R_F values refer to high-performance t.l.c. unless otherwise indicated. Molecular sieves were purchased from Nakarai Chemicals, Ltd. I.r. spectra were recorded with an EPI-G2 Hitachi spectrophotometer, using KBr pellets for the crystalline samples, and films for the liquid samples. ^{1}H-N.m.r. spectra were recorded with either a JNM-GX400 or a JNM-FX90Q n.m.r. spectrometer. ^{13}C-N.m.r. spectra were recorded with a JNM-FX 100FT n.m.r. spectrometer operated at 25.05 MHz. The values of δ_C and δ_H are expressed in p.p.m. downfield from the signal for internal Me_4Si, for solutions in $CDCl_3$, unless noted otherwise. Values of δ_H (D_2O) are expressed in p.p.m. downward from $Me_3Si(CD_2)_2CO_2Na$. Values of δ_C (D_2O) are expressed in p.p.m. downfield from Me_4Si, by reference to internal standards of 1,4-dioxane (67.4) or MeOH (49.8).

Allyl O-*(4-*O-*acetyl-2,3,6-tri-*O-*benzyl-α-*D-*glucopyranosyl)-[(1→4)-*O-*(2,3,6-tri-*O-*benzyl-α-*D-*glucopyranosyl)]$_6$-(1→4)-2,3,6-tri-*O-*benzyl-β-*D-*glucopyranoside* (**4**), *the isomer* (**17**), *and their deprotected products* (**16** *and* **19**). — *A.* To a stirred mixture of compound **14** (615 mg, 230 μmol), $AgOSO_2CF_3$ (710 mg, 2.8 mmol), $SnCl_2$ (530 mg, 2.8 mmol), and powdered 4A molecular sieves (1.5 g) in $Cl(CH_2)_2Cl$ (3 mL), was added dropwise a solution of compound **6** (450 mg, 490 μmol) in $Cl(CH_2)_2Cl$ (1 mL) at 0° under Ar. After stirring for 3 h at 20°, 2 mL of $Cl(CH_2)_2Cl$ was distilled off and an additional solution of compound **6** (300 mg, 320 μmol) in $Cl(CH_2)_2Cl$ (1 mL), was added. The mixture was stirred for 16 h at 20°, diluted with EtOAc, and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated *in vacuo*.

Chromatography of the residue over SiO_2 in 15:1 toluene–EtOAc gave a fraction containing **4**, **17**, and **21**, and a fraction containing **20** (430 mg, 41%). A mixture of **4**, **17**, and **21** was resolved on a column of Bio Beads S-X4 (Bio-Rad) in benzene to give a mixture of **4** and **17**, and pure **21** (270 mg, 23%). The mixture of **4** and **17** was chromatographed over Lober LiChroprep size B in 15:1 toluene–EtOAc to give **4** (170 mg, 21%). Fractions containing **17** were submitted first to high-pressure liquid chromatography over Senshu Pak Silica 50-5, 10 × 250 mm (SSC Co.) in 4:1 hexane–THF and then chromatography over SiO_2 in 18:1 toluene–EtOAc to give pure **17** (44 mg, 5.3%).

Compound **4** had $[\alpha]_D$ +65.9° (*c* 0.4), R_F 0.58 in 7:1 toluene–EtOAc; n.m.r.: δ_C 169.4 (C=O), 134.3 (*C*H=CH_2), 117.2 (CH=*C*H_2), 102.6 (C-1a), 96.9, 96.6, and 96.1 (in a ratio of 1:1:5, C-1bcdefgh), 84.7 (C-3a), 82.1 (C-2a), 81.6 (C-3bcdefg), 79.6 and 79.4 (C-4abcdefg and C-3h), and 20.9 (CO*C*H_3).

Anal. Calc. for $C_{221}H_{232}O_{42}\cdot 0.5\ C_6H_5CH_3$: C, 75.21; H, 6.61. Found: C, 75.49; H, 6.58.

Compound **17** had $[\alpha]_D$ +60.5° (*c* 0.2), R_F 0.48 in 7:1 toluene–EtOAc; n.m.r.: δ_C 169.4 (C=O), 134.3 (*C*H=CH_2), 117.2 (CH=*C*H_2), 102.6 (C-1a), 102.2 (C-1g), 96.9, 96.6, 96.4, 96.3, and 96.1 (in a ratio of 2:1:1:1:1, C-1bcdefh), and 20.8 (CO*C*H_3).

Anal. Calc. for $C_{221}H_{232}O_{42}$: C, 74.56; H, 6.57. Found: C, 74.51; H, 6.57.

Compound **20** had R_F 0.20 in 7:1 toluene–EtOAc. Compound **21** had R_F 0.48 in 7:1 toluene–EtOAc. Compounds **20** and **21** were identified by comparison with authentic samples[1].

B. To a stirred mixture of compound **22** (100 mg, 60 μmol), $AgOSO_2CF_3$ (50 mg, 200 μmol), $SnCl_2$ (40 mg, 200 μmol), and powdered 4A molecular sieves (100 mg) in $Cl(CH_2)_2Cl$ (0.5 mL) was added a solution of compound **23** (100 mg, 60 μmol) in $Cl(CH_2)_2Cl$ (0.5 mL) at 0° under Ar. The mixture was stirred for 19 h at 20° and processed as in *A*. Chromatography of the products over SiO_2 in 20:1 toluene–EtOAc afforded an inseparable 3:1 mixture (54 mg, 27%) of **4** and **24**, and **25** (27 mg, 29%).

Compound **4**, R_F 0.58 in 7:1 toluene–EtOAc, was identified by comparison with an authentic sample by t.l.c. Compound **24**, R_F 0.54 in 7:1 toluene–EtOAc, was presumed to be the β anomer. Compound **25**, R_F 0.29 in 7:1 toluene–EtOAc, was identified by comparison with an authentic sample by ^{1}H-n.m.r. spectroscopy[1].

A solution of compound **4** (18 mg, 5 μmol) in 1:1 MeOH–THF (0.4 mL) containing 0.5M NaOMe–MeOH (10 μL) was stirred for 19 h at 20°, and evaporated. Chromatography of the residue over SiO_2 in 16:1 toluene–EtOAc gave **15** (14.5 mg, 81%), R_F 0.50 in 7:1 toluene–EtOAc.

A mixture of compound **15** (14.5 mg), 10% Pd–C (20 mg), and HCO_2H (50 μL) in 2:2:1 MeOH–THF–H_2O (0.5 mL) was stirred for 1 h at 50° under Ar, and filtered through Celite. Work-up and chromatography over Sephadex G-25 in H_2O gave a quantitative yield of *propyl* O-α-D-*glucopyranosyl*-[*(1→4)*-O-α-D-*glucopyranosyl*]$_6$-*(1→4)*-β-D-*glucopyranoside* (**16**), R_F 0.56 in 2:2:1 BuOH–MeOH–

H_2O, n.m.r.: δ_H (D_2O) 5.419 (d, 7 H, *J* 2.8 Hz, H-1bcdefgh), 4.488 (d, 1 H, *J* 8.2 Hz, H-1a), 3.429 (t, 1 H, *J* 9.3 Hz, H-4a), 3.301 (t, 1 H, *J* 8.7 Hz, H-2a), and 0.924 (t, 3 H, *J* 7.3 Hz, CH_2CH_3).

A solution of compound **17** (23 mg, 6 μmol) in 1:1 MeOH–THF (0.4 mL) containing 0.5M NaOMe–MeOH (10 μL) was stirred for 19 h at 20°. Work-up and purification as for **15** afforded **18** (18 mg, 81%), R_F 0.40 in 7:1 toluene–EtOAc. A mixture of **18** (18 mg), 10% Pd–C (18 mg), and HCO_2H (5 μL) in 2:2:1 MeOH–THF–H_2O (0.5 mL) was stirred for 1 h at 50° under Ar. Work-up and purification as for **16** afforded *propyl* O-*α*-D-*glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl*-[*(1→4)*-*α*-D-*glucopyranosyl*]$_5$-*(1→4)*-O-*β*-D-*glucopyranoside* **19** (quantitative), R_F 0.55 in 2:2:1 BuOH–MeOH–H_2O; n.m.r.: δ_H (D_2O) 5.424 (d, 3 H, *J* 2.8 Hz) and 5.416 (d, 3 H, *J* 3.4 Hz, H-1bcdefh), 4.539 (d, 1 H, *J* 7.9 Hz, H-1g), 4.488 (d, 1 H, *J* 7.9 Hz, H-1a), 3.423 (t, 2 H, *J* 9.3 Hz, H-4ag), 3.358 (t, 1 H, *J* 9.5 Hz, H-2g), 3.300 (t, 1 H, *J* 8.5 Hz, H-2a), and 0.925 (t, 3 H, *J* 7.4 Hz, CH_2CH_3).

O-*(4-O-Acetyl-2,3,6-tri-O-benzyl-α-D-glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri-O-benzyl-α-D-glucopyranosyl*]$_6$-*(1→4)-2,3,6-tri-O-benzyl-D-glucopyranose* (**26**). — A mixture of compound **4** (148 mg, 42 μmol), $PdCl_2$ (75 mg, 420 μmol), and NaOAc (85 mg, 1 mmol) in 19:1 AcOH–H_2O (10 mL) was stirred for 3 h at 50°, filtered through Celite, and the filtrate evaporated. A solution of the residue in EtOAc was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 20:1 toluene–EtOAc afforded **26** (103 mg, 71%), $[\alpha]_D$ +76.4° (*c* 0.1); R_F 0.34 and 0.24 (t.l.c. in 8:1 toluene–EtOAc); n.m.r.: δ_C 169.4 (C=O), 96.9 and 96.1 (in a ratio of 2:5, 7 anomeric C).

Anal. Calc. for $C_{218}H_{228}O_{42}\cdot C_6H_5CH_3$: C, 74.81; H, 6.59. Found: C, 74.94; H, 6.56.

O-*(4-O-Acetyl-2,3,6-tri-O-benzyl-α-D-glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri-O-benzyl-α-D-glucopyranosyl)*]$_6$-*(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranosyl fluoride* (**27**). — A mixture of compound **26** (89 mg, 25 μmol), $SOCl_2$ (20 μL, 180 μmol) and trace of DMF in $Cl(CH_2)_2Cl$ (2 mL) was stirred for 16 h at 20°, and filtered through a thin bed of SiO_2. The filtrate was evaporated. A mixture of the residue and AgF (18 mg, 150 μmol) in CH_3CN (2 mL) was stirred for 16 h at 20°, diluted with EtOAc, and filtered through Celite. The filtrate was washed with aq. NaCl, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 40:1 toluene–EtOAc afforded **27** (59 mg, 66%), $[\alpha]_D$ +79.0° (*c* 0.1), R_F 0.50 in 8:1 toluene–EtOAc; n.m.r.: δ_H 5.667 (d, 3 H, *J* 3.4 Hz), 5.646 (d, 1 H, *J* 3.6 Hz), 5.621 (d, 1 H, *J* 3.7 Hz), 5.571 (d, 1 H, *J* 3.4 Hz), and 5.469 (d, 1 H, *J* 3.7 Hz, H-1bcdefgh), 5.353 (dd, 1 H, *J* 5.8 and 54.4 Hz, H-1a), 5.089 (t, 1 H, *J* 8.2 Hz, H-4h), and 1.782 (s, 3 H, Ac); δ_C 169.3 (C=O), 109.6 ($^1J_{CF}$ 219 Hz, C-1a), 96.8 and 96.1 (in a ratio of 2:5, C-1bcdefgh), and 20.8 ($COCH_3$).

Anal. Calc. for $C_{218}H_{227}O_{41}F$: C, 74.34; H, 6.50. Found: C, 74.08; H, 6.47.

O-*(2,3,6-Tri-O-benzyl-α-D-glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri-O-benzyl-α-D-glucopyranosyl)*]$_6$-*(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranosyl fluoride* (**3**). — A solution of compound **27** (26 mg, 8 μmol) in 1:1 THF–MeOH (0.4 mL, dried

over activated 4A molecular sieves) containing a trace of NaOMe was stirred for 8 h at 20° and for 10 min at 50°. Evaporation and chromatography of the residue over SiO_2 in 20:1 toluene–EtOAc afforded **3** (24 mg, 92%), $[\alpha]_D$ +67.2° (*c* 0.1), R_F 0.42 (t.l.c. in 8:1 toluene–EtOAc); n.m.r.: δ_H 5.688 (d, 1 H, *J* 3.4 Hz), 5.662 (bs, 3 H), 5.601 (d, 1 H, *J* 2.9 Hz), 5.566 (d, 1 H, *J* 3.4 Hz), and 5.466 (d, 1 H, *J* 3.7 Hz, H-1bcdefgh), and 5.351 (dd, 1 H, *J* 6.2 and 54.1 Hz, H-1a).

Anal. Calc. for $C_{216}H_{225}O_{40}$: C, 74.55; H, 6.52. Found: C, 74.59; H, 6.66.

Octakis(2,3,6-tri-O-benzyl)-gamma-cyclodextrin (**2**) *and gamma-cyclodextrin* (**1**). — *A.* To a stirred mixture of $AgOSO_2CF_3$ (7 mg, 30 μmol), $SnCl_2$ (5 mg, 3 μmol), and powdered 4A molecular sieves (100 mg) in Et_2O (3 mL) was added dropwise a solution of compound **3** (24 mg, 7 μmol) in $Cl(CH_2)_2Cl$ (0.7 mL) during 25 min at 0°. The mixture was stirred for 16 h at 20°, diluted with EtOAc, and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue twice over SiO_2 in 20:1 toluene–EtOAc afforded **2** (2.0 mg, 8.4%), **28** (4.2 mg, 17.5%), **29** (2.3 mg, 10%), and **30** (5.8 mg, 24%).

Compound **2** had R_F 0.54 in 8:1 toluene–EtOAc; n.m.r.: δ_H 5.183 (d, 1 H, *J* 3.4 Hz, H-1a), 5.113 (d, 1 H, *J* 10.7 Hz, C*H*Ph), 4.743 (d, 1 H, *J* 10.7 Hz, C*H*Ph), 4.487 (d, 1 H, *J* 12.3 Hz, C*H*Ph), 4.433 (d, 1 H, *J* 12.3 Hz, C*H*Ph), 4.352 (d, 1 H, *J* 12.2 Hz, C*H*Ph), 4.306 (d, 1 H, *J* 12.2 Hz, C*H*Ph), 3.990 (t, 1 H, *J* 8.7 Hz, H-3), 3.917 (t, 1 H, *J* 8.9 Hz, H-4), 3.905 (dd, 1 H, *J* 4.9 and 11.0 Hz, H-6), 3.854 (bd, 1 H, *J* 10.0 Hz, H-5), 3.456 (d, 1 H, *J* 9.8 Hz, H-6′), and 3.452 (dd, 1 H, *J* 3.2 and 9.8 Hz, H-2).

Compound **28** had R_F 0.36 in 8:1 toluene–EtOAc; n.m.r.: δ_H 6.357 (s, 1 H, H-1a), 5.690 (d, 1 H, *J* 3.4 Hz, H-1), 5.666 (d, 3 H, *J* 3.4 Hz, H-1 × 3), 5.635 (d, 1 H, *J* 3.4 Hz, H-1), 5.603 (d, 1 H, *J* 3.4 Hz, H-1) and 5.162 (d, 1 H, *J* 3.4 Hz, H-1b).

Compound **29** had R_F 0.19 in 8:1 toluene–EtOAc; n.m.r.: δ_H 5.690 (d, 1 H, *J* 3.4 Hz, H-1), 5.661 (bs, 2 H, H-1 × 2), 5.633 (d, 1 H, *J* 3.4 Hz, H-1), 5.599 (d, 1 H, *J* 3.4 Hz, H-1), 5.566 (d, 1 H, *J* 3.4 Hz, H-1), 5.478 (s, 1 H, H-1a), and 5.001 (d, 1 H, *J* 3.4 Hz, H-1b).

Compound **30** had R_F 0.08 and 0.09 in 8:1 toluene–EtOAc; n.m.r.: δ_H 5.688 (d, 1 H, *J* 3.4 Hz), 5.660 (bs, 3 H), 5.603 (bs, 2 H), 5.508 (d, 1 H, *J* 3.4 Hz) for 7 anomeric protons, and 5.217 (d, 0.7 H, *J* 3.4 Hz, H-1aα).

B. To a stirred suspension of NaH (50%, 240 mg, 5 mmol) in DMF (3 mL) was added natural gamma-cyclodextrin (200 mg, 150 μmol) and the mixture was stirred for 30 min at 20°. To this mixture was added $PhCH_2Br$ (590 μL, 5 mmol) at 0°. The mixture was stirred for 30 min at 0°, and for 2.5 h at 20°. After the excess of NaH had been decomposed with MeOH, the mixture was evaporated. A solution of the residue in EtOAc was washed with H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 30:1 toluene–EtOAc afforded **2** (222 mg, 42%), $[\alpha]_D$ +36.8° (*c* 0.2).

Anal. Calc. for $C_{216}H_{224}O_{40}$: C, 75.00; H, 6.53. Found: C, 74.76; H, 6.53.

A mixture of compound **2** (29 mg, 3 μmol, prepared by method *B*), 10% Pd–C (20 mg), and HCO_2H (50 μL) in 2:2:1 THF–MeOH–H_2O (0.5 mL) was stirred for 1 h at 50°, and filtered through Celite. The filtrate was evaporated and the residue purified by chromatography over Sephadex G-25 in H_2O to give gamma-cyclodextrin (**1**, 7 mg, 63%), R_F 0.49 in 2:2:1 BuOH–MeOH–H_2O; n.m.r.: δ_H (D_2O) 5.117 (d, 1 H, *J* 3.9 Hz, H-1). δ_C (D_2O) 102.3 (C-1), 81.4 (C-4), 73.7 (C-2), 73.1 (C-3), 72.6 (C-5) and 61.0 (C-6).

Allyl O-*(2,3-di-*O*-benzyl-6-*O*-monochloroacetyl-α-*D*-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**32**). — To a solution of compound **31** (12.0 g, 14 mmol) in $Cl(CH_2)_2Cl$ (150 mL) containing pyridine (4.6 mL, 60 mmol) was added dropwise a solution of $(ClCH_2CO)_2O$ (2.71 g, 16 mmol) in $Cl(CH_2)_2Cl$ (50 mL) during 30 min at −5 to 0°. The mixture was stirred for 1 h at 20°, diluted with EtOAc, washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 40:1 toluene–EtOAc afforded **32** (7.4 g, 56%) and its 4′,6′-di-*O*-monochloroacetyl derivative (2.6 g, 19%).

Compound **32** had $[\alpha]_D$ +20.8° (*c* 0.1), R_F 0.43 in 5:1 toluene–EtOAc; n.m.r.: δ_C 167.4 ($COCH_2Cl$), 134.2 ($CH=CH_2$), 117.3 ($CH=CH_2$), 102.6 (C-1a), 96.4 (C-1b), 84.7 (C-3a), 82.1 (C-2a), 81.0 (C-4a), 65.0 (C-6b), and 40.7 ($COCH_2Cl$).

Anal. Calc. for $C_{52}H_{57}ClO_{12}\cdot 0.2\ C_6H_5CH_3$: C, 68.67; H, 6.31. Found: C, 69.16; H, 6.38.

The 4′,6′-di-*O*-monochloroacetyl derivative had $[\alpha]_D$ +21.1° (*c* 0.5), R_F 0.67 in 5:1 toluene–EtOAc; n.m.r.: δ_C 166.9 ($COCH_2Cl$), 166.1 ($COCH_2Cl$), 134.0 ($CH=CH_2$), 117.3 ($CH=CH_2$), 102.6 (C-1a), 96.2 (C-1b), 84.4 (C-3a), 82.0 (C-2a), 79.3 (C-4a), 63.8 (C-6b), 40.5 ($COCH_2Cl$), and 40.4 ($COCH_2Cl$).

Anal. Calc. for $C_{54}H_{58}O_{13}Cl_2$: C, 66.87; H, 6.03. Found: C, 66.90; H, 6.09.

Allyl O-*(4-*O*-acetyl-2,3-di-*O*-benzyl-6-*O*-monochloroacetyl-α-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**33**). — A solution of compound **32** (8.0 g, 8.8 mmol) in pyridine (20 mL) and Ac_2O (10 mL) was stirred for 4 h at 20° and evaporated. A solution of the residue in EtOAc (50 mL) was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue in 20:1 toluene–EtOAc afforded **33** (7.5 g, 90%), $[\alpha]_D$ +23.8° (*c* 0.2), R_F 0.32 (t.l.c. in 8:1 toluene–EtOAc); n.m.r.: δ_C 169.5 ($COCH_3$), 166.9 ($COCH_2Cl$), 134.0 ($CH=CH_2$), 117.3 ($CH=CH_2$), 102.6 (C-1a), 96.3 (C-1b), 84.5 (C-3a), 82.0 (C-2a), 79.3 (C-4a), 63.9 (C-6b), 40.6 ($COCH_2Cl$), and 20.7 ($COCH_3$).

Anal. Calc. for $C_{54}H_{59}ClO_{13}$: C, 68.17; H, 6.25. Found: C, 68.08; H, 6.21.

O-*(4-*O*-Acetyl-2,3-di-*O*-benzyl-6-*O*-monochloroacetyl-α-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-*D*-glucopyranose* (**34**). — A mixture of compound **33** (1.88 g, 2.0 mmol), $PdCl_2$ (1.75 g, 9.9 mmol), and NaOAc (1.75 g, 21 mmol) in 19:1 AcOH–H_2O (20 mL) was stirred for 2 h at 50° and filtered through Celite. The filtrate was evaporated. A solution of the residue in EtOAc (50 mL) was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 10:1 toluene–EtOAc afforded **34** (1.54 g, 86%), $[\alpha]_D$ +31.2°

(*c* 0.5); R_F 0.28 and 0.21 in 8:1 toluene–EtOAc; n.m.r.: δ_H 3.999 (s, 2 H, $COCH_2Cl$), and 1.915 (s, 3 H, $COCH_3$); δ_C 169.3 ($COCH_3$), 166.8 ($COCH_2Cl$), 97.3 (C-1aβ), 96.4 (C-1bβ), 96.2 (C-1bα), 90.5 (C-1aα), 63.8 (C-6b), 40.4 ($COCH_2Cl$), and 20.5 ($COCH_3$).

Anal. Calc. for $C_{51}H_{55}ClO_{13}$: C, 67.21; H, 6.08. Found: C, 67.26; H, 6.08.

O-(4-O-Acetyl-2,3-di-O-benzyl-6-O-monochloroacetyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**13**). — To a solution of compound **34** (5.68 g, 6.0 mmol) in $Cl(CH_2)_2Cl$ (15 mL) containing a trace of DMF was added dropwise $SOCl_2$ (3.42 mL, 31.2 mmol). The mixture was stirred for 19 h at 20° and filtered through a bed of silica gel. The filtrate was evaporated. To a solution of the residue (**35**) in CH_3CN (20 mL) was added AgF (2.37 g, 18.7 mmol) and the mixture was stirred for 16 h at 20°, filtered through Celite, and the filtrate evaporated. Chromatography of the residue over SiO_2 in 20:1 toluene–EtOAc afforded **13** (4.57 g, 81%), $[\alpha]_D$ +39.2° (*c* 0.9), R_F 0.42 in 7:1 toluene–EtOAc; n.m.r.: δ_H 7.40–7.10 (m, 25 H, aromatic), 5.493 (d, 1 H, *J* 3.5 Hz, H-1b), 5.430 (dd, 1 H, *J* 5.6 and 53.6 Hz, H-1a), 4.002 (s, 2 H, $COCH_2Cl$), and 1.915 (s, 3 H, $COCH_3$); δ_C 169.3 ($COCH_3$), 166.8 ($COCH_2Cl$), 109.0 ($^1J_{C,F}$ 218.5 Hz, C-1a), 96.3 (C-1b), 82.4 ($^3J_{C,F}$ 7.3 Hz, C-3a), 79.8 ($^2J_{C,F}$ 25.6 Hz, C-2a), 79.3 (C-4a), 63.8 (C-6b), 40.8 ($COCH_2Cl$), and 20.5 ($COCH_3$).

Anal. Calc. for $C_{51}H_{54}ClFO_{12}$: C, 67.06; H, 5.96. Found: C, 67.18; H, 5.93.

Allyl O-(4-O-acetyl-2,3-di-O-benzyl-6-O-monochloroacetyl-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**38**), *allyl O-(4-O-acetyl-2,3-di-O-benzyl-6-O-monochloroacetyl-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-benzyl-β-D-glucopyranosyl-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl]$_3$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside* (**42**), *and the conversion of* **42** *into* **43**. — To a stirred mixture of $AgOSO_2CF_3$ (430 mg, 1.67 mmol), $SnCl_2$ (320 mg, 1.69 mmol), compound **22** (500 mg, 280 μmol), and powdered 4A molecular sieves (3 g) in $Cl(CH_2)_2Cl$ (5 mL) was added a solution of compound **13** (500 mg, 550 μmol) in $Cl(CH_2)_2Cl$ (1.5 mL) at 0°. After stirring for 16 h at 20°, additional solution of compound **13** (500 mg, 550 μmol) in $Cl(CH_2)_2Cl$ (1.5 mL) was added and the mixture was stirred for 19 h at 20°. After filtration through Celite, the filtrate was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 10:1 toluene–EtOAc afforded compound **37** (418 mg, 48%), and a mixture of other products that was passed through a column of Biobeads S-X4 in benzene to give compound **36** (270 mg, 28%) and a mixture of compounds **38**, **42**, and unreacted **22**. This mixture was chromatographed over Lobar LiChroprep size C in 10:1 toluene–EtOAc to give **38** (130 mg, 18%), and a mixture (200 mg) of **42** and **22** which was purified after removal of the monochloroacetyl group in the succeeding experiment. Compound **36** had R_F 0.36 in 7:1 toluene–EtOAc; n.m.r. data: δ_H 6.305 (s, 1 H, H-1a), 5.029 (d, 1 H, *J* 3.7 Hz, H-1b), and 1.946 (s, 3 H, $COCH_3$); δ_C 169.7 ($COCH_3$), 167.2 ($COCH_2Cl$), 97.0 (C-1b), 64.2 (C-6b), 40.8 ($COCH_2Cl$), and 20.8 ($COCH_3$).

Compound **37** had R_F 0.11 in 7:1 toluene–EtOAc; δ_H 5.492 (s, 1 H, H-1a), 4.894 (d, 1 H, *J* 3.7 Hz, H-1b), and 1.928 (s, 3 H, $COCH_3$).

Compound **38** had $[\alpha]_D$ +60.4° (*c* 0.2), R_F 0.42 in 7:1 toluene–EtOAc; n.m.r.: δ_C 169.5 ($COCH_3$), 167.0 ($COCH_2Cl$), 134.2 ($CH=CH_2$), 117.1 ($CH=CH_2$), 102.6 (C-1a), 96.4 (C-1 × 2), 96.3 (C-1), 96.1 (C-1 × 2), 84.7 (C-3a), 82.1 (C-2a), 81.5 (C-3bcde), 79.7 and 79.4 (C-3f and C-4abcde), 63.8 (C-6f), 40.7 ($COCH_2Cl$), and 20.8 ($COCH_3$).

Anal. Calc. for $C_{162}H_{171}ClO_{33}$: C, 72.56; H, 6.43. Found: C, 72.67; H, 6.40.

Compound **42** (60 mg, 8.2% calculated from the following experimental result) had R_F 0.39 in 7:1 toluene–EtOAc.

To a solution of a mixture of compounds **22** and **42** (200 mg) in 1:1 EtOH–THF (4 mL) containing pyridine (20 μL, 300 μmol) was added NH_2CSNH_2 (20 mg, 300 μmol). The mixture was stirred for 19 h at 70°, and evaporated. The residue was dissolved in $CHCl_3$ and filtered. The filtrate was evaporated. Chromatography of the residue over SiO_2 in 10:1 toluene–EtOAc afforded *allyl* O-*(4-O-acetyl-2,3-di-O-benzyl-α-*D-*glucopyranosyl)-(1→4)-*O-*(2,3,6-tri-O-benzyl-β-*D-*glucopyranosyl)-[(1→4)-*O-*(2,3,6-tri-O-benzyl-α-*D-*glucopyranosyl)]$_3$-(1→4)-2,3,6-tri-O-benzyl-β-*D-*glucopyranoside* **43** (58 mg) and recovered **22** (100 mg).

Compound **43** had R_F 0.26 in 5:1 toluene–EtOAc; n.m.r.: δ_C 170.7 ($COCH_3$), 134.2 ($CH=CH_2$), 117.2 ($CH=CH_2$), 102.6 (C-1a), 102.1 (C-1e), 96.7, 96.5, 96.4, 96.2 (C-1bcdf), 84.6 (C-3ae), 61.3 (C-6f), and 20.8 ($COCH_3$).

O-*(4-O-Acetyl-2,3-di-O-benzyl-6-O-monochloroacetyl-α-*D-*glucopyranosyl)-[(1→4)-*O-*(2,3,6-tri-O-benzyl-α-*D-*glucopyranosyl]$_4$-(1→4)-2,3,6-tri-O-benzyl-*D-*glucopyranose* (**39**). — A mixture of compound **38** (32 mg, 12 μmol), $PdCl_2$ (10 mg, 60 μmol), and NaOAc (10 mg, 120 μmol) in 19:1 AcOH–H_2O (0.5 mL) was stirred for 1.5 h at 50°, diluted with EtOAc (50 mL), and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 12:1 toluene–EtOAc gave **39** (20 mg, 66%), $[\alpha]_D$ +56.8° (*c* 0.1), R_F 0.26 and 0.29 in 7:1 toluene–EtOAc; n.m.r.: δ_C 169.4 ($COCH_3$), 167.0 ($COCH_2Cl$), 97.5 (C-1aβ), 96.8 (C-1), 96.1 (C-1 × 2), 95.9 (C-1 × 2), 63.7 (C-6f), 40.7 ($COCH_2Cl$), and 20.8 ($COCH_3$).

Anal. Calc. for $C_{152}H_{160}ClO_{33}$: C, 69.62; H, 6.45. Found: C, 69.38; H, 6.16.

O-*(4-O-Acetyl-2,3-di-O-benzyl-6-O-monochloroacetyl-α-*D-*glucopyranosyl-[(1→4)-*O-*(2,3,6-tri-O-benzyl-α-*D-*glucopyranosyl]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-*D-*glucopyranosyl fluoride* (**41**). — To a solution of compound **39** (17 mg, 6 μmol) in $Cl(CH_2)_2Cl$ (0.2 mL) was added $SOCl_2$ (3 μL, 30 μmol) and trace of DMF, and the mixture was stirred for 19 h at 20°. After dilution with $Cl(CH_2)_2Cl$ (5 mL), the mixture was filtered through a bed of SiO_2 and the filtrate was evaporated. To a solution of the residue (**40**) in CH_3CN (0.5 mL) was added AgF (5 mg, 40 μmol), and the mixture was stirred for 16 h at 20° in the dark. After filtration through Celite, the filtrate was evaporated. Chromatography of the residue over SiO_2 in 12:1 toluene–EtOAc afforded **41** (14 mg, 84%), $[\alpha]_D$ +71.3° (*c* 0.1), R_F 0.55 in 7:1 toluene–EtOAc; n.m.r.: δ_H 5.655 (d, 1 H, *J* 3.6 Hz, H-1), 5.636 (d, 1 H,

J 3.6 Hz, H-1), 5.615 (d, 1 H, *J* 3.6 Hz, H-1), 5.571 (d, 1 H, *J* 3.7 Hz, H-1), 5.475 (d, 1 H, *J* 3.7 Hz, H-1), 5.357 (dd, 1 H, *J* 6.0 and 54.0 Hz, H-1a), and 1.902 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{159}H_{166}ClFO_{32}$: C, 72.24; H, 6.33. Found: C, 72.07; H, 6.29.

O-*(2,3-Di*-O-*benzyl*-α-D-*glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri*-O-*benzyl*-α-D-*glucopyranosyl)*]$_4$-*(1→4)-2,3,6-tri*-O-*benzyl*-β-D-*glucopyranosyl fluoride* (**12**), *cyclization of* **12** *into* **7** *and* **9**, *and transformation of* **7** *and* **9** *into* **8** *and* **11**. — To a solution of compound **41** (12 mg, 4.8 μmol) in 1:1 THF–MeOH (0.4 mL, dried over activated 4A molecular sieves was added 0.7M NaOMe–MeOH (3 μL). The mixture was stirred for 19 h at 20° and evaporated. Chromatography of the residue over SiO_2 in 5:1 toluene–EtOAc afforded a quantitative yield of **12**, $[\alpha]_D$ +65.5° (*c 0.1*), R_F 0.58 (t.l.c. in 2:1 toluene–EtOAc); n.m.r.: δ_H 5.656 (d, 1 H, *J* 3.7 Hz, H-1), 5.624 (d, 1 H, *J* 3.4 Hz, H-1), 5.603 (d, 1 H, *J* 3.7 Hz, H-1), 5.567 (d, 1 H, *J* 3.4 Hz, H-1), 5.474 (d, 1 H, *J* 3.4 Hz, H-1), and 5.356 (dd, 1 H, *J* 6.2 and 54.1 Hz, H-1a).

Anal. Calc. for $C_{155}H_{163}FO_{30}$: C, 73.73; H, 6.51. Found: C, 74.02; H, 6.69.

To a stirred mixture of $AgOSO_2CF_3$ (10 mg, 40 μmol), $SnCl_2$ (10 mg, 50 μmol), and powdered 4A molecular sieves (60 mg) in $Cl(CH_2)_2Cl$ (0.3 mL) was added dropwise a solution of compound **12** (10.2 mg, 4 μmol) in $Cl(CH_2)_2Cl$ (0.4 mL) during 5 min at −5° under Ar. The mixture was stirred for 1 h at −5 to 0°, diluted with EtOAc (5 mL), and filtered through Celite. The filtrate was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 20:1, and then in 2:1, toluene–EtOAc afforded *cyclo*{*→4)*-O-*(2,3-di*-O-*benzyl*-α-D-*glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri*-O-*benzyl*-α-D-*glucopyranosyl)*]$_5$-*(1-)*} (**7**, 1.9 mg, 19%), *cyclo*{*→6)*-O-*(2,3-di*-O-*benzyl*-α-D-*glucopyranosyl)*-[*(1→4)*-O-*(2,3,6-tri*-O-*benzyl*-α-D-*glucopyranosyl)*]$_5$-*(1-)*} (**9**, 4.7 mg, 47%), and compound **44** (1.4 mg, 14%).

Compound **7** had $[\alpha]_D$ +17.7° (*c* 0.09), R_F 0.31 in 7:1 toluene–EtOAc; n.m.r.: δ_H 5.484 (d, 1 H, *J* 3.6 Hz, H-1), 5.459 (d, 1 H, *J* 3.3 Hz, H-1), 5.358 (d, 1 H, *J* 10.8 Hz, CH_2Ph), 5.309 (d, 1 H, *J* 10.8 Hz, CH_2Ph), 5.194 (d, 1 H, *J* 10.8 Hz, CH_2Ph), 5.153 (d, 1 H, *J* 10.8 Hz, CH_2Ph), 4.672 (d, 1 H, *J* 4.4 Hz, H-1), and 4.643 (d, 1 H, *J* 4.4 Hz, H-1).

Compound **9** had $[\alpha]_D$ +33.5° (*c* 0.1), R_F 0.48 in 7:1 toluene–EtOAc; n.m.r.: δ_H 5.377 (d, 1 H, *J* 11.0 Hz, CH_2Ph), 5.276 (d, 1 H, *J* 11.0 Hz, CH_2Ph), 5.217 (d, 1 H, *J* 3.7 Hz, H-1), 5.190 (d, 1 H, *J* 3.7 Hz, H-1), 5.080 (d, 1 H, *J* 3.4 Hz, H-1), 4.879 (d, 1 H, *J* 3.2 Hz, H-1), 4.745 (d, 1 H, *J* 3.7 Hz, H-1*), and 4.719 (d, 1 H, *J* 3.7 Hz, H-1*). The acetate **10** of compound **9** was prepared by treatment of **9** with pyridine–Ac_2O–DMAP for 24 h at 20°; R_F 0.55 in 7:1 toluene–EtOAc; n.m.r.: δ_H 1.901 (s, 3 H, $COCH_3$).

*These assignments are tentative.

Compound **44** had R_F 0 05 in 7.1 toluene–EtOAc, n m r · δ_H 5 628 (d, 1 H, *J* 3 7 Hz, H-1), 5 619 (d, 1 H, *J* 3 7 Hz, H-1), 5 599 (d, 1 H, *J* 3.7 Hz, H-1), 5 561 (d, 1 H, *J* 3.4 Hz, H-1), 5.479 (s, 1 H, H-1a), and 5 015 (d, 1 H, *J* 2.5 Hz, H-1b)

To a stirred solution of compound **7** (1.7 mg, 0 7 μmol) in DMF (0.1 mL) was added NaH (50%, 2 mg, 40 μmol) and benzyl bromide (1 μL, 8 μmol) The mixture was stirred for 16 h at 20° and excess NaH was decomposed with MeOH Conventional processing and chromatography over SiO_2 in 14 1 toluene–EtOAc gave *hexakis(2,3,6-tri-O-benzyl)-cyclomaltohexaose* (**8**, 0 9 mg, 51%). The 400-MHz ^{1}H-n.m r data of **8** were completely identical with those of authentic[1] **8**.

A mixture of compound **9** (3 mg, 1 2 μmol), 10% Pd–C (8 mg), and HCO_2H (40 μL) in 4 4:1 MeOH–THF–H_2O (0.45 mL) was stirred for 1 h at 60° under Ar After diluting with same solvent, the mixture was filtered through Celite and the filtrate was evaporated Chromatography of the residue over Sephadex G-25 in H_2O afforded *cyclo{→6)-O-α-D-glucopyranosyl-[(1→4)-O-α-D-glucopyranosyl]$_5$-(1-)}* (**11**, 1 mg, 86%), $[\alpha]_D$ +81° (*c* 0 05, H_2O), R_F 0 50 in 2:2:1 BuOH–MeOH–H_2O, n m.r . δ_H (D_2O) 5.293 (d, 1 H, *J* 3 2 Hz), 5.100 (d, 1 H, *J* 3 2 Hz), 5 089 (d, 1 H, *J* 3 7 Hz), 5.066 (d, 1 H, *J* 3 7 Hz), 5 055 (d, 1 H, *J* 3 9 Hz), and 4 953 (d, 1 H, *J* 3 2 Hz) for 6 anomeric protons

The peracetate of compound **11** was prepared by conventional treatment with pyridine–Ac_2O–DMAP for 2 days at 20°, R_F 0 51 in EtOAc, n.m r.· δ_H 2.177, 2 167, 2.158 (s, 3 H, Ac × 3), 2.136 (s, 6 H, Ac × 2), 2 126 (s, 6 H, Ac × 2), 2 117 (s, 9 H, Ac × 3), 2 112, 2 087 (s, 3 H, Ac × 2), 2.071 (s, 6 H, Ac × 2), 2 061, 2.017, 2 000, and 1 983 (s, 3 H, Ac × 4).

Allyl O-*(4-O-acetyl-2,3-di-O-benzyl-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl)]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside* (**45**) — To a solution of compound **38** (111 mg, 40 μmol) in 1 1 THF–EtOH (10 mL) was added $CS(NH_2)_2$ (10 mg, 130 μmol) and pyridine (10 μL) The mixture was stirred for 20 h at 70° and evaporated The residue was extracted with $CHCl_3$ and the organic layer was washed with H_2O, aq $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated Chromatography of the residue over SiO_2 in 10·1 toluene–EtOAc gave **45** (72 6 mg, 85 9%), $[\alpha]_D$ +50 1° (*c* 0 36), R_F 0 26 (t l c in 7.1 toluene–EtOAc); n m r · δ_C 170 5 (*C*OCH$_3$), 134 2 (–*C*H=CH$_2$), 117 1 (–CH=*C*H$_2$), 102 6 (C-1a), 96.8, 96 4, 96 3 and 96.1 (in a ratio of 1 1 1 2, C-1bcdef), 84 9 (C-3a), 61.4 (C-6a), and 20.8 (CO*C*H$_3$)

Anal. Calc for $C_{160}H_{170}O_{32}$: C, 73 77; H, 6.58 Found· C, 74 14, H, 6 65

Allyl O-*(4-O-acetyl-2,3-di-O-benzyl-6-O-p-tolylsulfonyl-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside* (**46**). — A mixture of compound **45** (33.3 mg, 13 μmol), TsCl (10 mg, 53 μmol), and DMAP (5 mg, 41 μmol) in pyridine (1 5 mL) was stirred for 20 h at 20° The mixture was evaporated *in vacuo* The residue was dissolved in EtOAc (20 mL) and the extract was washed with aq. $NaHCO_3$, H_2O, dried ($MgSO_4$), and evaporated Chromatography of the residue over SiO_2 in 25:1 toluene–EtOAc gave **46** (33 1 mg, 93.8%), $[\alpha]_D$ +61 4° (*c* 0 19), R_F 0 62 in 7.1

toluene–EtOAc; n.m.r.: δ_C 169.3 ($COCH_3$), 134.3 ($-CH=CH_2$), 117.2 ($-CH=CH_2$), 102.7 (C-1a), 96.6 and 96.2 (in a ratio of 3:2, C-1bcdef), 84.7 (C-3a), 82.1 (C-2a), 81.5 (C-3bcdef), 21.6 ($-C_6H_4CH_3$), and 20.8 ($COCH_3$); δ_H 2.351 (s, 3 H, $-C_6H_4CH_3$), and 1.831 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{167}H_{176}O_{34}S \cdot H_2O$: C, 72.22; H, 6.46. Found: C, 72.15; H, 6.36.

Allyl O-(4-O-acetyl-6-azido-2,3-di-O-benzyl-6-deoxy-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**47**). — A mixture of compoud **46** (33.1 mg, 12 μmol) and NaN_3 (12 mg, 180 μmol) in DMF (1 mL) was stirred for 20 h at 50°, cooled, poured into water, and extracted with EtOAc. The extract was washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 20:1 toluene–EtOAc gave **47** (23 mg, 73%), $[\alpha]_D$ +68.0° (*c* 0.1); R_F 0.58 in 7:1 toluene-EtOAc; ν_{max} 2120 cm^{-1}. N.m.r.: δ_C 134.3 ($-CH=CH_2$), 117.2 ($-CH=CH_2$), 102.7 (C-1a), 96.6 and 96.2 (in a ratio of 1:4, C-1bcdef), 84.7 (C-3a), 51.4 (C-6a), and 20.8 ($COCH_3$); δ_H 1.897 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{160}H_{169}N_3O_{31}$: C, 73.08; H, 6.48. Found: C, 72.92; H, 6.32.

O-(4-O-Acetyl-6-azido-2,3-di-O-benzyl-6-deoxy-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl)]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**49**). — A mixture of compound **47** (18.8 mg, 7 μmol), NaOAc (2 mg), and $PdCl_2$ (6 mg, 34 μmol) in AcOH (0.5 mL)–H_2O (3 μL) was stirred for 18 h at 20° and filtered through Celite. The filtrate was evaporated and the residue was extracted with EtOAc. The extract was successively washed by aq. $NaHCO_3$ and H_2O dried ($MgSO_4$), and evaporated. Chromatography of the residue over SiO_2 in 14:1 toluene–EtOAc afforded compound **48** (11.4 mg, 62%), $[\alpha]_D$ +65.8° (*c* 0.1), R_F 0.26 and 0.30 in 7:1 toluene–EtOAc. A mixture of compound **48** (11.4 mg, 4.4 μmol), $SOCl_2$ (3 μL), and DMF (0.1 μL) in $Cl(CH_2)_2Cl$ (0.5 mL) was stirred for 18 h at 20° and filtered through a thin layer of SiO_2. The filtrate was evaporated. To a solution of the residue in CH_3CN (0.5 mL) was added AgF (5 mg, 40 μmol). The mixture was stirred for 18 h at 20° and evaporated. Chromatography of the residue over SiO_2 in 22:1 toluene–EtOAc gave **49** (8.8 mg, 78% from **48**), $[\alpha]_D$ +85.2° (*c* 0.07), R_F 0.53 in 7:1 toluene–EtOAc; n.m.r.: δ_H 5.664 (d, 1 H, *J* 3.4 Hz), 5.647 (d, 1 H, *J* 3.7 Hz), 5.630 (d, 1 H, *J* 3.4 Hz), 5.576 (d, 1 H, *J* 3.4 Hz) and 5.478 (d, 1 H, *J* 3.7 Hz), H-1bcdef), 5.359 (dd, 1 H, *J* 6.1 and 54.0 Hz, H-1a), and 1.904 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{157}H_{164}FN_3O_{30} \cdot H_2O$: C, 72.25; H, 6.41. Found: C, 72.27; H, 6.23.

O-(6-Azido-2,3-di-O-benzyl-6-deoxy-α-D-glucopyranosyl)-[(1→4)-O-(2,3,6-tri-O-benzyl-α-D-glucopyranosyl)]$_4$-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**50**). — To a solution of compound **49** (11.6 mg, 4.5 μmol) in THF (dried over $LiAlH_4$, 0.1 mL)–MeOH (dried over powdered 4A molecular sieves, 0.1 mL) was added a trace of NaOMe. The mixture was stirred for 18 h at 20° and evaporated. Chromatography of the residue over SiO_2 in 14:1 toluene–EtOAc

afforded **50** (9.7 mg, 85%), $[\alpha]_D$ +59.2° (*c* 0.06), R_F 0.44 in 7:1 toluene–EtOAc; ν_{max} 2120 cm^{-1}; n.m.r.: δ_H 5.668 (d, 1 H, *J* 3.9 Hz), 5.658 (d, 1 H, *J* 4.2 Hz), 5.621 (d, 1 H, *J* 3.7 Hz), 5.566 (d, 1 H, *J* 3.4 Hz), and 5.473 (d, 1 H, *J* 3.7 Hz, H-1bcdef), and 5.355 (dd, 1 H, *J* 5.7 and 54.6 Hz, H-1a).

Anal. Calc. for $C_{155}H_{162}FN_3O_{29}$: C, 73.01; H, 6.40. Found: C, 72.87; H, 6.36.

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REFERENCES

1 Y. Takahashi and T. Ogawa, *Carbohydr. Res.*, 164 (1987) 277–296.
2 T. Mukaiyama, Y. Murai, and S. Shoda, *Chem. Lett.*, (1981) 431–432.
3 T. Ogawa and S. Nakabayashi, *Carbohydr. Res.*, 93 (1981) c1–c5; T. Ogawa, S. Nakabayashi, and T. Kitajima, *ibid.*, 114 (1983) 225–236.
4 M. S. Newman and P. K. Sujeeth, *J. Org. Chem.*, 43 (1978) 4367–4369; see also ref. 3.
5 B. Helferich and R. Gootz, *Ber.*, 62 (1929) 2505–2507.
6 L. D. Hall, J. F. Manville, and N. S. Bhacca, *Can. J. Chem.*, 47 (1969) 1–17; L. Phillips and V. Wray, *J. Chem. Soc. B*, (1971) 1618–1624.
7 B. ElAmin, G. M. Anantharamaiah, G. P. Royer, and C. E. Means, *J. Org. Chem.*, 44 (1979) 3442–3444; V. S. Rao, and A. S. Perlin, *Carbohydr. Res.*, 83 (1980) 175–177.
8 F. A. Cook and D. T. Maichuk, *J. Org. Chem.*, 35 (1970) 1940–1943.
9 B. Helferich, K. Bäuerlein, and F. Wiegand, *Ann.*, 447 (1926) 27–37.