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EFFICIENT CHEMICAL SYNTHESIS OF METHYL β-GLYCOSIDES OF β-(1→6)-LINKED D-GALACTO-OLIGOSACCHARIDES BY A STEPWISE AND A BLOCKWISE APPROACH*†

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ABSTRACT

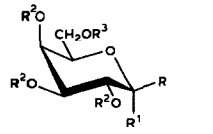
Bromoacetylation of methyl 2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (**1**) followed by cleavage of the methoxyl group from the resulting 6-*O*-bromoacetyl derivative **2** with 1,1-dichloromethyl methyl ether gave 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-α-D-galactopyranosyl chloride (**3**). Reaction of **3** with **1**, promoted by silver trifluoromethanesulfonate, afforded methyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (**12**), bearing at O-6 of its non-reducing end-group the selectively removable bromoacetyl group. This was *O*-debromoacetylated and the disaccharide nucleophile **15** formed was again treated with **3**, to give the analogous trisaccharide **18**. This sequence of reactions was repeated to afford the analogous tetrasaccharide **20**, showing the feasibility of stepwise construction of the title oligosaccharides. Similar reactions of **3** with 1,2,3,4-tetra-*O*-benzoyl-α- (**7**) and β-D-galactopyranose (**5**) gave, respectively, *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-D-galactopyranosyl)-(1→6)-1,2,3,4-tetra-*O*-benzoyl-α- (**14**) and β-D-galactopyranose (**13**). These could be separately converted into the same glycosyl halide, namely, α-(2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranosyl chloride (**16**), by cleavage with 1,1-dichloromethyl methyl ether. The chloride **16** was treated with tri- and tetra-saccharide nucleophiles analogous to **15** to give, respectively, the corresponding pentasaccharide **23** and the hexasaccharide **25**, demonstrating the possibility of the blockwise construction of higher β-(1→6)-linked D-galacto-oligosaccharides. The disaccharide **12** was also obtained by the reaction of 1,2,3,4-tetra-*O*-benzoyl-6-*O*-bromoacetyl-β-D-galactopyranose (**6**) with **1** in the presence of trimethylsilyl trifluoromethanesulfonate. Similarly, the trisaccharide **18** and the tetrasaccharide **20** were obtained by the treatment of **13**, respectively, with **1** and **15**, showing that, as with their 1-*O*-acetyl counterparts, β-1-benzoates of saccharides bearing at O-2 a group capable of neighboring-group participation can act under these conditions as

*Dedicated to Dr. Štefan Bauer, Dr. Sc.
†For a preliminary report of this work, see ref. 1.

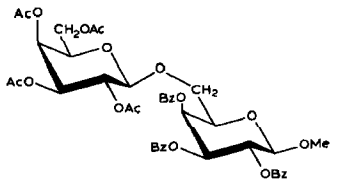
glycosyl donors. Crystalline methyl β-glycosides of (1→6)-β-D-galacto-tetraose (**22**), -pentaose (**24**) and -hexaose (**27**) have been obtained for the first time, by deacylation (Zemplén) of their fully protected precursors.

INTRODUCTION

Continuing studies on the interaction of (1→6)-β-D-galactan-specific monoclonal antibodies[2,3] with saccharides requires a series of methyl β-glycosides of (1→6)-β-D-galacto-oligosaccharides. Several approaches for synthesizing ligands of this type have been described, but difficulties prevented the synthesis of higher members of this series. The first systematic attempts were by Schuerch *et al.*, and



	R	R^1	R^2	R^3
1	OMe	H	Bz	H
2	OMe	H	Bz	$COCH_2Br$
3	H	Cl	Bz	$COCH_2Br$
4	H	OMe	Bz	$COCH_2Br$
5	OBz	H	Bz	H
6	OBz	H	Bz	$COCH_2Br$
7	H	OBz	Bz	H
8	OAc	H	Ac	Ac
9	H	Br	Bz	Bz
10	OMe	H	Bz	Ac



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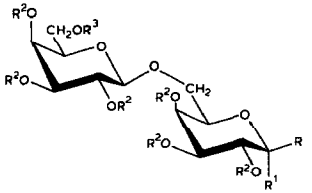
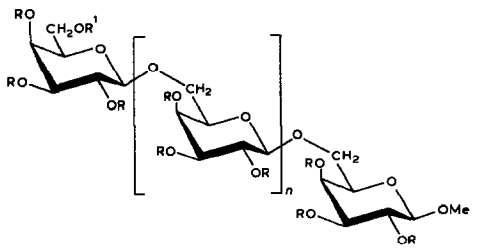


	R	R^1	R^2	R^3
12	OMe	H	Bz	$COCH_2Br$
13	OBz	H	Bz	$COCH_2Br$
14	H	OBz	Bz	$COCH_2Br$
15	OMe	H	Bz	H
16	H	Cl	Bz	$COCH_2Br$



	n	R	R^1
17	1	Bz	Bz
18	1	Bz	$COCH_2Br$
19	1	Bz	H
20	2	Bz	$COCH_2Br$
21	2	Bz	H
22	2	H	H
23	3	Bz	$COCH_2Br$
24	3	H	H
25	4	Bz	$COCH_2Br$
26	4	Bz	H
27	4	H	H

6-*O*-acetyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-*O*-tosyl-α-D-galactopyranose[4,5] or the 1-*O*-[(2,2,2-trifluoroethyl)sulfonyl] derivative[5] of a β-linked (1→6)-D-galactobiose were used as glycosyl donors. The preparation of 2,3,4-tri-*O*-acetyl-6-*O*-chloroacetyl-α-D-galactopyranosyl bromide in this laboratory and its use in the synthesis of (1→6)-β-D-galactobiose and galactotriose has been reported[6]. Recently, we have used[7] this bromide in the syntheses of related substances, but have found that *O*-dechloroacetylation was accompanied by extensive migration of acetyl groups present at other positions in the substrates. This difficulty was eliminated by temporarily protecting O-6 in the intermediates with the more readily removable *bromo*acetyl[8], instead of the chloroacetyl group. Using 2,3,4-tri-*O*-acetyl-6-*O*-bromoacetyl-α-D-galactopyranosyl bromide[9], a series of monofluorinated β-(1→6)-linked D-galacto-oligosaccharides, up to a tetrasaccharide, were synthesized[10]. The only fair yields[10] (~40–65%) of the desired products were attributed to transesterification that accompanied the silver trifluoromethanesulfonate (triflate)-promoted glycosylation reactions. This resulted in the formation of 6-*O*-acetylated nucleophiles at the expense of the target oligosaccharides. Recently, this difficulty has been overcome, and excellent yields of the desired disaccharides in the foregoing series were obtained[11,12] by using silver triflate and 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-α-D-galactopyranosyl bromide, respectively, as the promotor and the glycosyl donor. Here, we describe a further improvement in the synthesis of β-(1→6)-linked D-galacto-oligosaccharides, based on the use as glycosyl donors of the readily obtainable 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-α-D-galactopyranosyl chloride (**3**) and the appropriately protected glycosyl chloride (**16**) derived from β-(1→6)-linked-D-galactobiose.

RESULTS AND DISCUSSION

2,3,4-Tri-*O*-benzoyl-6-*O*-bromoacetyl-α-D-galactopyranosyl bromide proved to be an excellent glycosyl donor, but its large-scale preparation[11] required for the stepwise construction of oligosaccharides is somewhat tedious. It requires isolation of all intermediates by chromatography involving, *inter alia,* the separation of four isomeric tetra-*O*-benzoyl-D-galactoses to remove from the crude product the furanoid isomers formed during the benzoylation of 6-*O*-trityl-D-galactose. In the search for a more-efficient source of a related glycosylating reagent, we have now prepared 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-α-D-galactopyranosyl chloride (**3**): methyl 2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside[13] (**1**) was bromoacetylated under standard conditions[9,11] and the resulting 6-*O*-bromoacetyl derivative **2** was cleaved with 1,1-dichloromethyl methyl ether (DCMME) to yield **3** in 84% yield. As in the case of the cleavage[14] of methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranoside, the reaction was accompanied by anomerization. The methyl α-glycoside **4** formed was cleaved by DCMME much more slowly than **2** and it was impractical to prolong the reaction time until all **4** would be consumed. Consequently, **4** was isolated by chromatography in low yield from the crude product. The preparation

of **3** makes use of the commercially available DCMME and can be readily performed on a large scale. Chloride **3** has a long shelf-life and reacts smoothly in the silver triflate-promoted glycosylation reactions. In fact, in its reactions leading to the disaccharides **12–14**, and the trisaccharide **18**, the desired compounds were practically the only products formed, and they could be isolated from the crude products in excellent yields by crystallization, without recourse to chromatography.

The lower members of the title series of glycosides were first synthesized by a stepwise approach. Thus, the reaction of the initial nucleophile **1** with the chloride **3** gave the disaccharide **12** (91%) which was smoothly *O*-debromoacetylated to give the disaccharide nucleophile **15** having HO-6′ available to further glycosylation. Similar condensation of **3** with **15** and **19**, the latter being obtained by *O*-debromoacetylation of **18**, yielded the oligosaccharides **18** and **20** in 89 and 78% yield, respectively. Ogawa *et al.*[15] and Paulsen *et al.*[16,17] have reported stereospecific glycosylation promoted by trimethylsilyl (Me_3Si) triflate using as glycosyl donors β-1-acetates of sugars that bear at position O-2 substituents capable of neighboring-group participation. This methodology bypasses the preparation of glycosyl halides, and constitutes the most recent practical improvement in the synthesis of 1,2-*trans*-linked oligosaccharides. We have found that the corresponding 1-benzoates react similarly. Thus, the Me_3Si triflate-catalyzed reaction of the benzoate[11] **6** with **1** gave the disaccharide **12** in good yield.

To pursue the blockwise approach to the title oligosaccharides, two new glycosyl donors have been prepared, namely the disaccharide **13** and the glycosyl chloride **16**. The glycosylating ability of **13** was tested in the synthesis of trisaccharide **18** and tetrasaccharide **20**, and compared to those of the chlorides **3** and **16**. As fewer by-products were formed in reactions involving halides **3** and **16**, in the syntheses of the pentasaccharide **23** and the hexasaccharide **25** the crystalline disaccharide halide **16**, obtained readily from **13** or **14** by cleavage with DCMME, was used.

Paulsen's successful use[16,17] of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (**8**) as a glycosyl donor in the Me_3Si triflate-catalyzed glycosylations suggested that this inexpensive, commercially available glycosylating reagent could be used to form non-reducing β-D-galactopyranosyl end-group of the oligosaccharides described here. The reaction of **8** with methyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranoside[18] in the presence of Me_3Si triflate yielded[19] only a mixture of products, because of extensive migration of acetyl groups present in the nucleophile. Similar reaction of **8** with **1** was successful, but afforded the desired disaccharide derivative **11** in 54% yield only. The glycosylation was accompanied by a transesterification side-reaction, yielding methyl 6-*O*-acetyl-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (**10**), isolated crystalline in 28% yield. The formation of acetates of nucleophiles as by-products of triflate-catalyzed glycosylation reactions that involved acetylated glycosyl donors has been reported[10,20]. No such side-reaction was observed when the β-D-galactopyranosyl end-group was constructed by using 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (**9**), as exemplified in the preparation of the trisaccharide **17**.

Simultaneous *O*-debromoacetylation and debenzoylation of **20**, **23**, and **25**, which gave, respectively, the hitherto unknown title glycosides **22** (84%), **24** (78%), and **27** (90%) was achieved with sodium methoxide in toluene–methanol at 60–100°. Losses were due only to manipulation. Cleavage of the interglycosidic linkages, observed by others[5,21,22] during similar deacylations, was not observed.

EXPERIMENTAL

General methods. — Melting points were determined with a Büchi melting-point apparatus. Optical rotations were measured at 25° with a Perkin–Elmer automatic polarimeter, Model 241 MC. Thin-layer chromatography (t.l.c.) on pre-coated plates of silica gel (Analtech) was performed with mixtures of appropriately adjusted polarity consisting of *A*, toluene–acetone; *B*, carbon tetrachloride–acetone; *C*, dichloromethane–acetone; *D*, toluene–ethyl acetate, and *E*, chloroform–acetone. Detection was effected by charring with 5% (v/v) sulfuric acid in ethanol and, where applicable, by u.v. light. Preparative chromatography was performed by gradient elution from slurry-packed columns of Silica Gel 60 (Merck, Prod. No. 9385, 0.04–0.063 mm, or Prod. No. 1511, 0.015–0.04 mm). Except for the purification of glycosyl chlorides, the silica gel was deactivated[23] by addition of 5–10% of water.

^{1}H-N.m.r. and ^{13}C-n.m.r. spectra were recorded at room temperature for solutions in $CDCl_3$ (internal standard Me_4Si) or D_2O (internal standard MeOH, δ_{MeOH} *vs.* Me_4Si, 49.0 p.p.m.) with Varian FX-100, Varian HR-220 and Varian FX-300. The frequencies of measurements are listed, as required. Proton-signal assignments were made by first-order analysis of the spectra, comparison of their spectra with those of related compounds and, where feasible, by homonuclear selective decoupling. Carbon-signal assignments were made by mutual comparison of the spectra of related substances described here and elsewhere[7,11,18,24,25].

Trimethylsilyl trifluoromethanesulfonate was purchased from Aldrich Chemical Co., and used as supplied. Silver trifluoromethanesulfonate was obtained from Aldrich Chemical Co., and dried at 100°/133 Pa for 8 h. Dichloromethane of h.p.l.c. purity was dried before use with $CaCl_2$. Chloroform was washed consecutively with concentrated sulfuric acid (twice), water, dried with phosphorus pentaoxide, and distilled. Acetonitrile was dried with calcium hydride and distilled. Reactions requiring anhydrous conditions were performed under argon using common laboratory glassware, and reagents and solvents were handled with Hamilton, Series 1000 gas-tight syringes. Solutions in organic solvents were dried with anhydrous sodium sulfate and evaporated at 40°/2 kPa.

Methyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**11**). — Trimethylsilyl triflate (0.02 mL) was added at room temperature to a stirred solution of **8** (780 mg, 2 mmol) and **1** (1.12 g, 2 mmol), and the mixture was stirred at room temperature for 1 h. Two products were formed, as shown by t.l.c. (solvent *A*), one slightly slower and one much

faster-moving than **8**. The mixture was processed as described for the preparation of **12** (*a*) and the crude product was chromatographed to give first **10** (0.35 g, 28%), m.p. 127–128° (from ethanol), $[\alpha]_D$ +173° (*c* 0.78, chloroform; ^{1}H-n.m.r. (220 MHz, in $CDCl_3$): δ 5.88 (bd, 1 H, $J_{4,5}$ 1 Hz, H-4), 5.76 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 5.56 (dd, 1 H, $J_{3,4}$ 3 Hz, H-3), 4.71 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.40–4.15 (m, 3 H, H-5,6a,6b), 3.59 (s, 3 H, OCH_3), and 2.04 (s, 3 H, $COCH_2$).

Anal. Calc. for $C_{30}H_{28}O_{10}$: C, 65.68; H, 5.14. Found: C, 65.58; H, 5.20.

Eluted next was the disaccharide **11** (1 g, 54%), m.p. 215–216° (from ether), $[\alpha]_D$ +106° (*c* 1.1, chloroform); ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 5.85 (bd, 1 H, $J_{4,5}$ <1 Hz, H-4), 5.75 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 5.54 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 5.35 (bd, 1 H, $J_{4',5'}$ <1 Hz, H-4'), 5.21 (dd, 1 H, $J_{2',3'}$ 10 Hz, H-2'), 4.98 (dd, 1 H, $J_{3',4'}$ 3 Hz, H-3'), 4.70 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.56 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'), 4.23–3.78 (m, 6 H, H-5,5',6a,6b,6'a,6'b), and 3.60 (s, 3 H, OCH_3), 2.15, 2.06, 1.99 (3 × s, 9 H, 3 × $COCH_3$); ^{13}C-n.m.r. (25 MHz in $CDCl_3$): δ 102.4 (C-1), 102.0 (C-1'), 73.1 (C-5), 71.8 (C-3), 70.9, 70.8 (C-5,3'), 69.7 (C-2), 68.7, 68.6 (C-2', C-4), 67.7 (C-6), 67.0 (C-4'), 61.2 (C-6'), and 57.2 (OCH_3).

Anal. Calc. for $C_{42}H_{44}O_{18}$: C, 60.28; H, 5.30. Found: C, 60.35; H, 5.34.

*Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-bromoacetyl-β-*D*-galactopyranoside* (**2**). — Bromoacetyl bromide (8.8 mL, 100 mmol) was added dropwise at −20° to a stirred solution of **1** (35.5 g, 70 mmol) and 2,6-dimethylpyridine (13.6 mL, 115 mmol) in dichloromethane (350 mL). After 15 min, t.l.c. (solvent *A*) showed that no starting material was present and that a single product had been formed. The mixture was partitioned between ice–water and dichloromethane, the dichloromethane solution was washed with aqueous $NaHCO_3$, dried and decolorized by elution from a short column of silica gel (solvent *A*), to give pure, amorphous **2** (41 g, 93.2%), $[\alpha]_D$ +159° (*c* 1.2, chloroform); ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 5.90 (bd, 1 H, $J_{4,5}$ <1 Hz, H-4), 5.78 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 5.57 (dd, 1 H, $J_{3,4}$ 3 Hz, H-3), 4.73 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.50–4.20 (m, 3 H, H-5,6a,6b), 3.81 (s, 2 H, $COCH_2Br$), and 3.59 (s, 3 H, OCH_3); ^{13}C-n.m.r. (25 MHz in $CDCl_3$): δ 102.3 (C-1), 71.6 (C-3), 71.0 (C-5), 69.5 (C-2), 68.0 (C-4), 63.4 (C-6), 57.3 (OCH_3), and 25.2 (CH_2Br).

Anal. Calc. for $C_{30}H_{27}BrO_{10}$: C, 57.42; H, 4.33; Br, 12.73. Found: C, 57.37; H, 4.31; Br, 12.50.

*2,3,4-Tri-*O*-benzoyl-6-*O*-bromoacetyl-α-*D*-galactopyranosyl chloride* (**3**). — Freshly fused $ZnCl_2$ (~70 mg) was added to a solution of **2** (4.5 g) in DCMME* (9 mL) and the mixture was stirred at 80–85° (bath) in a round-bottomed flask, equipped with an efficient condenser and a Drierite drying tube. Two faster-migrating products were initially formed, in the ratio of ~1:1, as shown by t.l.c. (solvent *B*). After 8–10 h, when the mixture contained only traces of unchanged **2**, the mixture was concentrated with concomitant evaporation of toluene and the residue was eluted from a column of silica gel to give first the desired chloride **3** as

*Dichloromethyl methyl ether (DCMME) is a suspect carcinogen[26] and all operations involving this reagent should be conducted in a well-ventilated hood.

a colorless, amorphous solid (3.8 g, 84%), $[\alpha]_D$ +218° (*c* 1.6, chloroform); ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 6.63 (d, 1 H, 5 Hz, H-1), 6.12–5.78 (m, 3 H, H-2,3,4), 4.84 (bt, 1 H, $J_{5,6a}$ = 6.5 Hz, H-5), 4.38 (d, 2 H, H-6a,6b), and 3.79 (s, 2 H, $COCH_2Br$); ^{13}C-n.m.r. (25 MHz in $CDCl_3$): δ 91.3 (C-1), 69.7 (C-5), 68.5 (C-3), 68.1 (C-4), 67.8 (C-2), 63.0 (C-6), and 24.9 (CH_2Br).

Anal. Calc. for $C_{29}H_{24}BrClO_9$: C, 55.12; H, 3.82; Br, 12.64; Cl, 5.76. Found: C, 55.05; H, 3.82; Br, 12.65; Cl, 5.61.

Eluted next was the amorphous α-glycoside **4** (270 mg, 6%), $[\alpha]_D$ +186° (*c* 1, chloroform); ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 6.01–5.61 (m, 3 H, H-2,3,4), 5.30 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.50 (bt, 1 H, $J_{5,6a}$ = 6.5 Hz, H-5), 4.44–4.27 (m, 2 H, H-6a,6b), 3.79 (s, 2 H, $COCH_2Br$), and 3.47 (s, 3 H, OCH_3).

Anal. Calc. for $C_{30}H_{27}BrO_{10}$: C, 57.42; H, 4.33; Br, 12.73. Found: C, 57.15; H, 4.48; Br, 12.55.

Methyl O-(2,3,4-tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**12**). — (*a*) Trimethylsilyl triflate (1,5 mL, 7.76 mmol) was added dropwise at −5° to a stirred solution of **1** (1.52 g, 3 mmol) and **6** (2.18 g, 3 mmol) in dichloromethane (30 mL). After 1.5 h, when t.l.c. (solvent *A*) showed that the reaction was almost complete and that one major product was formed, solid $NaHCO_3$ was added, and the suspension was stirred until neutral (~15 min). After filtration, the dichloromethane solution was washed with aqueous NaCl solution, dried, and evaporated. Crystallization from toluene–ether yielded **12** (2.2 g). The material in the mother liquor was chromatographed to give more **12** (0.34 g, total yield 77%). Recrystallization of a portion gave the analytical sample of **12**, m.p. 258–259°, $[\alpha]_D$ +158° (*c* 0.7, chloroform). ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 5.88, 5.84 (2 × bd, 2 × 1 H, $J_{4,5} = J_{4',5'}$ <1 Hz, H-4,4'), 5.77, 5.69 (2 × dd, 2 × 1 H, $J_{2,3} = J_{2',3'}$ = 10 Hz, H-2,2'), 5.59–5.48 (m, 2 H, H-3,3'), 4.87 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'), 4.56 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.27–3.80 (m, 6 H, H-5,5',6a,6b,6'a,6'b), 3.69 (s, 2 H, $COCH_2Br$), and 3.25 (s, 3 H, OCH_3); ^{13}C-n.m.r. (25 MHz in $CDCl_3$): δ 102.2 (C-1), 101.3 (C-1'), 73.1 (C-5), 71.6, 71.5 (C-3,3'), 71.1 (C-5'), 69.7 (C-2'), 69.6 (C-2), 68.7 (C-4), 68.3 (C-6), 67.9 (C-4'), 63.2 (C-6'), 56.8 (OCH_3), and 24.9 (CH_2Br).

Anal. Calc. for $C_{57}H_{49}BrO_{18}$: C, 62.12; H, 4.48; Br, 7.25. Found: C, 62.04; H, 4.51; Br, 7.34.

(*b*) A solution of **1** (2.53 g, 5 mmol), **3** (3.79 g, 6 mmol) and 2,4,6-trimethylpyridine (0.727 mL, 5.5 mmol) in dichloromethane (20 mL) was added at room temperature to a suspension of silver triflate (1.7 g, 6.6 mmol) in dichloromethane (20 mL). Silver chloride started to separate almost immediately, the mixture turned acidic after ~15 min and, after a further 5 min, the solution was made neutral with 2,4,6-trimethylpyridine. T.l.c. (solvent *A*) showed that both starting compounds reacted completely, and that one major product was formed. The mixture was filtered, the solids wahed with CH_2Cl_2, and the combined filtrates were washed with aqueous $Na_2S_2O_3$, water, and evaporated. Crystallization from toluene–ether gave product **12** (5.01 g, 91%), m.p. 258–260°. T.l.c. of the material that remained in the mother liquor showed that it contained little of the same compound.

O-(2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-1,2,3,4-tetra-O-benzoyl-β-D-galactopyranose (**13**). — A solution of **3** (7.88 g, 12.5 mmol), **5** (6.2 g, 10.4 mmol), and 2,4,6-trimethylpyridine (1.6 mL, 12.1 mmol) in CH_2Cl_2 (50 mL) was added to a stirred mixture of silver triflate (3.85 g, 15 mmol) in CH_2Cl_2 (30 mL). The mixture turned acidic after ~15 min, and it was made neutral with 2,4,6-trimethylpyridine after an additional 10 min. After processing as described for the preparation of **12** (*b*), the solution of the crude product in dichloromethane was concentrated to a crystalline slurry and crystallization was completed by addition of ethanol to give **13** (10.64 g, 85.8%). Recrystallization of a portion gave the analytical sample, m.p. 128–129°, $[\alpha]_D$ +138° (*c* 0.7, chloroform); ^{1}H-n.m.r. (220 MHz in $CDCl_3$): δ 6.17 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 6.01 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 6.00 (bd, 1 H, $J_{4,5}$ <1 Hz, H-4), 5.80 (bd, 1 H, $J_{4',5'}$ <1 Hz, H-4'), 5.74 (dd, 1 H, $J_{2',3'}$ 10 Hz, H-2'), 5.69 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 5.51 (dd, 1 H, $J_{3',4'}$ 3.5 Hz, H-3), 4.39 (bt, 1 H, $J_{5',6'a} = J_{5,6'b}$ = ~6 Hz, H-5'), 4.22–3.90 (m, 5 H, H-5,6a,6b,6'a,6'b), and 3.66 (s, 2 H, CH_2Br); ^{13}C-n.m.r. (25 MHz in $CDCl_3$: δ 100.6 (C-1'), 93.1 (C-1), 74.3 (C-5), 71.7, 71.5 (C-3,3'), 71.0 (C-5'), 69.5 (C-2'), 68.8 (C-2), 68.2 (C-4), 67.8 (C-4'), 66.5 (C-6), 63.2 (C-6'), and 25.2 (CH_2Br).

Anal. Calc. for $C_{63}H_{51}BrO_{19}$: C, 63.47; H, 4.31; Br, 6.70. Found: C, 63.34; H, 4.34; Br, 6.80.

1,2,3,4-Tetra-O-benzoyl-α-D-galactopyranose (**7**). — A solution of crystalline[11] 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-α-D-galactopyranose (0.84 g, 1 mmol) in dichloromethane (5 mL) was added to a solution of sodium iodide (0.45 g, 3 mmol) in dry acetonitrile (10 mL). The solution was cooled in an ice bath and chlorotrimethylsilane (0.4 mL, 3.15 mmol) was added with stirring. Water (5 mL) was added after 3 min, and the mixture was partitioned between dichloromethane and aqueous sodium thiosulfate. The colorless organic phase was evaporated and the residue was eluted from a column of silica gel (solvent *B*) to give pure **7** (0.55 g, 92%) as a colorless foam, $[\alpha]_D$ +281° (*c* 1.85, chloroform); ^{1}H-n.m.r. (220 MHz, in $CDCl_3$): δ 6.90 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 6.15–5.99 (m, 3 H, H-2,3,4), 4.56 (t, $J_{5,6} = J_{5,6'}$ = 6.5 Hz, H-5), 3.80, 3.65 (2 × dd, 2 H, $J_{6,6'}$ 11.5 Hz, H-6,6'), and 2.61 (bs, 1 H, disappears on deuteration, OH).

Anal. Calc. for $C_{34}H_{28}O_{10}$: C, 68.44; H, 4.73. Found: C, 68.12; H, 4.75.

O-(2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-1,2,3,4-tetra-O-benzoyl-α-D-galactopyranose (**14**). — A solution of **7** (3 g, 5.03 mmol), **3** (3.8 g, 6 mmol), and 2,4,6-trimethylpyridine (0.72 mL, 5.5 mmol) in dichloromethane (25 mL) was added at room temperature to a suspension of silver triflate (1.67 g, 6.5 mmol) in dichloromethane (25 mL). When t.l.c. (solvent *A*) showed that all **3** had been consumed (~20 min), the mixture was processed as described for the preparation of **12** (*b*), and crystallization from dichloromethane–ether gave **14** (5 g, 83%). After recrystallization from the same solvent, the disaccharide **14** melted at 216–216.5° and showed $[\alpha]_D$ +190° (*c* 0.65, chloroform); ^{1}H-n.m.r. (300 MHz in $CDCl_3$): δ 6.80 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 6.12 (bd, 1 H, $J_{4,5}$ <1 Hz, H-4), 6.04 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 5.92 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-2),

5.79 (bd, 1 H, $J_{4',5'}$ <1 Hz, H-4'), 5.70 (dd, 1 H, $J_{2',3'}$ 10.3 Hz, H-2'), 5.48 (dd, 1 H, $J_{3',4'}$ 3.4 Hz, H-3'), 4.86 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.70 (bt, 1 H, $J_{5,6a} = J_{5,6b}$ = 5.9 Hz, H-5), 4.19–3.90 (m, 5 H, H-5',6a,6b,6'a,6',b), and 3.71 (s, 2 H, CH_2Br); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 100.94 (C-1'), 90.69 (C-1), 71.66 (C-3'), 71.08 (2C, C-5,5'), 69.49 (C-2'), 68.71, 68.55 (C-3,4), 67.86 (2C, C-2,4'), 67.13 (C-6), 63.11 (C-6'), and 25.21 (CH_2Br).

Anal. Calc. for $C_{63}H_{51}BrO_{19}$: C, 63.47; H, 4.31; Br, 6.20. Found: C, 63.20; H, 4.44; Br, 6.91.

Methyl O-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**15**). — A solution of thiourea (230 mg, 3 mmol) in methanol (10 mL) was added to a stirred solution of **12** (1.1 g, 1 mmol) in CH_2Cl_2 (20 mL). After 40 min, t.l.c. (solvent *A*) showed that only traces of **12** were present and that a slower-moving product had been formed. The mixture was partitioned between CH_2Cl_2 and aqueous NaCl, the organic phase was dried, and evaporated, and the residue was eluted from a short column of silica gel (solvent *C*), to remove some non-carbohydrate, base-line material, to give **15** (0.9 g, 92%), m.p. 139–140° (from CH_2Cl_2-ethanol), $[\alpha]_D$ +186° (*c* 1, chloroform); ^{1}H-n.m.r. (220 MHz in 1:10 MeOD–$CDCl_3$): δ 5.89, 5.85 (2 × bd, 2 × 1 H, $J_{4,5} = J_{4',5'}$ = <1 Hz, H-4,4'), 5.77, 5.67 (2 × dd, 2 × 1 H, $J_{2,3} = J_{2',3'}$ = 10.5 Hz, H-2,2'), 5.61–5.50 (m, 2 H, H-3,3'), 4.90 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.53 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.26–3.83 (m, 4 H, H-5,5',6a,6b), 3.71–3.48 (m, 2 H, H-6'a,6'b), and 3.25 (s, 3 H, OCH_3); in pure $CDCl_3$, the signal of OH appears as a bd at 2.93 p.p.m.; ^{13}C-n.m.r. (25 MHz in $CDCl_3$): δ 102.2 (C-1), 101.4 (C-1'), 74.1 (C-5'), 73.0 (C-5), 71.7 (2C, C-3,3'), 70.0, 69.8 (C-2,2'), 68.8 (C-4), 68.7 (C-4'), 68.2 (C-6), 60.6 (C-6'), and 56.9 (OCH_3).

Anal. Calc. for $C_{55}H_{48}O_{17}$: C, 67.33; H, 4.93. Found: C, 67.31; H, 4.97.

O-(2,3,4-Tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-α-D-galactopyranosyl chloride (**16**). — (*a*) DCMME (2 mL) followed by freshly fused $ZnCl_2$ (10 mg) was added to a solution of **13** (1.12 g, 1 mmol) in chloroform (2 mL), and the mixture was stirred for 45 min at 45–50° under the conditions described for the preparation of **3**. T.l.c. (solvent *B*) showed that all starting material was consumed and that a single, faster-moving product was formed. Toluene (10 mL) was added, the mixture was evaporated, and the residue was partitioned between dichloromethane and aqueous NaCl containing a little $NaHCO_3$. The organic layer was dried, evaporated, and the solid residue was crystallized from acetone–ether to give **16** (0.8 g), sufficiently pure for the next step. The material in the mother liquor was chromatographed to give more **16** (55 mg, total yield 85%), m.p. 225–227°, $[\alpha]_D$ +236° (*c* 0.4, chloroform); ^{1}H-n.m.r. (300 MHz in $CDCl_3$): δ 6.47 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 6.04 (bd, 1 H, $J_{4,5}$ <1 Hz, H-4), 5.99 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 5.86 (bd, 1 H, $J_{4',5'}$ <1 Hz), 5.78 (dd, 1 H, $J_{2',3'}$ 10.7 Hz, H-2'), 5.75 (dd, 1 H, $J_{2,3}$ 10.7 Hz, H-2), 5.56 (dd, 1 H, $J_{3',4'}$ 3.4 Hz, H-3'), 4.90 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.80 (bt, 1 H, $J_{5,6a} = J_{5,6b}$ = ~6 Hz, H-5), 4.15, 3.92 (2 × dd, $J_{6a,6b}$ 11 Hz, H-6a,6b), and 3.72 (s, 2 H, CH_2Br); ^{13}C-n.m.r.

(25 MHz in $CDCl_3$): δ 101.4 (C-1'), 91.3 (C-1), 71.6 (2C, C-5,3'), 71.1 (C-5), 69.5 (C-2'), 68.9, 68.5 (C-3,4), 67.9 (2C, C-2,4'), 67.3 (C-6), 63.2 (C-6'), and 25.2 (CH_2Br).

Anal. Calc. for $C_{56}H_{46}BrClO_{17}$: C, 60.79; H, 4.19; Br, 7.22; Cl, 3.20. Found: C, 60.67; H, 4.32; Br, 7.27; Cl, 3.23.

(*b*) DCMME (15 mL) followed by freshly fused zinc chloride (50 mg) was added to a solution of **14** (4.96 g) in chloroform (10 mL) and the mixture was stirred for 1 h at 65–70°. Toluene (20 mL) was added and, after evaporation, the residue was chromatographed (solvent *B*) to give the major product **14** (3.5 g, 76%), m.p. 225–227° (from acetone–ether).

Methyl O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**17**). — A solution of the glycosyl halide **9** (104 mg, 0.16 mmol) and 2,4,6-trimethylpyridine (0.020 mL, 0.15 mmol) in dichloromethane (2 mL) was added to a stirred suspension of silver triflate (50 mg, 0.19 mmol) and the nucleophile **15** (0.13 g, 0.13 mmol) in the same solvent (2 mL). After 15 min, the mixture was processed as described for the preparation of **12** (*b*), and the major product was isolated by chromatography to give **17** (165 mg, 80%), m.p. 250–251° (from dichloromethane–ethanol), $[\alpha]_D$ +115° (*c* 0.55, chloroform). Definite signals in the ^{1}H-n.m.r. spectrum (300 MHz in $CDCl_3$) were at δ 4.77 (d, 1 H, $J_{1'',2''}$ 7.8 Hz, H-1''), 4.71 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-1'), 4.56 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), and 3.24 (s, 3 H, OCH_3); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.18 (C-1), 101.15 (C-1'), 100.69 (C-1''), 72.94 (C-5), 72.62 (C-5'), 71.74, 71.64, 71.59 (C-3,3',3''), 71.22 (C-5''), 69.88 (3C, C-2,2',2''), 68.67 (C-4), 68.0, 67.88, 67.80 (C-6,4',4''), 66.34 (C-6'), 61.58 (C-6''), and 56.81 (OCH_3).

Anal. Calc. for $C_{89}H_{74}O_{26}$: C, 68.54; H, 4.78. Found: C, 68.47; H, 4.80.

Methyl O-(2,3,4-tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**18**). — (*a*) Trimethylsilyl triflate (0.060 mL, 0.3 mmol) was added at −5° to a solution of the nucleophile **1** (140 mg, 0.275 mmol) and the disaccharide **13** (300 mg, 0.25 mmol). Cooling was removed and, when the mixture had warmed to +5°, it was kept at that temperature until t.l.c. (solvents *A* and *B*) showed that only negligible amounts of starting materials remained (~1 h). The mixture was stirred with solid $NaHCO_3$ for 15 min, filtered, the filtrate washed with water, dried, and evaporated. The residue was chromatographed, and crystallization from dichloromethane–methanol yielded **18** (280 mg, 71% based on **13**), m.p. 233–234°, $[\alpha]_D$ +162° (*c* 0.8, chloroform). Definite signals in the ^{1}H-n.m.r. spectrum (300 MHz in $CDCl_3$) were at δ 5.93, 5.87, 5.80 (3 × bd, 3 × 1 H, $J_{4,5}$ <1 Hz, H-4,4',4''), 4.79 (d, 1 H, $J_{1'',2''}$ 8.3 Hz, H-1''), 4.67 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.58 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 3.67 (s, 2 H, CH_2Br), and 3.26 (s, 3 H, OCH_3); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.19 (C-1), 101.10 (C-1'), 100.72 (C-1''), 72.92 (C-5), 72.60 (C-5'), 71.73, 71.59 (1C, 2C, C-3,3',3''), 70.94 (C-5''), 69.88, 69.82 (C-2',2''), 69.61 (C-2), 68.63 (C-4), 68.00, 67.78 (1C, 2C, C-6,4',4''), 66.56 (C-6'), 63.15 (C-6''), 56.88 (OCH_3), and 25.32 (CH_2Br).

Anal. Calc. for $C_{84}H_{71}BrO_{26}$: C, 64.00; H, 4.54; Br, 5.12. Found: C, 63.99; H, 4.58; Br, 5.12.

(*b*) A solution of the nucleophile **15** (2.94 g, 3 mmol), chloride **3** (2.27 g, 3.6 mmol) and 2,4,6-trimethylpyridine (0.436 mL, 3.3 mmol) in CH_2Cl_2 (15 mL) was added to a suspension of silver triflate (1.03 g, 4 mmol) in CH_2Cl_2 (15 mL). Silver chloride slowly precipitated and the mixture turned acidic to litmus after ~15 min. T.l.c. (solvent *A*) showed that the reaction was complete and that essentially a single product was formed. After an additional 15 min, the mixture was made neutral with 2,4,6-trimethylpyridine and processed as described for the preparation of **12** (*b*). Crystallization from dichloromethane–methanol gave material (4.2 g, 89%) indistinguishable from the aforementioned substance.

Methyl O-*(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)*-*(1→6)*-*(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)*-*(1→6)*-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**19**). — A solution of **18** (4.2 g, 2.66 mmol) in dichloromethane (50 mL) was treated with a solution of thiourea (630 mg, 8.26 mmol) in methanol (25 mL) and, after 40 min, the mixture was processed as described for the preparation of **15**. Crystallization from acetone–methanol gave pure **19** (3.6 g, 93%), m.p. 221–222°, $[\alpha]_D$ +146° (*c* 0.6, chloroform). Definite signals in the ^{1}H-n.m.r. spectrum (300 MHz in $CDCl_3$) were at δ 5.98, 5.88, 5.75 (3 × bd, 3 × 1 H, $J_{4,5}$ <1 Hz, H-4,4′,4″), 4.78 (d, 1 H, $J_{1'',2''}$ 7.8 Hz, H-1″), 4.65 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′), 4.57 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 3.26 (s, 3 H, OCH_3), and 2.54 (t, 1 H, disappears on deuteration, OH); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.17 (C-1), 101.10 (C-1′), 100.98 (C-1″), 74.15 (C-5″), 72.89 (C-5), 72.40 (C-5′), 71.83, 71.76, 71.66 (C-3,3′,3″), 69.93 (2C, C-2′,2″), 69.83 (C-2), 68.73 (C-4), 68.57 (C-4″), 68.01 (C-6), 67.68 (C-4′), 66.69 (C-6′), 60.67 (C-6″), and 56.79 (OCH_3).

Anal. Calc. for $C_{82}H_{70}O_{25}$: C, 67.66; H, 4.85. Found: C, 67.71; H, 4.94.

Methyl O-*(2,3,4-tri*-O-*benzoyl-6*-O-*bromoacetyl*-β-D-*galactopyranosyl)*-*(1→6)*-*(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)*-*(1→6)*-*(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)*-*(1→6)*-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**20**). — (*a*) Trimethylsilyl triflate (0.25 mL, 1.3 mmol) was added at 0° to a solution of **13** (1.19 g, 1 mmol and **15** (0.98 g, 1 mmol) in dichloromethane (15 mL). Cooling was removed and the temperature was allowed to rise slowly to +5°. After 1 h, t.l.c. (solvent *A*) showed that only traces of starting compounds remained unchanged and that several products were formed, with one predominating. The solution was stirred with solid $NaHCO_3$ until neutral, filtered, evaporated, and the main product was isolated by chromatography to give pure **20** (1.47 g, 72%), m.p. 273–275°, $[\alpha]_D$ +104° (*c* 0.7, chloroform). Definite signals in the ^{1}H-n.m.r. spectrum (300 MHz in $CDCl_3$) were at δ 5.92, 5.86, 5.83, 5.77 (4 × bd, 4 × 1 H, $J_{4,5}$ <1 Hz, H-4,4′,4″,4‴), 4.78 (d, 1 H, $J_{1''',2'''}$ 7.8 Hz, H-1‴), 4.56, 4.47 (m, 2 H, d, 1 H, *J* 7.8 Hz, H-1,1′,1″), 3.62 (s, 2 H, CH_2Br), and 3.22 (s, 3 H, OCH_3); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.16 (C-1), 101.21, 100.89 (C-1′,C-1″), 100.66 (C-1‴), 72.94 (C-5), 72.28 (2C, C-5′,5″), 71.71, 71.50 (3C, 1C, C-3,3′,3″,3‴), 70.96 (C-5‴), 69.85 (3C, C-2′,2″,2‴), 69.65 (C-2), 68.63 (C-4), 67.80 (4C, C-6,4′,4″,4‴), 66.65, 66.08 (C-6′,6″), 63.12 (C-6‴), 56.78 (OCH_3), and 25.24 (CH_2Br).

Anal. Calc. for $C_{111}H_{93}BrO_{34}$: C, 65.00; H, 4.57; Br, 3.89. Found: C, 64.79; H, 4.61; Br, 3.88.

(*b*) A solution of the nucleophile **19** (1.9 g, 1.3 mmol), the glycosyl donor **3** (0.99 g, 1.56 mmol) and 2,4,6-trimethylpyridine (0.185 mL, 1.4 mmol) in CH_2Cl_2 (10 mL) was added to a stirred suspension of silver triflate (0.41 g, 1.6 mmol) in CH_2Cl_2 (5 mL). When the mixture turned acidic to litmus (~20 min), t.l.c. showed that **3** had been consumed but that ~20% of **9** was still present. The reaction was completed by addition of an equimolar amount of solid **3** and silver triflate and, after neutralization with 2,4,6-trimethylpyridine, the major product **20** (2.1 g, 78.4%) was isolated by chromatography (solvent *C*), m.p. 273–274°.

Methyl O-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**21**). — A solution of thiourea (0.53 g, 6.4 mmol) in methanol (15 mL) was added with stirring to a solution of **20** (4.75 g, 2.31 mmol) in dichloromethane (50 mL) and, after 40 min, the mixture was processed as described for the preparation of **15**. Chromatography (solvent *C*) afforded pure **21** (3.3 g, 74%) as a solid foam, $[\alpha]_D$ +121° (*c* 0.5, chloroform); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.14 (C-1), 101.14, 101.03 (C-1′,1″), 100.63 (C-1‴), 74.19 (C-5‴), 72.87 (C-5), 72.12 (2C, C-5′,5″), 71.74 (4C, C-3,3′,3″,3‴), 69.92 (3C, C-2′,2″,2‴), 69.84 (C-2), 68.75 (C-4), 68.59 (C-4‴), 67.77 (2C, C-4′,4″), 67.68 (C-6), 66.62, 65.93 (C-6′, C-6″), 60.75 (C-6‴), and 56.77 (OCH_3).

Anal. Calc. for $C_{109}H_{92}O_{33}$: C, 67.83; H, 4.80. Found: C, 67.54; H, 5.02.

Methyl O-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside (**22**). — Methanolic sodium methoxide (M, 3 mL) was added to a hot solution of **20** (0.55 g) in toluene (20 mL), followed immediately by an addition of hot methanol (100 mL), whereupon all precipitate that had formed dissolved. The solution was kept at 50–60° overnight, and then cooled in an ice bath, made neutral with Dowex 50 W (H^+-form), and evaporated. The residue was dissolved in water (1 mL), the mixture filtered, and methanol (~5 mL) was added to the filtrate. Compound **22** slowly crystallized (154 mg, 84%) and, after drying at 105°/133 Pa, showed m.p. 180–185° and $[\alpha]_D$ −10.3° (*c* 0.77, water); ^{13}C-n.m.r. (75 MHz in D_2O): δ 103.86 (C-1), 103.42 (2C, C-1′,1″), 103.31 (C-1‴), 75.16 (C-5‴), 73.76 (3C, C-5,5′,5″), 72.80 (C-3), 72.61 (3C, C-3,3′,3″), 70.73 (4C, C-2,2′,2″,2‴), 69.35, 69.25, 69.21 (C-6,6′,6″), 68.69 (4C, C-4,4′,4″,4‴), 61.06 (C-6‴), and 57.40 (OCH_3).

Anal. Calc. for $C_{25}H_{44}O_{21}$: C, 44.11; H, 6.51. Found: C, 43.98; H, 6.68.

Methyl O-(2,3,4-tri-O-benzoyl-6-O-bromoacetyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**23**). — A solution of **19** (1.45 g, 1 mmol), **16** (1.32 g, 1.2 mmol), ad 2,4,6-trimethylpyridine 0.143 mL, 1.08 mmol) in dichloromethane (10 mL) was added to a suspension of silver triflate (345 mg, 1.35 mmol) in dichloromethane (10 mL). The mixture turned acidic after 10 min

and, after an additional 5 min, it was processed as described for the preparation of **12** (*b*). The crude product was chromatographed (solvent *D*) and crystallization from dichloromethane–ether gave pure **23** (1.7 g, 67.7%), m.p. 263–264°, $[\alpha]_D$ +86° (*c* 0.55, chloroform); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.12 (C-1), 101.10, 100.98, 100.77 (1C, 1C, 2C, C-1′,1″,1‴,1⁗), 72.83 (C-5), 72.19, 72.10 (2C, 1C, C-5′,5″,5‴), 71.78, 71.70, 71.52 (1C, 3C, C-3,3′,3″,3‴,3⁗), 71.00 (C-5⁗), 69.91 (4C, C-2′,2″,2‴,2⁗), 69.64 (C-2), 68.57 (C-4), 67.81, 67.68 (2C, 3C, C-6,4′,4″,4‴,4⁗), 66.65, 66.21 (1C, 2C, C-6′,6″,6‴), 63.14 (C-6⁗), 56.76 (OCH_3), and 25.28 (CH_2Br).

Anal. Calc. for $C_{138}H_{115}BrO_{42}$: C, 65.63; H, 4.59; Br, 3.16. Found: C, 65.48; H, 4.62; Br, 3.26.

Methyl O-β-D-*galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside* (**24**). — Methanolic sodium methoxide (M, 8 mL) was added to a solution of **23** (400 mg) in hot toluene (15 mL), followed immediately by the addition of hot methanol (100 mL). The strongly alkaline solution was kept overnight at 55–60°. After cooling in an ice bath, the separated solid was filtered, washed with a little methanol, dissolved in water, and treated with Dowex 50 W (H^+-form). The neutral solution was concentrated to ~1 mL and on addition of methanol compound **24** slowly crystallized as a dihydrate (103 mg, 78%), m.p. 275° (dec), with softening at ~180°, $[\alpha]_D$ −9.7° (*c* 1.03, water); ^{13}C-n.m.r. (75 MHz in D_2O): δ 103.86 (C-1), 103.42 (4C, shoulder, C-1′,1″,1‴,1⁗), 75.14 (C-5⁗), 73.73 (4C, C-5,5′,5″,5‴), 72.80 (C-3), 72.65 (4C, C-3′,3″,3‴,3⁗), 70.73 (5C, C-2,2′,2″,2‴,2⁗), 69.45, 69.32, 69.26, 69.17 (C-6,6′,6″,6‴), 68.67 (5C, C,4,4′,4″,4‴,4⁗), 61.05 (C-6⁗), and 57.36 (OCH_3).

Anal. Calc. for $C_{31}H_{54}O_{26} \cdot 2\ H_2O$: C, 42.36; H, 6.65. Found: C, 42.53; H, 6.61.

Methyl O-*(2,3,4-tri*-O-*benzoyl-6*-O-*bromoacetyl*-β-D-*galactopyranosyl)-(1→6)-2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)-(1→6)-(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)-(1→6)-(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)-(1→6)-(2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranosyl)-(1→6)-2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**25**). — A solution of **21** (2.9 g, 1.5 mmol), **16** (2 g, 1.8 mmol) and 2,4,6-trimethylpyridine (0.211 mL, 1.6 mmol) in dichloromethane (20 mL) was added to a stirred suspension of silver triflate (0.154 g, 2 mmol) in dichloromethane (10 mL). The mixture turned acidic after 10 min and it was made neutral with 2,4,6-trimethylpyridine after an additional 5 min. After conventional processing, the crude product was chromatographed (solvent *B*) to give pure **25** (3 g, 66%), m.p. 303–304° (from chloroform–ether), $[\alpha]_D$ +74° (*c* 0.75, chloroform); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.13 (C-1), 101.18, 101.10, 100.91, 100.85, 100.73 (C-1′,1″,1‴,1⁗,1⁗⁗), 72.83 (C-5), 72.22, 72.04, 71.88, 71.83 (C-5′,5″,5‴,5⁗), 71.71, 71.48 (5C, 1C, C-3, C-3′,3″,3‴,3⁗, C-3⁗⁗), 71.18 (C-5⁗⁗), 69.97, 69.92 (2C, 3C, C-2′,2″,2‴,2⁗,2⁗⁗), 69.72 (C-2), 68.65 (C-4), 67.82, 67.70, 67.62 (3 × 2C, C-6, C-4′,4″,4‴,4⁗,4⁗⁗), 66.86, 66.24, 66.12 (1C, 2C, 1C, C-6′,6″,6‴,6⁗), 63.23 (C-6⁗⁗), 56.75 (OCH_3), and 25.29 (CH_2Br).

Anal. Calc. for $C_{165}H_{137}BrO_{50}$: C, 66.06; H, 4.60; Br, 2.66. Found: C, 65.96; H, 4.58; Br, 2.75.

Methyl O-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzoyl-β-D-galactopyranosyl)-(1→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (**26**). — A solution of **25** (0.93 g, 0.3 mmol) in chloroform (60 mL) was treated with a solution of thiourea (135 mg, 1.8 mmol) in methanol (5 mL), and the solution was kept at room temperature until t.l.c. (solvent *A*) showed that only traces of uncharged starting material remained. The mixture was processed as described for the preparation of **15**, and the crude product was chromatographed (solvent *E*) to give pure **26** (0.7 g, 81%), m.p. 328–330° (dec), $[\alpha]_D$ +86.5° (*c* 0.63, chloroform); ^{13}C-n.m.r. (75 MHz in $CDCl_3$): δ 102.12 (C-1), 101.20, 101.13, 100.74, 100.66 (3 × 1C, 2C, C-1′,1″,1‴,1⁗,1⁗′), 74.30 (C-5⁗′), 72.86 (C-5), 71.92, 71.83, 71.74, 71.63 (2 × 2C, 4C, 2C, C-3,3′,3″,3‴,3⁗,3⁗′,5′,5″,5‴,5⁗′), 69.96, 69.88 (4C, 2C, C-2,2′,2″,2‴,2⁗,2⁗′), 68.77 (C-4), 69.88 (C-4⁗′), 67.73 (4C, C-4′,4″,4‴,4⁗′), 67.64 (C-6), 67.45, 66.77, 65.88 (2 × 1C, 2C, C-6′,6″,6‴,6⁗′), 60.81 (C-6⁗′), and 56.77 (OCH_3).

Anal. Calc. for $C_{163}H_{136}O_{49}$: C, 68.00; H, 4.76. Found: C, 67.44; H, 4.83.

Methyl O-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside (**27**). — Methanolic sodium methoxide (M, 5 mL) was added to a hot suspension of **25** (605 mg) in toluene, followed immediately by addition of hot methanol (100 mL). A clear solution formed, and a solid soon separated. The mixture was kept overnight at 55–60°, and processed as described for the preparation of **24**. Compound **27** crystallized readily from water–methanol as a dihydrate, m.p. 277–278° (dec), $[\alpha]_D$ −9.6° (*c* 0.8, water). ^{13}C-n.m.r. (75 MHz in D_2O): δ 103.89 (C-1), 103.46 (4C, C-1′,1″,1‴,1⁗), 103.35 (C-1⁗′), 75.20 (C-5⁗′), 73.79 (5C, C-5,5′,5″,5‴,5⁗), 72.84 (C-3), 72.66 (5C, C-3,3′,3″,3‴,3⁗,3⁗′), 70.77 (6C, C-2,2′,2″,2‴,2⁗,2⁗′), 69.50, 69.38, 69.30, 69.23 (2C, 3 × 1C, C-6,6′,6″,6‴,6⁗), 68.70 (6C, C-4,4′,4″,4‴,4⁗,4⁗′), 61.09 (C-6⁗′), and 57.41 (OCH_3).

Anal. Calc. for $C_{37}H_{64}O_{31} \cdot 2\ H_2O$: C, 42.69; H, 6.58. Found: C, 42.60; H, 6.46.

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