Carbohydrate Research, 245 (1993) 81–96
Elsevier Science Publishers B.V., Amsterdam

Synthesis of the laminara-oligosaccharide methyl β-glycosides of dp 3–8

Kenichi Takeo *, Kazumi Maki, Yoshikuni Wada and Shinichi Kitamura

Department of Agricultural Chemistry, Kyoto Prefectural University, Shimogamo, Kyoto 606 (Japan)

(Received August 10th, 1992; accepted in revised form January 16th, 1993)

ABSTRACT

Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-glucopyranoside has been prepared in a good yield by anomerization of the corresponding β-thioglucoside with tin(IV) chloride and transformed, in three steps, into ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**18**). Chloroacetylation of **18**, followed by treatment of the product with chlorine gave crystalline 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-D-glucopyranosyl chloride (**20**). This was coupled with methanol in the presence of silver carbonate-silver perchlorate and the product was *O*-dechloroacetylated to afford methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**22**). Silver triflate-promoted glucosylation of **18** with **20** gave a β-(1 → 3)-linked disaccharide derivative, reaction of which with chlorine yielded crystalline *O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl chloride (**24**). Likewise, condensation of **22** with **20** gave a β-(1 → 3)-linked disaccharide glycoside, which was partially deprotected to give methyl *O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1 → 3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**26**). The methyl β-glycosides of a homologous series of (1 → 3)-linked β-D-gluco-oligosaccharides from the tri- to the octa-saccharide have been synthesized in a blockwise manner by using **22** and **26** as the glycosyl acceptors, **24** as the disaccharide donor, and silver triflate as the promoter.

INTRODUCTION

Further extension of our physicochemical studies of (1 → 6)-branched (1 → 3)-β-D-glucans having antitumor activity[1] required the preparation of the methyl β-glycosides of a homologous series of (1 → 3)-linked β-D-gluco-oligosaccharides (laminara-oligosaccharides) up to and including the octasaccharide. Of the methyl β-glycosides of the laminara-oligosaccharide series, only methyl β-laminarabioside (**1**) has been synthesized, by the reaction of hepta-*O*-acetyl-α-laminarabiosyl bromide with methanol, followed by *O*-deacetylation[2,3]. Recently, methyl β-laminarahexaoside (**5**) has been prepared as its hexakis(2-*O*-benzoyl-4,6-*O*-ethylidene) derivative, from 1,2-*O*-benzylidene-4,6-*O*-ethylidene-α-D-glucopyranose[4] as the starting material. We first considered that the isolation[5] of laminara-oligosac-

* Corresponding author.

charides from partial acid hydrolyzates of (1 → 3)-β-D-glucans such as pachyman[5] and curdlan[6], followed by conversion of each member of the series into the respective methyl β-glycoside via the corresponding α-D-glycosyl halide, as for the synthesis[2,3] of **1**, would be a straightforward way to prepare the needed compounds. However, we studied an alternative synthetic route, as this enabled us to develop mono- and di-saccharide derivatives that are not only useful for the preparation of glycosides of the laminara-oligosaccharides but also can serve as versatile intermediates for the synthesis of various (1 → 6)-branched (1 → 3)-β-D-gluco-oligosaccharides[7].

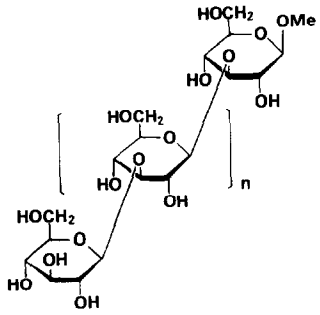
We now report a systematic synthesis, by a blockwise approach, of the methyl β-glycosides of the complete series of laminara-oligosaccharides from laminaratriose, through laminara-octaose (compounds **2**–**7**).

RESULTS AND DISCUSSION

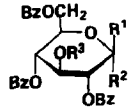
A prerequisite for the synthesis of a homologous series of laminara-oligosaccharide glycosides is to obtain as a starting material a derivative of a D-glucopyranosyl halide or a 1-thio-D-glucopyranoside bearing a substituent on O-2 capable of neighboring-group participation, and a selectively removable protecting group on O-3. It first appeared to us that 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-α-D-glucopyranosyl bromide (**9**) might fulfill this requirement. Treatment of easily accessible[8] 1,2,4,6-tetra-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranose (**8**) with hydrogen bromide in acetic acid–dichloromethane gave **9**, which was reacted with 2-(trimethylsilyl)ethanol in the presence of silver carbonate–silver perchlorate[9] to afford **10**. Catalytic hydrogenolysis of **10** provided **11** having HO-3 unsubstituted. However, an attempted glucosylation of **11** with **9** in the presence of silver triflate[10] was unsuccessful; no reaction took place.

Next, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[11] (**12**) was considered as a starting material. However, isolation of **12** from the mixture obtained by the selective phase-transfer benzoylation of methyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside requires a chromatographic separation[11], making the method impractical for the preparation of large amounts of **12**. In view of the greater reactivity of HO-2 towards partial benzoylation in methyl 4,6-*O*-benzylidene-α-D-glucopyranoside compared to that in the corresponding β-D-glucoside[12,13], we investigated the preparation of ethyl 1-thio-α-D-glucopyranoside[14] (**16**), the precursor to ethyl 4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**17**).

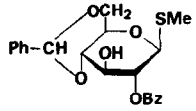
Contour et al.[15] reported that thioglucosidation of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**13**) with ethanethiol in dichloromethane in the presence of zirconium(IV) chloride for 16 h at 0°C affords 74% of ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**14**), whereas when the same reaction is conducted at room temperature for 16 h, thioglucosidation is accompanied by anomerization, to give a mixture from which **14** and the α anomer **15** are obtained in 32 and 38% yields, respectively, after column chromatography. In our hands, however, the



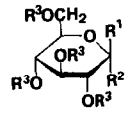
	n
1	0
2	1
3	2
4	3
5	4
6	5
7	6



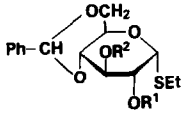
	R1	R2	R3
8	OBz	H	Bn
9	H	Br	Bn
10	OSE	H	Bn
11	OSE	H	H



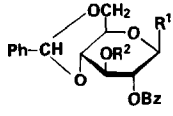
12



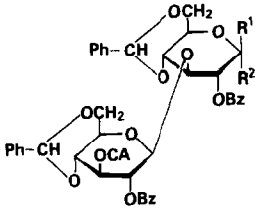
	R1	R2	R3
13	OAc	H	Ac
14	SEt	H	Ac
15	H	SEt	Ac
16	H	SEt	H



	R1	R2
17	H	H
18	Bz	H
19	Bz	CA



	R1	R2
20	Cl	CA
21	OMe	CA
22	OMe	H



	R1	R2
23	H	SEt
24	Cl	H

CA : $ClCH_2CO$; SE : $Me_3SiCH_2CH_2$

reaction of **13** with ethanethiol in dichloromethane in the presence of zirconium(IV) chloride under almost identical conditions proceeded much faster than reported[15]. Thus, reaction at 0°C for 20 min gave a mixture from which **14** was isolated in 84% yield by fractional crystallization. When the same process was run for 16 h at room temperature, the mixture contained **14** and **15**, together with some byproducts (TLC). In this case, the formation of significant amounts of an unidentified byproduct moving marginally faster than **15** prevented the complete recovery of **15** from the mixture by column chromatography. By contrast, when compound **14** was treated with tin(IV) chloride[16] in dichloromethane at room temperature equilibrium was reached after 8 h at a ~1:2 ratio of **14** and **15**, and virtually no

formation of the side products occurred. Compound **15** was isolated in 45% yield from the mixture by fractional crystallization. The mother liquor was then further subjected to anomerization with tin(IV) chloride, giving another 22% of **15**, similarly isolated by fractional crystallization. *O*-Deacetylation of **15** gave **16** (ref 14) in quantitative yield.

Benzylidenation of **16** with α,α-dimethoxytoluene–*p*-toluenesulfonic acid in *N*,*N*-dimethylformamide[17] afforded the 4,6-*O*-benzylidene derivative (**17**), partial benzoylation of which with 1-(benzoyloxy)benzotriazole–triethylamine[13] in dichloromethane gave the crystalline 2-*O*-benzoate **18**, directly isolated in 83% yield from the mixture by crystallization. The ^{1}H NMR spectrum of **18** showed a doublet of doublets ($J_{1,2}$ 5.7, $J_{2,3}$ 9.4 Hz) for H-2 at δ 5.21, confirming the position of the benzoyloxy group in **18**. Esterification of **18** with chloroacetyl chloride–pyridine[8] in dichloromethane gave **19**, which was transformed by treatment with chlorine[18] into the corresponding crystalline β-chloride **20** (84%). The configuration at C-1 in **20** could not be determined by the ^{1}H NMR spectrum, since it showed an overlapped 4-proton multiplet centered at δ 5.53 for H-1, H-2, H-3, and the C*H* of the benzylidene group. However, the negative optical rotation ($[\alpha]_D$ −23°), the absence of a signal for H-1 diagnostic[19] for the α configuration, and the mode of synthesis[18] of **20** indicated the configuration at C-1 to be β.

In attempts to obtain methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-D-glucopyranoside (**21**), compound **19** did not react with methanol in the presence of dimethyl(methylthio)sulfonium triflate[20] (DMTST) or *N*-iodosuccinimide (NIS)–triflic acid[21], whereas condensation of **20** with methanol in the presence of silver carbonate–silver perchlorate did give **21** in 84% yield. *O*-Dechloroacetylation of **21** with thiourea in the presence of 2,6-dimethylpyridine[22] provided methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside[23] (**22**, 92%).

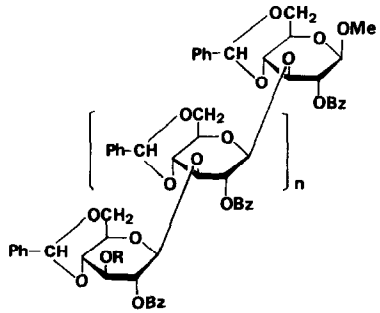
Glucosylation of **22** with **19**, promoted by NIS–triflic acid, gave methyl *O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**25**, 71%). However, no coupling took place between **19** and **22** in attempted condensations in the presence of DMTST or methyl triflate[24]. Compound **25** (88%) could also be obtained by condensation of **22** with **20**, assisted by silver triflate in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP)[25].

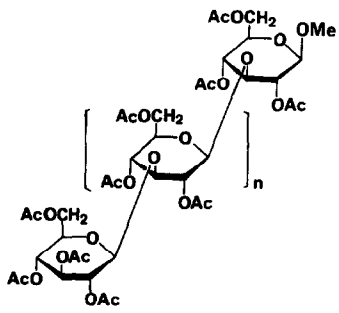
O-Dechloroacetylation of **25**, as for **21**, gave the disaccharide derivative **26** having HO-3^2 unsubstituted. Glucosylation of **18** with **20** in the presence of silver triflate–DTBMP afforded ethyl *O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**23**, 90%), which was converted by treatment with chlorine[18], as for **19**, into the corresponding crystalline β-chloride **24** (82%), a disaccharide building-block bearing a selectively removable protecting group[8,22] on O-3^2, the site of further chain extension.

Having prepared a mono- (**22**) and a di-saccharide acceptor (**26**), and a disaccharide glycosyl donor (**24**), we were able to carry out the synthesis of methyl

β-glycosides of laminara-oligosaccharides by a blockwise elongation of the oligosaccharide chain, using a combination of silver triflate as the promoter and DTBMP as the proton acceptor for all the glycosylation steps. Glycosylation of **22** with **24** gave the trisaccharide derivative **27**, which was *O*-dechloroacetylated to give **28**, having HO-3[3] unsubstituted. Coupling of **28** with **24** yielded the pentasaccharide derivative **29**, which was partially deprotected to afford the pentasaccharide derivative **30** having HO-3[5] unsubstituted. Reaction of **30** with **24** gave the heptasaccharide derivative **31**. In a similar way, the tetra- (**32** and **33**), hexa- (**34** and **35**), and octa-saccharide (**36**) derivatives were prepared by a sequence involving glycosylation of **26** with **24** (→ **32**), followed by *O*-dechloroacetylation (→ **33**), reaction with **24** (→ **34**), *O*-dechloroacetylation (→ **35**), and coupling with **24** (→ **36**). In the ^{13}C NMR spectra of compounds **29–36** the signals for some anomeric and/or benzylic carbon atoms appeared at abnormally high fields, up to δ 96.7, suggesting steric crowding[26] of the substituents in the inner glucosidic residues.

Removal of the benzylidene groups from **27** by treatment with ethylene glycol–*p*-toluenesulfonic acid[27] in acetonitrile, followed by deacylation with sodium methoxide in boiling methanol[28], and acetylation, gave methyl β-laminaratrioside decaacetate (**37**), saponification of which as above gave **2**. In an analogous manner, compounds **32**, **29**, **34**, **31**, and **36** were transformed into the per-*O*-acetyl derivatives **38**, **39**, **40**, **41**, and **42**, respectively, and these were *O*-deacetylated as before to furnish **3**, **4**, **5**, **6**, and **7**, respectively. Compounds **2–7** were homogeneous by LC and gave ^{13}C NMR spectra consistent with the structures assigned.





	n	R		n	R
25	0	CA	**31**	5	CA
26	0	H	**32**	2	CA
27	1	CA	**33**	2	H
28	1	H	**34**	4	CA
29	3	CA	**35**	4	H
30	3	H	**36**	6	CA

	n
37	1
38	2
39	3
40	4
41	5
42	6

EXPERIMENTAL

General methods.—Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were determined with an Applied Electronic automatic polarimeter model MP-1T. NMR spectra (^{1}H at 90 MHz, ^{13}C at 22.6 MHz) were recorded with a Hitachi R-90H spectrometer for solutions in $CDCl_3$ and Me_2SO-d_6 (internal Me_4Si) or D_2O (internal sodium 4,4-dimethyl-4-silapentanoate-d_4). ^{1}NMR spectra (270 MHz) of compounds **20** and **24** and ^{13}C NMR spectra (67.8 MHz) of compounds **27–36** were recorded with a Jeol JNM GX-270 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). ^{13}C NMR spectra (100.4 MHz) of compounds **2–7** and **37–42** were recorded with a Jeol JNM GX-400 spectrometer for solutions in D_2O (internal 1,4-dioxane δ_C 67.40) or $CDCl_3$ (internal Me_4Si). HPLC was performed with a Jasco 880-PU instrument equipped with a Shodex SE-61 r.i. detector and a column of YMC-pack polyamine (250 × 4.6 mm, i.d., YMC, Kyoto) using 60:40 MeCN–H_2O as eluent. Retention times (t_R) are given relative to that of methyl β-D-glucopyranoside. Organic solutions were dried over anhyd Na_2SO_4 or $MgSO_4$. Solutions were concentrated at temperatures < 40°C under diminished pressure. TLC was performed on Silica Gel 60 (No. 7734, Merck), with detection by charring with H_2SO_4. Column chromatography was performed on Waco Gel C-300. The following solvent systems (v/v) were used: (*1*) 1:1 hexane–EtOAc, (*2*) 1:1 Et_2O–hexane, and PhMe–EtOAc (*3*) 20:1, (*4*) 15:1, (*5*) 10:1, (*6*) 1:1.

2-(Trimethylsilyl)ethyl 2,4,6-tri-O-benzoyl-3-O-benzyl-β-D-glucopyranoside (**10**).—To a solution of **8** (5.0 g) in CH_2Cl_2 (50 mL) at 0°C was added a saturated (at 0°C) solution of HBr in AcOH (20 mL). The mixture was stirred for 30 min at 0°C, and then diluted with CH_2Cl_2. The solution was washed successively with ice–H_2O, aq $NaHCO_3$, and H_2O, dried, and concentrated. Column chromatography (solvent *1*) of the residue gave amorphous **9** (4.14 g, 88%), $[\alpha]_D^{20}$ +127° (*c* 1.5, CH_2Cl_2); NMR ($CDCl_3$): δ_H 8.38–7.03 (m, 20 H, 4 Ph), 6.80 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.27, and 5.17 (2 d, 197°2 H, PhCH_2); δ_C 165.8, 164.95, and 164.7 (*C*=O), 137.0, 133.5, 133.4, and 132.9 (aromatic C-1), 88.2 (C-1), 77.2 (C-3), 75.1, 73.2, and 72.8 (C-2,5, PhCH_2), 69.45 (C-4), and 62.0 (C-6).

A solution of **9** (3.85 g, 6 mmol) in CH_2Cl_2 (30 mL) was added dropwise during 1 h at 0°C to a stirred solution of 2-(trimethylsilyl)ethanol (1.28 mL, 8.9 mmol) in CH_2Cl_2 (20 mL) containing Ag_2CO_3 (1.65 g, 6 mmol), $AgClO_4$ (124 mg, 0.6 mmol), and powdered 4A molecular sieves (15 g). The mixture was allowed to attain room temperature, and then stirred overnight. Insoluble material was collected on a Celite layer, washed with CH_2Cl_2, and the combined filtrate and washings was concentrated. Crystallization of the residue from EtOH gave **10** (3.34 g, 82%); mp 120–122°C; $[\alpha]_D^{22}$ +6° (*c* 1.2, $CHCl_3$); NMR ($CDCl_3$): δ_H 4.74 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1); δ_C 169.95, 164.9, and 164.0 (*C*=O), 137.1, 133.2, and 132.9 (2 C) (aromatic C-1), 100.5 (C-1), 79.6 (C-3), 73.8, 73.6, 72.0, and 71.3 (C-2,5, PhCH_2,

$CH_2CH_2SiMe_3$), 67.2 (C-4), 63.5 (C-6), 17.9 ($CH_2CH_2SiMe_3$), and −1.5 ($SiMe_3$) Anal. Calcd for $C_{39}H_{42}O_9Si$: C, 68.60; H, 6.20. Found: C, 68.66; H, 6.28.

2-(Trimethylsilyl)ethyl 2,4,6-tri-O-benzoyl-β-D-glucopyranoside (**11**).—A solution of **10** (3.02 g) in 1,4-dioxane (90 mL) was hydrogenolyzed overnight in the presence of 10% Pd–C (0.5 g) at atmospheric pressure and room temperature. The suspension was filtered through a Celite layer and washed with Me_2CO, and the filtrate and washings was concentrated. The residue was crystallized from Et_2O–hexane to afford **11** (2.41 g, 92%); mp 156–157°C; $[\alpha]_D^{22}$ −2° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 165.85 (2 C) and 165.8 (*C*=O), 133.2, 133.0, and 132.8 (aromatic C-1), 100.2 (C-1), 74.85, 73.8, 72.4, and 71.8 (C-2,3,5, $CH_2CH_2SiMe_3$), 67.2 (C-4), 63.5 (C-6), 17.9 ($CH_2CH_2SiMe_3$), and −1.5 ($SiMe_3$). Anal. Calcd for $C_{32}H_{36}O_4Si$: C, 64.85; H, 6.12. Found: C, 64.93; H, 6.08.

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (**14**).—To a stirred solution of **13** (91.7 g, 0.235 mol) in CH_2Cl_2 (750 mL) at 0°C was added ethanethiol (29.6 mL, 0.4 mol), followed by $ZrCl_4$ (55.3 g, 0.24 mol), and the mixture was stirred for 20 min at 0°C, whereupon TLC (solvent *2*) showed complete conversion of **13** (R_f 0.17) into the product (R_f 0.27). The mixture was poured into ice–H_2O, and the organic layer was separated, washed successively with aq $NaHCO_3$, and H_2O, dried, and concentrated. The resulting solid was recrystallized from EtOH to give **14** (77.5 g, 84%); mp 82–83°C; $[\alpha]_D^{22}$ −27° (*c* 1.9, $CHCl_3$); lit.[15] mp 82–83°C; $[\alpha]_D$ −26.7°.

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-glucopyranoside (**15**).—A solution of $SnCl_4$ (42.5 mL, 0.36 mol) in CH_2Cl_2 (200 mL) was added dropwise at 0°C to a stirred solution of **14** (142.5 g, 0.36 mol) in CH_2Cl_2 (600 mL). The mixture was stirred for 8 h at room temperature and then processed as described for the preparation of **14**. The residue was crystallized from Et_2O–hexane and recrystallized twice from EtOH to give **15** (64 g, 45%); mp 90–92°C; $[\alpha]_D^{22}$ +197° (*c* 1.4, $CHCl_3$); lit.[15] mp 91–93°C; $[\alpha]_D$ +197°; NMR ($CDCl_3$): δ_H 5.68 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1), 2.57 (m, 2 H, SCH_2CH_3), 2.08, 2.06, 2.03, and 2.01 (4 s, 12 H, 4 $COCH_3$), and 1.28 (t, 3 H, SCH_2CH_3); δ_C 170.25, 169.6 and 169.3 (*C*=O), 81.7 (C-1), 70.7, 70.5, 68.7, 67.5 (C-2,3,4,5), 61.9 (C-6), 24.2 (SCH_2CH_3), 20.6 ($COCH_3$), and 14.7 (SCH_2CH_3).

The mother liquors from the crystallization of **15** were concentrated, and the residue was dried by repeated additions and evaporations of PhMe. A solution of this residue (96.8 g) in CH_2Cl_2 (400 mL) was treated at 0°C with $SnCl_4$ (29.1 mL, 0.25 mol) in CH_2Cl_2 (130 mL), and the mixture was processed as just described, to afford additional **15** (31.4 g, 22%).

Ethyl 1-thio-α-D-glucopyranoside (**16**).—A solution of **15** (85.4 g) in dry MeOH (300 mL) was treated with a catalytic amount of methanolic NaOMe. The mixture was kept for 3 h at room temperature, made neutral with Amberlite IR-120 (H^+) resin, filtered, and concentrated. The residue was crystallized from EtOAc to give **16** (47.3 g, 97%); mp 115–116°C; $[\alpha]_D^{22}$ +263° (*c* 1.3, H_2O); lit.[14] mp 117°C; $[\alpha]_D$ +269° (*c* 1.3, H_2O); NMR (D_2O): δ_H 5.43 (d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 2.65 (m, 2 H,

SCH_2CH_3), and 1.28 (t, 3 H, SCH_2CH_3); δ_C 87.6 (C-1), 76.3, 74.85, 73.6, 72.6, and 72.3 (C-2,3,4,5), 63.2 (C-6), 26.8 (SCH_2CH_3), and 16.9 (SCH_2CH_3).

*Ethyl 4,6-*O*-benzylidene-1-thio-α-*D*-glucopyranoside* (**17**).—A mixture of **16** (44.2 g, 0.2 mol), α,α-dimethoxytoluene (44.3 mL, 0.3 mol), and *p*-toluenesulfonic acid · H_2O (0.1 g) in *N*,*N*-dimethylformamide (200 mL) was stirred for 2 h at 50°C under diminished pressure (~ 4 kPa). Triethylamine (1 mL) was added and the mixture was concentrated. Crystallization of the residue from $CHCl_3$–hexane gave **17** (52.3 g, 85%); mp 144–145°C; $[\alpha]_D^{22}$ +238° (*c* 1.5, $CHCl_3$); NMR (Me_2SO-d_6); δ_H 7.95–7.07 (m, 5 H, Ph), 5.58 (s, 1 H, benzylic H), 5.37 (d, 1 H, $J_{1,2}$ 5.05 Hz, H-1), 2.51 (m, 2 H, SCH_2CH_3), and 1.21 (t, 3 H, SCH_2CH_3); δ_C 137.5 (aromatic C-1), 100.7 (benzylic C), 85.7 (C-1), 81.0 (C-4), 71.9 (C-2), 70.3 (C-3), 67.9 (C-6), 62.9 (C-5), 23.0 (SCH_2CH_3), and 14.8 (SCH_2CH_3). Anal. Calcd for $C_{15}H_{20}O_{15}S$: C, 57.67; H, 6.45. Found: C, 57.71; H, 6.49.

*Ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-α-*D*-glucopyranoside* (**18**).—To a stirred solution of **17** (56.0 g, 0.18 mol) and 1-(benzoyloxy)benzotriazole (46.0 g, 0.18 mol) in CH_2Cl_2 (700 mL) was added Et_3N (30 mL, 0.22 mol). The mixture was stirred for 2 h at room temperature, diluted with CH_2Cl_2, washed successively with aq $NaHCO_3$ and H_2O, dried, and concentrated. Crystallization of the residue from EtOH gave **18** (62.0 g, 83%); mp 166–167°C; $[\alpha]_D^{22}$ +160.5° (*c* 1.3, $CHCl_3$); NMR ($CDCl_3$): δ_H 8.12–7.32 (m, 10 H, 2 Ph), 5.75 (d, 1 H, $J_{1,2}$ 5.7 Hz, H-1), 5.55 (s, 1 H, benzylic H), 5.21 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 2.54 (m, 2 H, SCH_2CH_3), and 1.21 (t, 3 H, SCH_2CH_3); δ_C 165.65 (C=O), 136.9 and 133.2 (aromatic C-1), 101.95 (benzylic C), 82.8 (C-1), 81.3 (C-4), 73.6 and 69.3 (C-2,3), 68.6 (C-6), 62.6 (C-5), 24.5 (SCH_2CH_3), and 14.8 (SCH_2CH_3). Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.45; H, 5.81. Found C, 63.40; H, 5.78.

*Ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-1-thio-α-*D*-glucopyranoside* (**19**).—A solution of **18** (32.5 g) in CH_2Cl_2 (200 mL) containing pyridine (9.5 mL) was cooled to −10°C, treated with a solution of $ClCH_2COCl$ (7.5 mL) in CH_2Cl_2 (50 mL), and kept for 20 min at 0°C. The mixture was diluted with CH_2Cl_2 and poured into ice–H_2O, then the organic layer was separated, washed successively with dil HCl, aq $NaHCO_3$, and H_2O, dried, and concentrated. A solution of the residue in 1:1 hexane–EtOAc (100 mL) was filtered through a layer of silica gel (100 g), which was washed with 1:1 hexane–EtOAc (130 mL). The combined filtrate and washings was concentrated, and the residue was crystallized from Et_2O–hexane to give **19** (35.8 g, 93%); mp 140–141°C; $[\alpha]_D^{22}$ +156° (*c* 1.2, $CHCl_3$); NMR ($CDCl_3$): δ_H 8.07–7.23 (m, 10 H, 2 Ph), 5.83 (d, 1 H, $J_{1,2}$ 5.7 Hz, H-1), 5.73 (t, 1 H, $J_{3,4}$ 9.8 Hz, H-3), 5.54 (s, 1 H, benzylic H), 5.29 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 3.95 (s, 2 H, $COCH_2Cl$), 2.55 (m, 2 H, SCH_2CH_3), and 1.21 (t, 3 H, SCH_2CH_3); δ_C 166.1 and 165.2 (C=O), 133.6 and 133.5 (aromatic C-1), 101.6 (benzylic C), 82.8 (C-1), 78.75 (C-4), 71.8 and 71.2 (C-2,3), 68.5 (C-6), 62.9 (C-5), 40.4 ($COCH_2Cl$), 24.4 (SCH_2CH_3), and 14.75 (SCH_2CH_3). Anal. Calcd for $C_{24}H_{25}ClO_7S$: C, 58.47; H, 5.11. Found: C, 58.68; H, 5.05.

*2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-*D*-glucopyranosyl chloride* (**20**).

—A solution of Cl_2 (7.3 g, 91 mmol) in $CHCl_3$ (55 mL) was added at 0°C to a solution of **19** (22.5 g, 46 mmol) in CCl_4 (30 mL). After 5 min, the solvents were evaporated off and volatile non-carbohydrate byproducts[18] were removed by repeated additions and evaporations of PhMe. Crystallization of the residue from CH_2Cl_2–hexane gave **20** (17.9 g, 84%); mp 168–170°C; $[\alpha]_D^{22}$ − 23° (*c* 0.9, CH_2Cl_2); ^{13}C NMR ($CDCl_3$): δ 166.3 and 164.8 (*C*=O), 136.2 and 133.6 (aromatic C-1), 101.6 (benzylic C), 87.9 (C-1), 77.4 (C-4), 74.4, 73.5, 69.8, and 68.1 (C-2,3,5,6), and 40.3 ($COCH_2Cl$). This compound decomposes on TLC. Anal. Calcd for $C_{22}H_{20}Cl_2O_7$: C, 56.55; H, 4.31. Found: C, 56.40; H, 4.45.

Methyl-2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranoside (**21**). —A solution of **20** (5.1 g, 10.9 mmol) in CH_2Cl_2 (50 mL) was added dropwise during 1 h at 0°C to a stirred mixture of MeOH (1 mL, 24.5 mmol), Ag_2CO_3 (3.1 g, 11.2 mmol), $AgClO_4$ (0.23 g, 1.1 mmol), and powdered 4A molecular sieves (25 g) in CH_2Cl_2 (45 mL). The mixture was stirred for 6 h at room temperature, and processed as described for the preparation of **10** to give **21** (4.24 g, 84%); mp 155–156°C (from EtOH); $[\alpha]_D^{22}$ −15° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.35 and 165.0 (*C*=O), 133.6 and 133.2 (aromatic C-1), 102.35 (C-1), 101.4 (benzylic C), 78.1 (C-4), 73.4 and 72.2 (C-2,3), 68.5 (C-6), 66.3 (C-5), 57.2 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{23}H_{23}O_8Cl$: C, 59.68; H, 5.01. Found: C, 59.61; H, 4.95.

Methyl 2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**22**).—A mixture of **21** (3.84 g, 8.3 mmol), $(NH_2)_2C$=S (3.16 g, 41.5 mmol), and 2,6-dimethylpyridine (0.96 mL, 8.3 mmol) in MeOH (60 mL) and CH_2Cl_2 (40 mL) was boiled under reflux overnight. The mixture was concentrated and the residue was extracted with CH_2Cl_2. The extract was washed successively with cold dil HCl, aq $NaHCO_3$, and H_2O, dried, and concentrated. The residue was crystallized from EtOH to give **22** (2.95 g, 92%); mp 201–202°C; $[\alpha]_D^{22}$ −33° (*c* 0.9, $CHCl_3$); lit.[23] mp 195–196°C; $[\alpha]_D$ − 34°.

Methyl O-(2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**25**).—(*a*) To a stirred mixture of **19** (0.44 g, 8.9 mmol), **22** (0.31 g, 8 mmol), NIS (0.22 g, 9.8 mmol), and powdered 4A molecular sieves (4 g) in CH_2Cl_2 at 0°C was added dropwise a solution of CF_3SO_3H (0.1 μL) in Et_2O (2 mL) and CH_2Cl_2 (5 mL). After 10 min, the mixture was made neutral with Et_3N, diluted with CH_2Cl_2, and filtered through a Celite pad which was washed with CH_2Cl_2. The combined filtrate and washings was washed successively with aq $Na_2S_2O_3$, aq $NaHCO_3$, and H_2O, dried, and concentrated. Column chromatography (solvent *2*) of the product gave **25** (0.47 g, 71%); mp 235–236°C (from MeOH–Me_2CO); $[\alpha]_D^{22}$ +1.6° (*c* 0.9, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.3, 164.6, and 164.4 (*C*=O), 102.1, 101.3 (2 C), and 100.3 (C-1^1, 1^2, 2 benzylic C), 56.7 (OMe), and 40.3 ($COCH_2Cl$). Anal. Calcd for $C_{43}H_{41}O_{14}Cl$: C, 63.20; H, 5.06. Found: C, 63.32; H, 5.13.

(*b*) A solution of **20** (4.94 g, 10.6 mmol) in CH_2Cl_2 (40 mL) was added dropwise at 0°C to a stirred mixture of **22** (3.55 g, 9.2 mmol), silver triflate (3.26 g, 12.7

mmol), DTBMP (1.7 g, 8.3 mmol), and powdered 4A molecular sieves (5 g) in CH_2Cl_2 (100 mL) and PhMe (25 mL). The mixture was allowed to reach room temperature and stirred for 1 h. The insoluble material was collected on a Celite pad and washed with CH_2Cl_2, and the combined filtrate and washings was washed successively with H_2O, aq $Na_2S_2O_3$, aq $NaHCO_3$, and H_2O, dried, and concentrated. The residue was subjected to column chromatography, as just described, to afford **25** (6.61 g, 88%).

Methyl O-(*2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl*)-(*1 → 3*)-*2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside* (**26**).—A mixture of **25** (6.0 g), $(NH_2)_2C{=}S$ (3.26 g), and 2,6-dimethylpyridine (0.85 mL) in MeOH (90 mL) and CH_2Cl_2 (70 mL) was boiled under reflux overnight, and processed as described for **21** to afford **26** (4.95 g, 91%); mp 214–216°C (from MeOH–Me_2CO); $[\alpha]_D^{22}$ −15° (*c* 1.3, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 165.35 and 164.5 (*C*=O), 102.0, 101.4 (2 C), and 100.15 (C-1^1, 1^2, 2 benzylic C), and 56.6 (OMe). Anal. Calcd for $C_{41}H_{40}O_{13}$: C, 66.48; H, 5.44. Found: C, 66.61; H, 5.50.

Ethyl O-(*2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl*)-(*1 → 3*)-*2-O-benzoyl-4,6-O-benzylidene-1-thio α-D-glucopyranoside* (**23**).—A mixture of **18** (8.1 g, 19.4 mmol), silver triflate (6.0 g, 23.4 mmol), DTBMP (3.6 g, 17.5 mmol), and powdered 4A molecular sieves (10 g) in CH_2Cl_2 (70 mL), PhMe (35 mL), and $MeNO_2$ (15 mL) was treated with a solution of **20** (10.5 g, 22.5 mmol) in CH_2Cl_2 (100 mL) as described for the preparation of **25**. The residue was crystallized from EtOH to give **23** (14.85 g, 90%); mp 218–219.5°C, $[\alpha]_D^{22}$ +83° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.2 and 164.7 (2 C) (*C*=O), 101.3 (2 C) and 100.8 (C-1^2, 2 benzylic C), 82.5 (C-1^1), 40.3 ($COCH_2Cl$), 24.2 (SCH_2CH_3), and 14.7 (SCH_2CH_3). Anal. Calcd for $C_{44}H_{43}ClO_{13}S$: C, 62.37; H, 5.12. Found: C, 62.30; H, 5.20.

O-(2-O-Benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl chloride (**24**).—A solution of Cl_2 (1.9 g , 26.8 mmol) in $CHCl_3$ (15 mL) was added at 0°C to a solution of **23** (10.1 g, 11.9 mmol) in CH_2Cl_2 (20 mL) and CCl_4 (40 mL). The mixture was processed as described for the preparation of **20** to give **24** (8.0 g, 82%); mp 215–218°C (from CH_2Cl_2–petroleum ether); $[\alpha]_D^{22}$ +2.5° (*c* 0.7, CH_2Cl_2); NMR ($CDCl_3$): δ_H 5.30 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1^1) and 5. 01 (d, 1 H, $J_{1,2}$, 7.0 Hz, H-1^2); δ_C 166.3, 164.7, and 164.2 (*C*=O), 136.7, 136.5, 133.3, and 132.9 (aromatic C-1), 101.5, 101.3, and 100.15 (C-1^2, 2 benzylic C), 88.0 (C-1^1), and 40.3 ($COCH_2Cl$). This compound decomposes on TLC. Anal. Calcd for $C_{42}H_{38}Cl_2O_{13}$: C, 61.40; H, 4.66. Found: C, 61.27; H, 4.79.

Methyl O-(*2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl*)-(*1 → 3*)-O-(*2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl*)-(*1 → 3*)-*2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside* (**27**).—A mixture of **22** (1.52 g, 3.9 mmol), silver triflate (1.46 g, 5.7 mmol), DTBMP (0.73 g, 3.6 mmol), and powdered 4A molecular sieves (5 g) in CH_2Cl_2 (60 mL) and PhMe (15 mL) was treated with a solution of **24** (3.88 g, 4.7 mmol) in CH_2Cl_2 (60 mL) as described for the preparation of **25**. The residue was subjected to column chromatography (solvent

2) to give **27** (3.87 g, 84%); mp 207–208°C (from MeOH–Me_2CO), $[\alpha]_D^{22}$ +10° (*c* 1.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.95, 101.7, 101.25, 100.6, 98.7, and 98.3 (C-1^1, 1^2, 1^3, 3 benzylic C), 56.6 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{63}H_{59}ClO_{20}$: C, 64.59; H, 5.08. Found: C, 64.77; H, 5.15.

Methyl O-*(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)-O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside* (**28**).—*O*-Dechloroacetylation of **27** (2.94 g) as described for **21**, followed by column chromatography (solvent *5*) of the product, gave amorphous **28** (2.34 g, 85%); $[\alpha]_D^{22}$ −0.7° (*c* 1.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.0, 101.7, 101.55, 100.4, 98.2, and 97.2 (C-1^1, 1^2, 1^3, 3 benzylic C), and 56.7 (OMe). Anal. Calcd for $C_{61}H_{58}O_{19}$: C, 66.90; H, 5.34. Found: C, 67.17; H, 5.45.

Methyl O-(2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-tris[O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)]-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**29**).—The product obtained by condensation of **28** (2.02 g, 1.8 mmol) with **24** (1.82 g, 2.2 mmol), as described for the preparation of **25**, was subjected to column chromatography (solvent *4*) to afford amorphous **29** (2.83 g, 82%); $[\alpha]_D^{22}$ +31° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.9, 101.3, 101.1 (2 C), 100.7, 98.8, 98.1, 97.4, and 96.7 (C-1^1, 1^2, 1^3, 1^4, 1^5, 5 benzylic C), 56.8 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{103}H_{95}O_{32}$: C, 65.79; H, 5.09. Found: C, 65.90; H, 5.13.

Methyl O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)-tris-[O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)(1 → 3)]-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**30**).—*O*-Dechloroacetylation of **29** (1.63 g) as described for **21**, followed by column chromatography (solvent *5*) of the product, gave amorphous **30** (1.28 g, 82%); $[\alpha]_D^{22}$ +20° (*c* 1.3, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.0, 101.8, 101.5, 101.2, 100.9, 100.5, 98.35, 98.0, 97.1, and 96.8 (C-1^1, 1^2, 1^3, 1^4, 1^5, 5 benzylic C), and 56.8 (OMe). Anal. Calcd for $C_{101}H_{94}O_{31}$: C, 67.25; H, 5.25. Fond: C, 67.34; H, 5.35.

Methyl O-(2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-pentakis[O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)]-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**31**).—The product obtained by reaction of **30** (1.02 g, 565 μmol) with **24** (0.56 g, 682 μmol), as described for the preparation of **25**, was subjected to column chromatography (solvent *5*) to give amorphous **31** (1.16 g, 79%); $[\alpha]_D^{22}$ +40° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.9, 101.3 (2 C), 101.0 (3 C), 100.7, 98.9, 98.2, 97.2, 97.0, 96.9, and 96.8 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 1^7, 7 benzylic C), 56.9 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{143}H_{131}ClO_{44}$: C, 66.34; H, 5.10. Found: C, 66.55; H, 5.21.

Methyl O-(2-O-benzoyl-4,6-O-benzylidene-3-O-chloroacetyl-β-D-glucopyranosyl)-(1 → 3)-bis[O-(2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1 → 3)]-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**32**).—The product obtained by glycosylation of **26** (2.57 g, 3.5 mmol) with **24** (3.33 g, 4.05 g), as described for the preparation of **25**, was subjected to column chromatography to give amorphous **32** (4.34 g, 82%); $[\alpha]_D^{22}$ +19° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.8, 101.3,

100.8 (2 C), 99.2, 98.0, and 97.1 (C-1^1, 1^2, 1^3, 1^4, 4 benzylic C), 56.8 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{88}H_{77}ClO_{26}$: C, 65.33; H, 5.09. Found: C, 65.50; H, 5.17.

Methyl O-*(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)-bis[*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)]-2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside* (**33**).—*O*-Dechloroacetylation of **32** (3.11 g) by the procedure described above, followed by column chromatography (solvent *5*) of the residue, afforded amorphous **33** (2.39 g, 81%), $[\alpha]_D^{22}$ +11° (*c* 1.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.7 (2 C), 101.1, 100.7, 98.7, 98.3, and 97.0 (C-1^1, 1^2, 1^3, 1^4, 4 benzylic C), and 56.8 (OMe). Anal. Calcd for $C_{81}H_{76}O_{25}$: C, 67.12; H, 5.29. Found: C, 67.28; H, 5.40.

Methyl O-*(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-*D*-glucopyranosyl)-(1 → 3)-tetrakis[*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)]-2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside* (**34**).—The product obtained by reaction of **33** (2.09 g, 1.4 mmol) with **24** (1.42 g, 1.7 mmol), as described for the preparation of **25**, was subjected to column chromatography (solvent *4*) to give amorphous **34** (2.58 g, 80%); $[\alpha]_D^{22}$ +37° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.9, 101.3, 101.2 (3 C), 101.0, 100.8, 99.0, 98.3, 97.2, and 96.9 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 6 benzylic C), 56.8 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{123}H_{113}ClO_{38}$: C, 66.11; H, 5.10. Found: C, 65.94; H, 5.22.

Methyl O-*(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)-tetrakis[*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)]-2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside*. (**35**).—*O*-Dechloroacetylation of **34** (1.61 g) by the procedure described above, followed by column chromatography (solvent *5*) of the residue, gave amorphous **35** (1.24 g, 80%); $[\alpha]_D^{22}$ +31° (*c* 1.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.8, 101.7, 102.2 (3 C), 100.6, 98.4 (2 C), 97.2, 97.1, and 97.0 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 6 benzylic C), and 56.8 (OMe). Anal. Calcd for $C_{121}H_{112}O_{37}$: C, 67.34; H, 5.23. Found: C, 67.56; H, 5.11.

Methyl O-*(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-β-*D*-glucopyranosyl)-(1 → 3)-hexakis[*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1 → 3)]-2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside* (**36**).—The product obtained by reaction of **35** (0.94 g, 436 μmol) with **24** (0.43 g, 523 μmol), as described for the preparation of **25**, was subjected to column chromatography (solvent *5*) to give amorphous **36** (1.03 g, 80%); $[\alpha]_D^{22}$ +43° (*c* 1.6, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 102.1, 101.8, 101.2 (3 C), 101.1, 101.05, 101.0, 100.7, 98.9, 98.1, 97.1, 97.05, 96.8 (2 C), and 96.7 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 1^7, 1^8, 8 benzylic C), 56.8 (OMe), and 40.4 ($COCH_2Cl$). Anal. Calcd for $C_{163}H_{149}ClO_{50}$: C, 66.51; H, 5.10. Found: C, 66.74; H, 5.25.

Methyl O-*(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-*O*-acetyl-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-glucopyranoside* (**37**).—To a solution of **27** (0.72 g, 615 μmol) and ethylene glycol (0.69 mL, 12.4 mmol) in MeCN (8 mL) was added *p*-toluenesulfonic acid · H_2O (15 mg). The mixture was stirred overnight at room temperature, made neutral with Et_3N, concentrated, and

extracted with CH_2Cl_2. The extract was washed with H_2O, dried, and concentrated. A solution of the residue in MeOH (15 mL) containing M methanolic NaOMe (0.5 mL) was boiled under reflux for 3 h and then processed as described for the preparation of **16**. The residue was acetylated with 1:1 Ac_2O–pyridine (5 mL) for 1 h at 80°C. The crude product, obtained after removal of the solvents with the aid of repeated additions and evaporations of PhMe, was subjected to column chromatography (solvent *6*) to give amorphous **37** (0.48 g, 83%); $[\alpha]_D^{20}$ −51° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.4, 101.1, and 100.7 (C-1^1, 1^2, 1^3), 79.0 and 78.3 (C-3^1, 3^2), 68.4, 68.2, and 68.1 (C-6^1, 6^2, 6^3), and 56.6 (OMe). Anal. Calcd for $C_{39}H_{54}O_{26}$: C, 49.89, H, 5.80 Found: C, 49.97; H, 5.90.

The sequence of reactions used for **27** was applied to **32**, **29**, **34**, **31**, and **36** to give:

Methyl O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)*-*bis[*O-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)]*-*2,4,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**38**), 81%, amorphous solid; $[\alpha]_D^{20}$ −57° (*c* 1.1., $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.5, 101.0, 100.8, and 100.5 (C-1^1, 1^2, 1^3, 1^4), 78.9, 78.3, and 78.2 (C-3^1, 3^2, 3^3), 62.2, 62.1, 61.95, and 61.7 (C-6^1, 6^2, 6^3, 6^4), and 56.7 (OMe). Anal. Calcd for $C_{51}H_{70}O_{34}$: C, 49.92; H, 5.75. Found: C, 49.84; H, 5.88.

Methyl O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)*-*tris[*O-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)]*-*2,4,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**39**), 82%, amorphous solid; $[\alpha]_D^{20}$ −59° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.5, 101.0, 100.8, 100.6, and 100.5 (C-1^1, 1^2, 1^3, 1^4, 1^5), 78.95, 78.3, and 78.2 (2 C) (C-3^1, 3^2, 3^3, 3^4), 62.2, 62.1, 62.05, 61.9, and 61.7 (C-6^1, 6^2, 6^3, 6^4, 6^5), and 56.7 (OMe). Anal. Calcd for $C_{63}H_{86}O_{42}$: C, 49.94; H, 5.72. Found: C, 50.16; H, 5.88.

Methyl O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)*-*tetrakis[*O-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)]*-*2,4,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**40**), 79%, amorphous solid; $[\alpha]_D^{20}$ −60° (*c* 1.3 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.5, 101.0, 100.8, 100.7 (2 C), and 100.5 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6), 79.0, 78.35 (2 C), 78.3, and 78.25 (C-3^1, 3^2, 3^3, 3^4, 3^5), 62.2, 62.1, 62.0 (2 C), 61.9, and 61.7 (C-6^1, 6^2, 6^3, 6^4, 6^5, 6^6), and 56.75 (OMe). Anal. Calcd for $C_{75}H_{102}O_{50}$: C, 49.95; H, 5.70. Found: C, 49.79; H, 5.80.

Methyl O-*2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)*-*pentakis[*O-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)]*-*2,4,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**41**), 80%, amorphous solid; $[\alpha]_D^{20}$ −61° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 101.45, 101.0, 100.8, 100.7 (3 C), and 100.5 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 1^7), 79.0, 78.4 (2 C), and 78.3 (3 C) (C-3^1, 3^2, 3^3, 3^4, 3^5, 3^6), 62.2, 62.0 (4 C), 61.9, and 61.7 (C-6^1, 6^2, 6^3, 6^4, 6^5, 6^6, 6^7) and 56.7 (OMe). Anal. Calcd for $C_{87}H_{118}O_{58}$: C, 49.95; H, 5.69. Found: C, 50.10; H, 5.77.

Methyl O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)*-*hexakis[*O-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)*-*(1 → 3)]*-*2,4,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**42**), 81%, amorphous solid; $[\alpha]_D^{20}$ −62° (*c* 0.9, $CHCl_3$); ^{13}C NMR: δ 101.5, 101.05, 100.8, 100.7 (4 C), and 100.5 (C-1^1, 1^2, 1^3, 1^4, 1^5, 1^6, 1^7, 1^8), 79.0, 78.3 (4 C), and 78.3 (2 C) (C-3^1, 3^2, 3^3, 3^4, 3^5, 3^6, 3^7), 62.2, 62.0 (5 C), 61.9, and 61.7 (C-6^1, 6^2, 6^3, 6^4,

6^5, 6^6, 6^7, 6^8), and 56.7 (OMe). Anal. Calcd for $C_{99}H_{134}O_{66}$: C, 49.96; H, 5.68. Found: C, 50.14; H, 5.55.

Methyl O-β-D-*glucopyranosyl-(1 → 3)*-O-β-D-*glucopyranosyl-(1 → 3)*-β-D-*glucopyranoside* (**2**).—A solution of **37** (0.37 g) in MeOH (20 mL) containing M methanolic NaOMe (0.5 mL) was boiled under reflux for 2 h, and then processed as described for the preparation of **16**. The residue was purified by elution from a column of Bio-Gel P2 with H_2O to give **2** (0.18 g, 95%); mp 240–242°C (from EtOH–Me_2CO); $[\alpha]_D^{20}$ −29° (*c* 1.1, H_2O); LC: t_R 1.47; ^{13}C NMR (D_2O); δ 103.8 and 103.6 (C-1^1, 1^3), 103.35 (C-1^2), 85.3 (C-3^1), 85.1 (C-3^2), 76.8 (C-5^3), 76.45 and 76.4 (2C), (C-3^3, 5^1, 5^2), 74.3 (C-2^3), 74.0 (C-2^2), 73.6 (C-2^1), 70.4 (C-3^4), 69.0 and 68.95 (C-4^1, 4^2), 61.5 (3 C) (C-6^1, 6^2, 6^3), and 58.05 (OMe). Anal. Calcd for $C_{19}H_{34}O_{16}$: C, 44.02; H, 6.61. Found: C, 44.08; H, 6.70.

Similar *O*-deacetylation of **38–42** afforded:

Methyl O-β-D-*glucopyranosyl-(1 → 3)-bis[*O-β-D-*glucopyranosyl-(1 → 3)]*-β-D-*glucopyranoside* (**3**), 92%, amorphous solid; $[\alpha]_D^{20}$ −27° (*c* 1.5, H_2O); LC: t_R 1.78; ^{13}C NMR (D_2O): δ 103.8 and 103.6 (C-1^1, 1^4), 103.4 (2 C, C-1^2, 1^3), 85.4 (C-3^1), 85.1 (C-3^2), 84.95 (C-3^3), 76.8 (C-5^4), 76.4 (4 C) (C-3^4, 5^1, 5^2, 5^3), 74.3 (C-2^4), 74.1 and 74.05 (C-2^2, 2^3), 73.6 (C-2^1), 70.4 (C-4^4), 69.0, 68.95, and 68.9 (C-4^1, 4^2, 4^3), 61.5 (4 C) (C-6^1, 6^2, 6^3, 6^4), and 58.05 (OMe). Anal. Calcd for $C_{25}H_{44}O_{21}$: C, 44.12; H, 6.52. Found: C, 44.01; H, 6.60.

Methyl O-β-D-*glucopyranosyl-(1 → 3)-tris[*O-β-D-*glucopyranosyl-(1 → 3)]*-β-D-*gluco-pyranoside* (**4**), 91%, amorphous solid; $[\alpha]_D^{20}$ −26° (*c* 1.0, H_2O); LC: t_R 2.19; ^{13}C NMR (D_2O): δ 103.8 and 103.65 (C-1^1, 1^5), 103.4 (3 C) (C-1^2, 1^3, 1^4), 85.4 (C-3^1), 85.2 (C-3^2), 85.0 (2 C) (C-3^3, 3^4), 76.8 (C-5^5), 76.45 and 76.4 (5 C) (C-3^5, 5^1, 5^2, 5^3, 5^4), 74.3 (C-2^5), 74.1 (3C) (C-2^2, 2^3, 2^4), 73.6 (C-2^1), 70.4 (C-4^5), 69.0 and 68.9 (4 C) (C-4^1, 4^2, 4^3, 4^4), 61.55 (5 C) (C-6^1, 6^2, 6^3, 6^4, 6^5), and 58.05 (OMe). Anal. Calcd for $C_{31}H_{54}O_{26}$: C, 44.18; H, 6.46; Found: C, 44.06; H, 6.58.

Methyl O-β-D-*glucopyranosyl-(1 → 3)-tetrakis[*O-β-D-*glucopyranosyl-(1 → 3)]*-β-D-*glucopyranoside* (**5**), 92%, amorphous solid; $[\alpha]_D^{20}$ −25° (*c* 1.2, H_2O); LC: t_R 2.67; ^{13}C NMR (D_2O): δ 103.8 and 103.65 (C-1^1, 1^6), 103.4 (4 C) (C-1^2, 1^3, 1^4, 1^5), 85.4 (C-3^1), 85.2 (C-3^2), 85.0 (3 C) (C-3^3, 3^4, 3^5), 76.8 (C-5^6), 76.45 and 76.4 (6 C) (C-3^6, 5^1, 5^2, 5^3, 5^4, 5^5), 74.3 (C-2^6), 74.1 (4 C) (C-2^2, 2^3, 2^4, 2^5), 73.6 (C-2^1), 70.4 (C-4^6), 69.0 and 68.9 (5 C) (C-4^1, 4^2, 4^3, 4^4, 4^5), 61.5 (6 C) (C-6^1, 6^2, 6^3, 6^4, 6^5, 6^6), and 58.05 (OMe). Anal. Calcd for $C_{37}H_{64}O_{31}$: C, 44.22; H, 6.42. Found: C, 44.14; H, 6.58.

Methyl O-β-D-*glucopyranosyl-(1 → 3)-pentakis[*O-β-D-*glucopyranosyl-(1 → 3)]*-β-D-*glucopyranoside* (**6**), 90%, amorphous solid; $[\alpha]_D^{20}$ −23° (*c* 1.4, H_2O); LC: t_R 3.27; ^{13}C NMR (D_2O): δ 103.8 and 103.6 (C-1^1, 1^7), 103.4 (5 C) (C-1^2, 1^3, 1^4, 1^5, 1^6), 85.35 (C-3^1), 85.1 (C-3^2), 85.0 (4 C) (C-3^3, 3^4, 3^5, 3^6), 76.8 (C-5^7), 76.45 and 76.4 (7 C) (C-3^7, 5^1, 5^2, 5^3, 5^4, 5^5, 5^6), 72.3 (C-2^7), 74.1 (5 C) (C-2^2, 2^3, 2^4, 2^5, 2^6), 73.6 (C-2^1), 70.4 (C-4^7), 69.0 and 68.9 (6 C) (C-4^1, 4^2, 4^3, 4^4, 4^5, 4^6), 61.5 (7 C) (C-6^1, 6^2, 6^3, 6^4, 6^5, 6^6, 6^7), and 58.05 (OMe). Anal. Calcd for $C_{43}H_{74}O_{36}$: C, 44.26; H, 6.39. Found: C, 44.14; H, 6.45.

Methyl O-β-D-glucopyranosyl-(1 → 3)-hexakis[O-β-D-glucopyranosyl-(1 → 3)]-β-D-glucopyranoside (7), 91%, amorphous solid; $[\alpha]_D^{20}$ −21° (*c* 1.0, H_2O); LC: t_R 4.07; ^{13}C NMR (D_2O): δ 103.8 and 103.7 (C-1^1, 1^8), 103.4 (6 C) (C-1^2, 1^3, 1^4, 1^5, 1^6, 1^7), 86.4 (C-3^1), 85.1 (C-3^2), 85.0 (5 C) (C-3^3, 3^4, 3^5, 3^6, 3^7), 76.8 (C-5^8), 76.45 and 76.4 (8 C) (C-3^8, 5^1, 5^2, 5^3, 5^4, 5^5, 5^6, 5^7), 74.3 (C-2^8), 74.1 (6 C) (C-2^2, 2^3, 2^4, 2^5, 2^6, 2^7), 73.6 (C-2^1), 70.4 (C-4^8), 69.0 and 68.9 (7 C) (C-4^1, 4^2, 4^3, 4^4, 4^5, 4^6, 4^7), 61.5 (8 C) (C-6^1, 6^2, 6^3, 6^4, 6^5, 6^6, 6^7, 6^8), and 58.05 (OMe). Anal. Calcd for $C_{49}H_{84}O_{41}$: C, 44.28; H, 6.37. Found: C, 44.16; H, 6.47.

ACKNOWLEDGMENTS

The authors thank Dr. Y. Nitta (University of Osaka Prefecture) and Jeol Ltd. for recording the 270 and 400 MHz NMR spectra, respectively. This work was supported in part by a grant (to K.T.) from Taito Co., Ltd.

REFERENCES

1 S. Kitamura, T. Hori, K. Takeo, T. Kuge, B.T. Stokke, A. Elgsaeter, C. Hara, W. Ito, and K. Tabata, *Abstr. XIIIth Jpn. Carbohydr. Symp.*, (1991) pp 151–152.
S. Kitamura, E. Nakagawa, M. Yoshikawa, and K. Takeo, *Nippon Nogei Kagaku Kaishi*, 66 (1992) 303; T. Hori, S. Kitamura, B.T. Stokke, M. Mimura, K. Kajihara, S. Ohno, and K. Takeo, *ibid.*, 66 (1992) 305; B.T. Stokke, A. Elgsaeter, C. Hara, S. Kitamura, and K. Takeo, *Biopolymers*, (1993) in press.
2 P. Bächli and E.G.V. Percival, *J. Chem. Soc.*, (1952) 1243–1246.
3 K. Takeo, *Carbohydr. Res.*, 77 (1979) 241–251.
4 P.M. Collins and M.H. Ali, *Tetrahedron Lett.*, 31 (1990) 4517–4520.
5 W.J. Whelan, *Methods Carbohydr. Chem.*, 1 (1962) 330–333.
6 L.-X. Wang, N. Sakairi, and H. Kuzuhara, *Carbohydr. Res.*, 219 (1991) 133–148.
7 K. Takeo and S. Tei, *Carbohydr. Res.*, 145 (1986) 293–306.
8 M. Bertolini and C.P.J. Glaudemans, *Carbohydr. Res.*, 15 (1970) 263–270.
9 K.P.R. Kartha, A. Kameyama, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 145–158.
10 S. Hanessian and J. Banoub, *Methods Carbohydr. Chem.*, 8 (1980) 247–250.
11 P. Fügedi, W. Birberg, P.J. Garegg, and A. Pilotti, *Carbohydr. Res.*, 164 (1987) 297–312.
12 Y. Kondo, *Agric. Biol. Chem.*, 41 (1977) 2089–2090, and references therein.
13 S. Kim, H. Chang, and W.J. Kim, *J. Org. Chem.*, 50 (1985) 1751–1752.
14 P. Brigl, K. Gronemeier, and A. Shulz, *Ber.*, 72 (1939) 1052–1059.
15 M.-O. Contour, J. Defaye, M. Little, and E. Wong, *Carbohydr. Res.*, 193 (1989) 283–287.
16 E. Pacsu, *Ber.*, 61 (1928) 137–144; J. Banoub and D.R. Bundle, *Can. J. Chem.*, 57 (1979) 2085–2090.
17 M.E. Evans, *Carbohydr. Res.*, 21 (1972) 168–169.
18 M.L. Wolfrom and W. Groebke, *J. Org. Chem.*, 28 (1963) 2986–2988; P. Kováč and L. Lerner, *Carbohydr. Res.*, 184 (1988) 87–112.
19 K. Jansson and G. Magnusson, *Tetrahedron*, 46 (1990) 59–64.
20 P. Fügedi and P.J. Garegg, *Carbohydr. Res.*, 149 (1986) c9–c11.
21 P. Konradsson, U.E. Udodong, B. Fraser-Reid, *Tetrahedron Lett.*, 31 (1990) 4313–4316; G.H. Veeneman, S.H. van Leeuwen, and J.H. van Boom, *ibid.*, 31 (1990) 1331–1334.
22 P. Kováč, H.J.C. Yeh, and C.P.J. Glaudemans, *Carbohydr. Res.*, 140 (1985) 277–288.
23 P.M. Collins, D. Gardier, S. Kumar, and W.G. Overend, *J. Chem. Soc., Perkin Trans. 1*, (1972) 2596–2610.
24 H. Lönn, *J. Carbohydr. Chem.*, 6 (1987) 301–306.

25 M. Nilsson and T. Norberg, *Carbohydr. Res.*, 183 (1988) 71–82.
26 D.E. Dorman and J.D. Roberts, *J. Am. Chem. Soc.*, 92 (1971) 1355–1361.
27 T.C. Wong, W. Haque, S.Z. Abbas, and A.A. Noujaim, *J. Carbohydr. Chem.*, 9 (1990) 745–753.
28 K. Takeo, T. Nakaji, and K. Shinmitsu, *Carbohydr. Res.*, 133 (1984) 275–287;
Z. Szurmai, A. Liptâk, and G. Snatzke, *ibid.*, 200 (1990) 201–208, and references therein.