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Glycosylation via locked anomeric configuration: stereospecific synthesis of oligosaccharides containing the β-D-mannopyranosyl and β-L-rhamnopyranosyl linkage[1]

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Abstract

cis-1,2-Stannylene acetals of D-mannose and L-rhamnose, formed preferentially from the free sugars treated with dibutyltin oxide, are capable of displacing the trifluoromethanesulfonyl (triflyl) leaving groups in carbohydrates to give, with retention of configuration at the anomeric center in the nucleophile, *cis*-1,2-linked oligosaccharides. In the case of secondary triflates, the new glycosidic linkage is formed with complete inversion of configuration in the electrophile. Both the reactivity of the electrophile and nucleophilicity of oxygens in the stannylene complex affect the overall outcome of the reaction. From the comparison of results of a number of glycosylations via stannylene acetals, it appears that nucleophilicity of oxygens involved in the *cis*-1,2-acetals decreases in the order: equatorial anomeric > equatorial non-anomeric > axial anomeric. Consequently, treatment of the stannylene acetal prepared from D-mannose (mainly the *cis*-1,2-stannylene compound in admixture with a small proportion of the *cis*-2,3-stannylene acetal) with methyl 2,3,4-tri-*O*-benzoyl-6-*O*-trifluoromethanesulfonyl-α-D-glucopyranoside yielded, in addition to the expected β-D-mannopyranoside (major), a product of non-anomeric alkylation at O-3. On the other hand, glycosylation of the stannylene acetal derived from maltose with methyl 2,3,6-tri-*O*-benzoyl-4-*O*-trifluoromethanesulfonyl-α-D-galactopyranoside gave almost exclusively a non-glycosidically, (2→4)-linked pseudo-trisaccharide. Combination of the glycosylation via locked anomeric configuration with conventional glycosylations, to yield higher oligosaccharides, is also demonstrated. © 1998 Elsevier Science Ltd. All rights reserved

Keywords: Stereospecific β-D-mannosylation ; Stereospecific β-L-rhamnosylation ; *cis*-1,2-*O*-stannylene acetals ; Stereospecific glycosylation ; Oligosaccharide synthesis

1. Introduction

The involvement of oligosaccharide structures in vital biological processes has markedly increased the interest in synthetic oligosaccharides [1,2]. Thus, the efforts to develop new methods for the synthesis of oligosaccharides, chemical or chemoenzymatic, have escalated during the past decade [3–5]. Of the many, principally diverse methods available for oligosaccharide synthesis, most efficient are those where the stereochemical outcome of the reaction is facilitated by neighboring group

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participation. While the latter methods work very satisfactorily to synthesize *trans*-1,2-glycosides/oligosaccharides, the synthesis of their *cis*-counterparts, particularly β-L-rhamno- and β-D-manno-linked oligosaccharides, is still a formidable task [6]. Recently, we reported [7] on a fundamentally new method for the stereospecific synthesis of the β-L-rhamno- and β-D-mannopyranosyl linkage. It is based on the increased nucleophilicity of the anomeric oxygen, when it becomes part of a stannylene acetal. Formally, the method involves anomeric alkylation, pioneered by Schmidt and his co-workers [8–10]. In our case, contrary to the latter approach where the sodium salt of the anomeric hydroxyl group is present in both α- and β-forms, the anomeric oxygen is conveniently locked in the 1,2-*cis* configuration. We have confirmed by ^{1}H and ^{13}C NMR spectroscopy [11] that the acetal preferentially formed from L-rhamnose treated with dibutyltin oxide is, indeed, the *cis*-1,2-acetal. Consequently, while classical anomeric alkylation normally yields a mixture of anomers, our mannosylation or rhamnosylation via locked anomeric configuration affords, stereospecifically, the *cis*-1,2-oligosaccharides.

The concept of using *cis*-1,2-stannylene acetals of otherwise protected sugars for simple anomeric alkylations with alkyl halides has been previously used [12,13]. Our approach [7] extends the use of 1,2-stannylene acetals to a simple, high yielding, stereospecific synthesis of the β-D-mannopyranosyl and β-L-rhamnopyranosyl linkages, and is superior to previous protocols in that protection of hydroxyl groups in sugars to be converted to stannylene acetals is not required.

The present paper describes the scope and limitations of the new method, experimental details for preparations reported in our recent short communication [7], and full characterization of relevant substances synthesized. Also, we demonstrate the potential the new method has, in combination with conventional glycosylation techniques, in syntheses of more complex oligosaccharides.

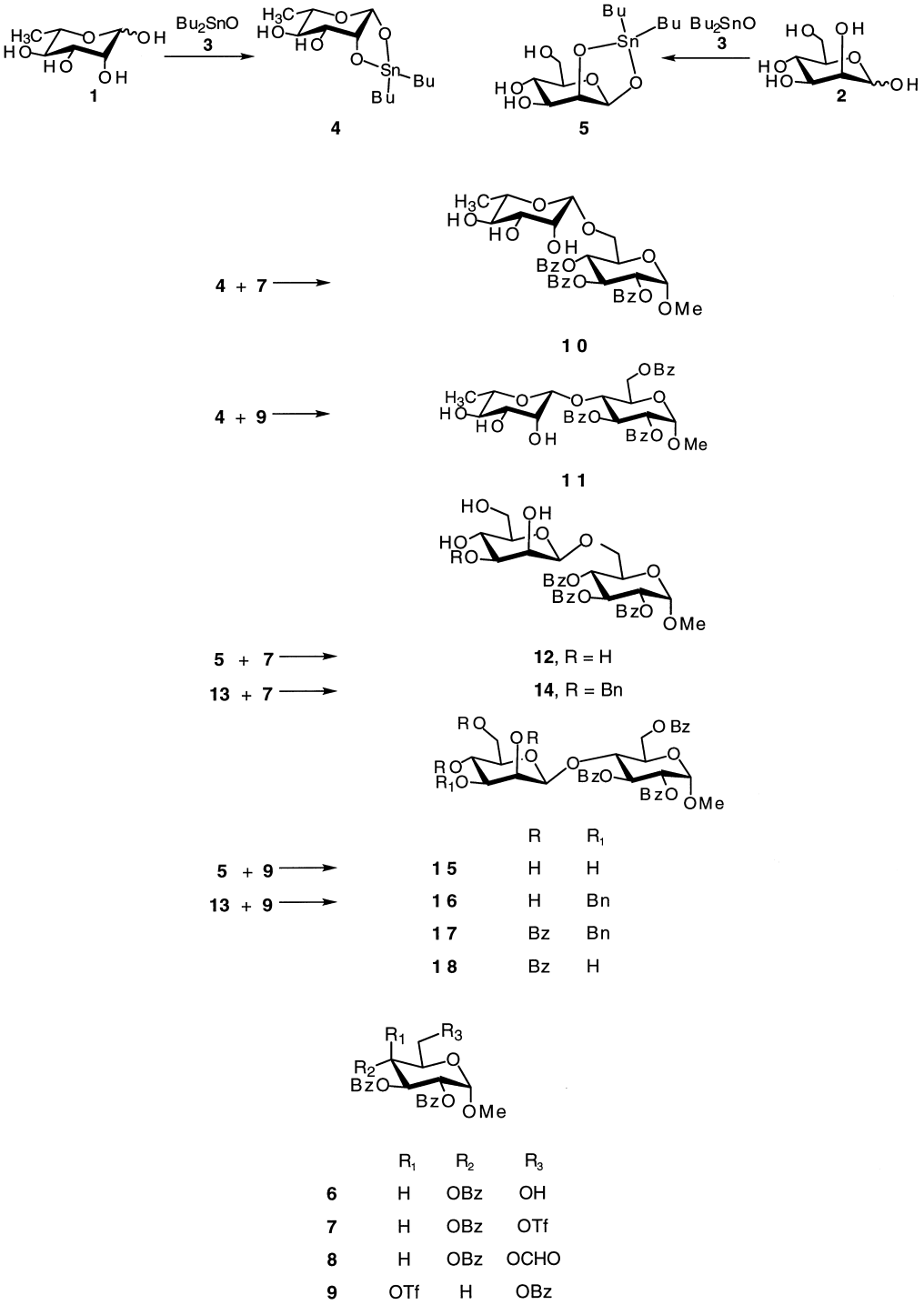
2. Results and discussion

When an unprotected sugar, e.g., mannose (**2**) or rhamnose (**1**), is treated with one equivalent of dibutyltin oxide (**3**) isomeric acetals may be formed. Thus, a high yield of the β-product, resulting from a displacement reaction involving the anomeric oxygen as the nucleophile, can be obtained from such a mixture only if the 1,2-*O*-acetal predominates. Therefore, the objective of our initial treatments of unprotected sugars with **3** was to ascertain the nature of stannylene acetals present when the equilibrium among possible isomers is reached. The presence of a high proportion of **4** in the product after treatment of L-rhamnose (**1**) with **3** was indicated when subsequent acetylation yielded [11] the β-per-*O*-acetyl derivative in >80% yield. The same was confirmed by NMR spectral data obtained [11] for the product of the stannylation of L-rhamnose (**1**). Other important information obtained during that work was that the formation of stannylene acetals from free sugars may be accompanied by epimerization, and that the extent of that side reaction can be controlled [11]. Having been able to minimize the occurrence of epimerization by conducting the acetal-forming reaction with a limited amount of the reagent under mild conditions [11,14], we turned our attention to replacement of leaving groups in carbohydrates using 1,2-*O*-stannylene acetals as nucleophiles. No reaction was observed ([15], TLC) when 6-deoxybromo, or 6-deoxyiodo derivatives of D-mannose (**2**), or the corresponding mesylate, were treated with 1,2-*O*-stannylene acetals, but the use of the trifluoromethanesulfonyl (triflyl) leaving group was successful. When necessary, the solubility of stannylene complexes could be enhanced by addition of CsF or phase-transfer salts, e.g., Bu_4NF, to reaction mixtures.

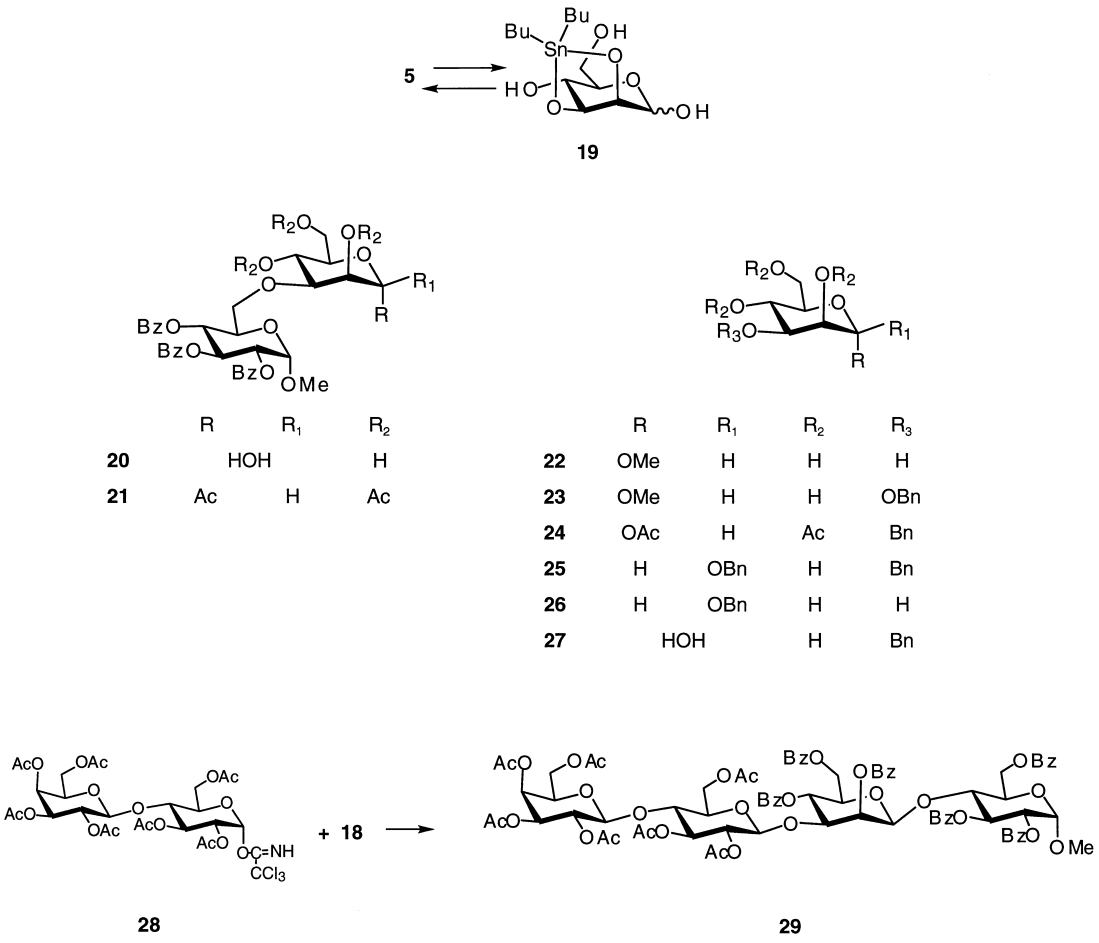
Initially, we tried the anomeric alkylation of the *cis*-1,2-stannylene acetal of L-rhamnose (**4**) with the primary triflate **7**, prepared from **6** [16] by the method of Ambrose and Binkley [17] (Scheme 1). When the reaction was conducted at ambient temperature in DMF as the solvent, the yield of the desired β-L-rhamnoside **10** was ~50%. As a result of a reaction between triflate **7** and DMF, formate **8** was also produced, and it was isolated in a yield of ~25%. The formation of this unwanted side product could be minimized when the same reaction was performed at −5 °C. The yield of the target disaccharide **10** increased then to 88%. In these reactions, the readily available dibutyltin acetal of L-rhamnose (**4**) was used in large excess (4–6 equivalents). This enhanced the rate of the desired alkylation, thereby largely avoiding the accompanying side reaction of the starting triflate.

The stannylene acetal **4** also reacted smoothly with the less reactive secondary triflate **9** [18]. The extent of formylation at the secondary position in **9** was minimal even when the reaction was conducted at 25 °C and, after a reaction time of 2.5 h, the desired disaccharide **11** was obtained in 78% yield. This is a notable improvement compared to the highest yield of the β-L-Rha-(1→4)-D-Glc linkage reported thus far (43%) [19].

Reactions of the analogous tin acetal **5** prepared from D-mannose (**2**) were less successful. The β-linked disaccharide **12**, formed from triflate **7**, could be obtained only in 40%, together with a by-product **20** (Scheme 2) isolated in 23% yield. The



Scheme 1.



Scheme 2.

mass spectrum of **20** showed a pseudomolecular ion peak at *m*/*z* 686, showing that the compound was isomeric with the desired β-mannoside **12**. Compound **20**, an α,β-mixture, was treated with pyridine–Ac_2O, and characterized as the corresponding peracetate **21**. That **20** was not the α-linked isomer of **12**, but the product of non-anomeric alkylation at position-3 of the mannose residue, followed from the analysis of spectral data obtained for **21**. The ^{13}C NMR spectrum showed only one signal at 60–65 ppm, showing that the triflyl group has undergone a substitution reaction. In agreement with this finding, the signal for C-6^I appeared downfield (δ 68.80). In the anomeric region of the ^{13}C NMR spectrum of the substance there were two signals, one of which (δ 96.77, $J_{C,H}$ 172.9 Hz) showed chemical shift similar to that of C-1^I of **12**. This, together with the chemical shifts of other ring carbons of the glycoside residue, which were found to be close to those present in the ^{13}C NMR spectrum of **12** (see Experimental), indicated that the aglycon bearing residue of the main product **12** and **21** are virtually identical. The other signal in the anomeric region of the ^{13}C NMR spectrum of **21** appeared at δ 90.93 ($J_{C,H}$ 177.2 Hz), indicating that the anomeric position of the second sugar ring was not involved in an interglycosidic linkage but was acetylated. Structure **21**, i.e., per-*O*-acetylated-α-D-mannopyranose linked ethereally through its position-3 to position-6 of methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside, was corroborated by its 2D ^1H–^{13}C correlated (HETCOR) spectrum. There, the ring ^{13}C signal appearing at the lowest field, indicative of its involvement in an ether linkage, showed a cross-peak with H-3 of the per-*O*-acetylated mannose residue. A plausible explanation for the formation of **20** from **5** and **7** is the isomerisation of the *cis*-1,2-acetal **5** into *cis*-2,3-acetal **19**, thus activating the oxygen at C-3 in D-mannose, which becomes a competing nucleophile in the substitution reaction. The yield and the ratio of products of the reaction **5** + **7** → **12** + **20** was found to be solvent dependent. When *N*,*N*-dimethylacetamide (DMA) was used

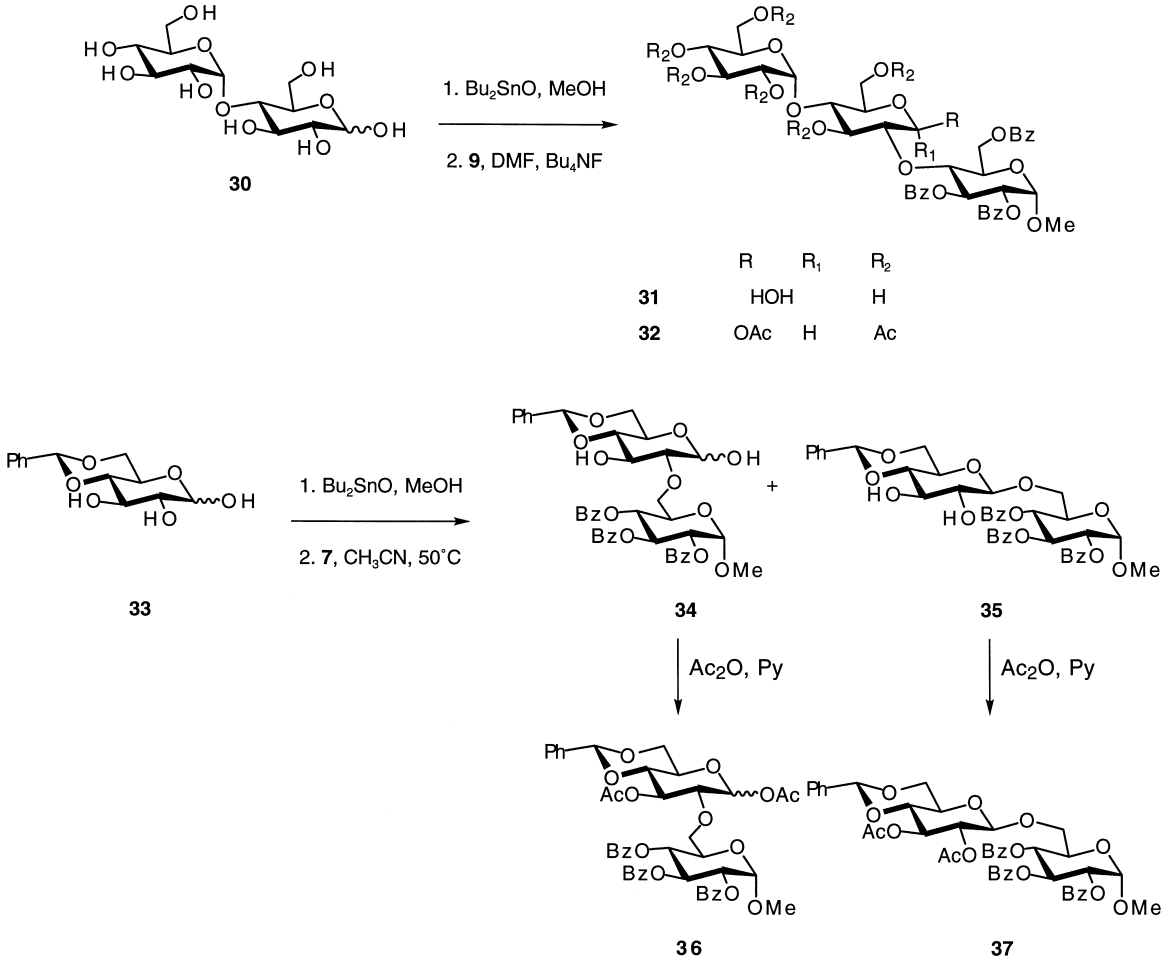
[15], the products **12** and **20** were formed in a ratio of ~1:1 (TLC). This indicates, firstly, that the isomerisation of **5** to **19** is solvent dependent and, secondly, that in solvents of higher dielectric constants the difference between the nucleophilicity of equatorial anomeric and a non-anomeric oxygens diminishes. The best yield of **12** (57%) was obtained when the reaction **5**+**7** was performed in acetonitrile in the presence of Bu_4NF. The effect of solvent upon the outcome of the reaction of the secondary triflate **9** could be further demonstrated in the series of experiments involving different solvents (for a tabular presentation of results obtained, see ref [7].). As the polarity of the solvent increased, the reactivity of reactants and, consequently, the yield of the desired S_N2 reaction increased as well. Thus, when reactions were conducted at 25 °C, the yield of the disaccharide **15** was 40% in DMF as solvent after 5 days, 53% in DMA after 3 days, and 59% in DMSO after 2 days. The above-mentioned isomerisation of **5** into **19** could be completely eliminated when the 1,2-stannylene acetal **13** of 3-*O*-benzyl-D-mannose (**27**) was used as the nucleophile. Accordingly, reactions of **13** with triflates **7** and **9**, gave the β-linked disaccharides **14** and **16** in increased yields of β-mannopyranosyl linkages (~73 and 67%, respectively). The mannose derivative **27** used in the foregoing experiments was obtained as follows. The 2,3-stannylene acetal of methyl α-D-mannopyranoside (**22**) was benzylated affording **23** (~73%). The latter was subjected to acetylation/acetolysis (→**24**, 90%), and subsequent deacetylation of **24** then gave the target 3-*O*-benzyl derivative **27**.

The isomerisation **5**→**19** suggested above is evident from the results of alkylation of **5** with benzyl bromide. In addition to unchanged D-mannose, and benzyl 3-*O*-benzyl-β-D-mannopyranoside (**25**, 18%), the main product was a 1.2:1 mixture of 3-*O*-benzyl-D-mannose (**27**) and benzyl β-D-mannopyranoside (**26**, ~40%; since the latter mixture could be only partially resolved by chromatography, the structure and the ratio of components were established by NMR spectroscopy). Again, formation of **25** and **27** must have been preceded by isomerisation of the *cis*-1,2-acetal **5** into the *cis*-2,3-acetal **19**. When a solution of **5** in DMA was kept overnight at 25 °C and then subjected to similar benzylation [15], the ratio of **27** to **26** formed was only slightly changed, to 1.5:1. This indicates that the isomerisation is a much faster process than the alkylation itself.

The successful preparation of the partially benzylated disaccharide **16** prompted us to explore the feasibility of application of the new glycosylation technique to synthesizing more complex oligosaccharides, by combination with conventional glycosylation methods. A suitable glycosyl acceptor **18** was obtained from **16** by perbenzoylation (→**17**), followed by hydrogenolytic cleavage of the benzyl group. Compound **18** was glycosylated using lactosyl imidate **28** [20] in the presence of BF_3·etherate affording the tetrasaccharide **29** in 70% yield.

In order to explore the utility of the glycosylation via locked anomeric configuration to synthesizing *cis*-1,2-oligosaccharides in the *gluco* series, we prepared the 1,2-stannylene complex of maltose (**30**) (Scheme 3) and treated it with triflate **9** under conditions proven favorable in similar situations (vide supra). The major product formed under these conditions was an α,β-mixture of the (2→4)-linked pseudo-oligosaccharide **31**. This showed that when the *equatorially* oriented oxygen at C-2 becomes part of the *cis*-1,2-stannylene acetal, it becomes a stronger nucleophile than the similarly engaged, *axially* oriented anomeric oxygen.

To elucidate the structure of the product **31** resulting from attempted glycosylation with **30** as the glycosyl donor, the pure material isolated by chromatography was acetylated. An α,β-mixture was formed, and the β-1-*O*-acetyl derivative **32** was isolated in admixture with a small proportion (~10%) of the α-isomer. The mass spectral and NMR characteristics observed for such material showed that it was isomeric with the desired trisaccharide. The diagnostically significant observations supporting the presence of the O-2→O-4-ether linkage in **32**, rather than the (1→4)-glycosidic linkage expected to be present in the targeted trisaccharide, follow (for complete ^1H and ^{13}C NMR data, see Experimental): The CIMS spectrum contained a quasi molecular ion peak at *m*/*z* 1142. That the nucleophilic substitution at position-4 in compound **9** had occurred with inversion of configuration was evident from the appearance of $H\text{-}4^I$ signal as a triplet (J 10.1 Hz), as would be expected for the axially oriented H-4 proton in a D-glucose residue interacting with two axially oriented protons at C-3 and C-5. Also, in the ^1H NMR spectrum of **32**, the doublet of $H\text{-}1^{II}$ appears downfield (δ 5.61, $J_{1,2}$ 7.5 Hz) as expected for signal of a proton which is part of a $CH_3CO\text{–}O\text{–}C\text{–}H$



Scheme 3.

group, showing that position to be acetylated. At the same time, the ^{13}C signal for C-2^{II} and C-4^{I} appeared downfield (δ 76.87 and 75.32, respectively) as is common for ring carbons in carbohydrates that are engaged in an interglycosidic linkage.

Finally, when the 1,2-stannylene derivative prepared from 4,6-*O*-benzylidene-D-glucose (**33**) was treated with triflate **7**, the main product was the β-Glc-(1→6)-Glc disaccharide **35**, isolated in 57% yield. A small amount of a byproduct was also formed and isolated by chromatography. The pseudomolecular ion peak present in the CI mass spectrum of this material indicated that it could be methyl 4,6-*O*-benzylidene-α,β-D-glucopyranos-2-yl-(2→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**34**), a compound isomeric with **35**. Mass spectral analysis of the substance formed from **34** upon acetylation, **36**, supported the same. The ^{1}H NMR spectrum of **36** showed (see Experimental) low-field signals for anomeric protons of the *O*-benzylidenated D-glucose residue, showing that position not to be involved in an interglycosidic linkage, but that it was acetylated. The high-field signal found for H-2 of the same moiety showed that that proton was not part of an H–C–$OCOCH_3$ group. This, together with the cross-peak in the ^{1}H–^{13}C heteronuclear correlation NMR spectrum showing connectivity between H-2^{II} and the ^{13}C signal appearing at δ 80.19, provided concluding evidence that the material was the (2→6)-ether linked substance **36**, analogous to the ether-type pseudodisaccharides obtained from similar reactions. The explanation for the formation of **34** and **35** is not straightforward. It is not inconceivable, however, that in the most stable conformation of the 1,2-*O*-stannylene acetal of compound **33**, the orientation of the anomeric oxygen is close to equatorial, and then the two equatorially oriented oxygen atoms, O-1 and O-2, that are part of the stannylene acetal are competing species in displacing the leaving group in the electrophile.

3. Experimental

Unless stated otherwise, optical rotations were measured at ambient temperature for solutions in chloroform (c~1), with a Perkin–Elmer automatic polarimeter, Model 241 MC, or Model 341. All reactions were monitored by thin-layer chromatography (TLC) on glass slides coated with Silica Gel 60 (Whatman or Analtech), with solvent mixtures of appropriately adjusted polarity consisting of components listed in the Experimental. Column chromatography was performed by gradient elution from columns of silica gel. Solvent mixtures slightly less polar than those used for TLC were used at the onset of development. Assignments of NMR signals were made by first-order analysis of the spectra, and, when feasible, the assignments were supported by homonuclear decoupling experiments or homonuclear and heteronuclear 2-dimensional correlation spectroscopy, run with the software supplied with the spectrometers. When reporting assignments of NMR signals, sugar residues in oligosaccharides are serially numbered, beginning with the one bearing the methyl aglycone, and are identified by a Roman numeral superscript in listings of signal assignments. 4,6-*O*-Benzylidene-D-glucose was purchased from Sigma Chemical Company. Unless indicated otherwise, solutions in organic solvents were dried with anhydrous Na_2SO_4 and concentrated at 40 °C/2 kPa.

Methyl 2,3,4-tri-O-*benzoyl-6*-O-*formyl*-α-D-*glucopyranoside* (**8**) *and methyl* β-L-*rhamnopyranosyl-(1→6)-2,3,4-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**10**).—(a) A mixture of L-rhamnose monohydrate (**1**, 0.114 g, 0.628 mmol) and dibutyltin oxide (**3**, 0.152 g, 0.612 mmol) in anhyd methanol (3 mL) was stirred at 70 °C (bath) until a clear solution was obtained (~35 min). Toluene (1 mL) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/2 kPa for 2.5 h to assure dryness, was dissolved in DMF (2 mL). After addition of **7** (0.1 g, 0.157 mmol), the mixture was stirred vigorously at 20 °C for 2 h, and concentrated. The residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography (dichloromethane–methanol) of the residue gave first the largely unstable **8** (0.03 g, 24.6%). ^{1}H NMR (C_6D_6): δ 7.58 (s, 1 H, CH=O), 6.60 (t, 1 H, *J* 10.0 Hz, H-3), 5.80 (t, 1 H, *J* 10.0 Hz, H-4), 5.46 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 10.4 Hz, H-2), 5.16 (d, 1 H, H-1), 4.20 (d, 2 H, H-6a,b), 4.10 (m, 1 H, H-5), 2.97 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 159.98 (HC=O), 97.44 (C-1), 72.42 (C-2), 70.99 (C-3), 69.94 (C-4), 67.92 (C-5), 61.76 (C-6), 55.23 (OCH_3); CIMS: *m/z* 552 ($[M+18]^+$).

Second eluted was **10** (0.06 g, 49.2%): mp 150.5–151.5 °C (from EtOH), $[\alpha]_D$ +126.6°. ^{1}H NMR ($CDCl_3$): δ 6.13 (t, 1 H, *J* 9.7 Hz, H-3^I), 5.74 (t, 1 H, *J* 9.9 Hz, H-4^I), 5.31–5.24 (m, 2 H, H-1^I,2^I), 4.52 (bs, 1 H, H-1^{II}), 4.25 (dbt, 1 H, H-5^I), 4.13 (dd, 1 H, $J_{5,6_a}$ 3.9, $J_{5_a,6_b}$ 11.4 Hz, H-6a^I), 4.00 (bd, 1 H, H-2^{II}), 3.78 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b^I), 3.46 (s, 3 H, OCH_3), 3.43–3.40 (m, 2 H, H-3^{II},4^{II}), 3.22–3.13 (m, 1 H, H-5^{II}), 1.07 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6^{II}); ^{13}C NMR ($CDCl_3$): δ 99.13 (C-1^{II}, $J_{C,H}$ 157.8 Hz), 97.20 (C-1^I, $J_{C,H}$ 172.7 Hz), 74.17 (C-3^{II}), 72.92 (C-4^{II}), 72.15 (C-2^I), 71.79 (C-5^{II}), 70.52 (2 C, C-3^I,2^{II}), 68.98 (C-4^I), 68.41 (C-5^I), 66.11 (C-6^I), 55.70 (OCH_3), 17.02 (C-6^{II}); CIMS: *m/z* 670 ($[M+18]^+$). Anal Calcd for $C_{34}H_{36}O_{13}\cdot H_2O$: C, 61.72; H, 5.64. Found: C, 61.89; H, 5.61.

(b) A mixture of L-rhamnose (**1**, 0.713 g, 3.92 mmol) and dibutyltin oxide (**3**, 0.877 g, 3.52 mmol) in anhyd methanol (25 mL) was stirred at 60 °C (bath) until a clear solution was obtained (~1.5 h). CsF (0.714 g, 4.7 mmol) and toluene (5 mL) were added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.3 kPa for 2.5 h to assure dryness, was dissolved in DMF (5 mL), molecular sieves (4 Å, 0.5 g) were added, and the solution was cooled to −5 °C. After addition of **7** (0.5 g, 0.79 mmol), the mixture was stirred vigorously at −5 °C for 80 min, and concentrated. The residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, the solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography of the residue gave **10** (0.45 g, 88.2%).

Methyl β-L-*rhamnopyranosyl-(1→4)-2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**11**).—A mixture of L-rhamnose (**1**, 0.713 g, 3.92 mmol) and dibutyltin oxide (**3**, 0.877 g, 3.52 mmol) in anhyd methanol (25 mL) was stirred at 60 °C until a clear solution was obtained (~1.5 h). CsF (0.714 g, 4.7 mmol) and toluene (5 mL) were added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa, for 2.5 h, was dissolved in DMF (5 mL), and molecular sieves (4 Å, 0.5 g) were added. After addition of **9** (0.5 g, 0.79 mmol), the

mixture was stirred vigorously at 20 °C for 140 min and then concentrated. The residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, the solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography gave **11** (0.4 g, 78.4%): $[\alpha]_D + 142.0°$. ^{1}H NMR ($CDCl_3$): δ 6.03 (dd, 1 H, $J_{3,4}$ 8.8, $J_{4,5}$ 10.3 Hz, H-3^I), 5.22 (dd, 1 H, $J_{1,2}$ 3.4, $J_{2,3}$ 10.3 Hz, H-2^I), 5.15 (d, 1 H, H-1^I), 4.74 (bd, 1 H, H-6^{I}a), 4.66 (dd, $J_{5,6}$ 4.0, $J_{6a,6b}$ 12.0 Hz, H-6^{I}b), 4.48 (s, 1 H, H-1^{II}), 4.22–4.13 (m, 2 H, H-4^I,5^I), 3.68 (bd, 1 H, $J_{2,3}$ ~3.1 Hz, H-2^{II}), 3.40 (s, 3 H, OCH_3), 3.32 (t, 1 H, J 9.3 Hz, H-4^{II}), 3.08–3.00 (m, 2 H, H-3^{II},5^{II}), 1.12 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 100.20 (C-1^{II}, $J_{C,H}$ 156.5 Hz), 96.85 (C-1^I, $J_{C,H}$ 170.8 Hz), 74.81 (C-4^I), 73.90 (C-3^{II}), 72.65 (C-3^I), 72.55 (C-4^{II}), 72.08 (C-5^{II}), 71.66 (C-2^I), 70.70 (C-2^{II}), 68.48 (C-5^I), 63.42 (C-6^I), 55.30 (OCH_3), 17.04 (C-6^{II}); CIMS: m/z 670 ($[M+18]^+$). Anal. Calcd for $C_{34}H_{36}O_{13}$: C, 62.57; H, 5.56. Found: C, 62.33; H, 5.61.

Methyl β-D-*mannopyranosyl-(1→6)-2,3,4-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**12**) *and methyl 2,3,4-tri*-O-*benzoyl-6*-O-*(1,2,4,6-tetra*-O-*acetyl*-α-D-*glucopyranos-3-yl)*-α-D-*glucopyranoside* (**21**).—Triflic anhydride (1.2 mL, 7.1 mmol) was added at −20 °C to a stirred solution of methyl 2,3,4-tri-O-benzoyl-α-D-glucopyranoside [16] (**6**, 3.0 g, 5.92 mmol) and 2,4-di-*tert*-butyl-4-methylpyridine (1.82 g, 8.88 mmol) in anhyd CH_2Cl_2 (30 mL), and the mixture was kept at the same temperature for 2 h. After concentration, the residue was triturated with ether, and the solids were filtered off and washed with ether. The combined filtrates were concentrated, and the residue was chromatographed to give methyl 2,3,4-tri-*O*-benzoyl-6-*O*-trifluoromethanesulfonyl-α-D-glucopyranoside (**7**) that was used immediately for the next step. ^{1}H NMR ($CDCl_3$): δ 6.19 (m, 1 H, H-3), 5.47 (t, 1 H, J 9.8 Hz, H-4), 5.30–5.26 (m, 2 H, H-1,2), 4.69 (dd, 1 H, $J_{5,6a}$ 6.6, $J_{6a,6b}$ 11.3 Hz, H-6a), 4.62 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 4.38 (ddd, 1 H, H-5), 3.50 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 97.11 (C-1), 73.93 (C-6), 71.60 (C-2), 69.87 (C-3), 69.03 (C-4), 67.50 (C-5); CIMS: m/z 656 ($[M+18]^+$).

(a) A mixture of D-mannose (**2**, 0.253 g, 1.4 mmol) and dibutyltin oxide (**3**, 0.312 g, 1.25 mmol) in anhyd methanol (10 mL) was stirred at 60 °C until a clear solution was obtained (~50 min). Toluene (2 mL) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd DMF (2.0 mL), and molecular sieves (4 Å, 0.2 g) were added. After addition of **7** (0.19 g, 0.298 mmol), the mixture was stirred vigorously at 0 °C for 4 h and then concentrated. The residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, the solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography (CH_2Cl_2–MeOH) gave first **20** 0.045 g, 22.6%) as mixture of α- and β-anomers, m/z 686 ($[M+18]^+$).

For characterization, the material was acetylated with acetic anhydride in pyridine at 20 °C to give, after column chromatography (hexane–ethyl acetate, pure **21**: $[\alpha]_D + 56°$. ^{1}H NMR ($CDCl_3$): δ 6.12 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.5 Hz, H-3^I), 6.06 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1^{II}), 5.43 (dd, 1 H, $J_{4,5}$10.4 Hz, H-4^I), 5.30 (t, partially overlapped, J ~10.0 Hz, H-4^{II}), 5.29 (dd, partially overlapped, H-2^{II}), 5.23 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10.0 Hz, H-2^I), 5. 17 (d, 1 H, H-1^I), 4.26 (dd, 1 H, $J_{5,6a}$ 5.1, $J_{6a,6b}$ 12.4 Hz, H-6^{II}a), 4.10 (dd, partially overlapped, $J_{5,6b}$ 2.4 Hz, H-6^{II}b), 4.08 (m, partially overlapped, H-5^I), 3.96 (ddd, 1 H, H-5^{II}), 3.87 (dd, partially overlapped, $J_{2,3}$ 3.5 Hz, H-3^{II}), 3.82 (dd, partially overlapped, H-6^{I}a), 3.58 (dd, 1 H, $J_{5,6b}$ 6.0 Hz, H-6^{I}b), 3.43 (s, 3 H, OCH_3), 2.14, 2.13, 2.12, 2.09 (4 s, 3 H each, 4 $COCH_3$); ^{13}C NMR ($CDCl_3$): δ 96.77 (C-1^I, $J_{C,H}$ 172.9 Hz), 90.93 (C-1^{II}, $J_{C,H}$ 177.2), 75.91 (C-3^{II}), 72.05 (C-2^I), 70.68 (C-5^{II}), 70.50 (C-3^I), 69.25 (C-4^I), 69.00 (C-5^I), 68.80 (C-6^I), 67.08 (C-2^{II}), 66.96 (C-4^{II}), 62.36 (C-6^{II}), 55.36 (OCH_3); CIMS: m/z 855 ($[M+18]^+$). Anal. Calcd for $C_{42}H_{44}O_{18}$: C, 60.28; H, 5.30. Found: C, 60.01 ; H, 5.39.

Later eluted was **12** (0.08 g, 40.2%) $[\alpha]_D + 30.2°$; ^{1}H NMR ($CDCl_3 + D_2O$): δ 6.13 (t, 1 H, J 9.7 Hz, H-3^I), 5.65 (t, 1 H, J 9.7, H-4^I), 5.31–5.22 (m, 2 H, H-1^I,2^I), 4.47 (bs, H 1, H-1^{II}), 4.25–4.19 (m, 1 H, H-5^I), 4.15–4.10 (m, 2 H, H-2^{II},6^{I}a), 3.94–3.87 (m, 2 H, H-4^{II},6^{II}a), 3.78 (bd, 1 H, $J_{6a,6b}$ ~11 Hz, H-6^{II}b), 3.67 (dd, 1 H, $J_{5,6b}$ 4.5, $J_{6a,6b}$ 12.2 Hz, H-6^{I}b), 3.56 (dd, 1 H, $J_{2,3}$ 3.8, $J_{3,4}$ 9.8 Hz, H-3^{II}), 3.41 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3 + D_2O$): δ 101.10 (C-1^{II}, $J_{C,H}$ 158.3 Hz), 96.98 (C-1^I, $J_{C,H}$ 175.9 Hz), 76.17 (C-5^{II}), 73.81 (C-3^{II}), 71.98 (C-2^I), 70.71 (C-2^{II}), 70.53 (C-3^I), 69.10 (C-4^I), 68.88 (C-5^I), 67.69 (C-6^I), 66.19 (C-4^{II}), 60.95 (C-6^{II}), 55.70 (OCH_3); CIMS: m/z 686 ($[M+18]^+$). Anal. Calcd for $C_{34}H_{36}O_{14}$: C, 61.07; H, 5.42. Found: C, 60.89; H, 5.51.

(b) A mixture of D-mannose (**1**, 0.253 g, 1.4 mmol) and dibutyltin oxide (**3**, 0.312 g,

1.27 mmol) in anhyd methanol (15 mL) was stirred at 60 °C until a clear solution was obtained (~70 min). Toluene (2 mL) and tetrabutylammonium fluoride monohydrate (0.125 g, 0.47 mmol) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd acetonitrile (3.0 mL), and molecular sieves (4 Å, 0.2 g) were added. After addition of **7** (0.3 g, 0.47 mmol), the mixture was stirred vigorously at 20 °C for 24 h, and concentrated. The resulting suspension was filtered through a pad of Celite, the solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography (CH_2Cl_2–MeOH) gave first **20** (0.055 g, 17.5%).

Eluted second was **12** (0.18 g, 57.3%).

*Methyl 3-*O*-benzyl-α-*D*-mannopyranoside* (**23**).—A mixture of methyl α-D-mannopyranoside (**22**, 10.0 g, 51.5 mmol) and dibutyltin oxide (**3**, 12.82 g, 51.5 mmol) in anhyd methanol (100 mL) was stirred under reflux for 3.5 h, at the end of which time a clear solution was obtained. Toluene (10 mL) and cesium fluoride (15.64 g, 103.0 mmol) were added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd DMF (70 mL), and molecular sieves (4 Å, 5 g) were added. After addition of benzyl bromide (12.24 mL, 103.0 mmol), the mixture was stirred at room temperature for 20 h, and concentrated. The residue was triturated with methanol, and the solids were filtered off. After addition of water to the filtrate, the mixture was kept overnight at 0 °C, the solids were filtered off and washed with methanol, the combined filtrate was concentrated, and the residue was chromatographed (CH_2Cl_2–MeOH), to give amorphous **23** (11 g, 72.6%): $[\alpha]_D + 35.2°$ (*c* 1, EtOH). Lit [21]., $[\alpha]_D + 36°$ (*c* 1.2, EtOH). The NMR data agreed with those reported [21].

*3-*O*-Benzyl-1,2,4,6-tetra-*O*-acetyl-α-*D*-mannopyranose* (**24**).—A solution of **23** (4.0 g) in 50:20:0.5 (v/v) Ac_2O–AcOH–H_2SO_4 (35 mL) was stirred at 20 °C for 4 h. The reaction mixture was poured into ice-water (30 mL), and, when the excess of Ac_2O was hydrolyzed, it was partitioned between dichloromethane and aq $NaHCO_3$. The organic layer was dried, concentrated, and chromatography (hexane–ethyl acetate) gave amorphous **24** (5.3 g, 89.0%): $[\alpha]_D + 0.20°$. Lit [22]. $[\alpha]_D + 0.28°$. The NMR data agreed with those reported [21].

*3-*O*-Benzyl-α-*D*-mannopyranose* (**27**).—Compound **24** (12.3 g) was deacetylated (Zemplén) to give **27** (7.13 g, 94%): $[\alpha]_D + 3.0°$. Lit [22]. $[\alpha]_D + 2.8°$.

Attempted anomeric benzylation of D-*mannose via the 1,2-stannylene acetal.*—A mixture of D-mannose (**2**, 2 g, 11.1 mmol) and dibutyltin oxide (**3**, 2.76 g, 11.1 mmol) in anhyd methanol (70 mL) was stirred at 60 °C until a clear solution was obtained (~3 h). Toluene (10 mL) was added, and the mixture was concentrated. The residue after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd *N*,*N*-dimethylacetamide (15 mL), molecular sieves (4 Å, 1.0 g) were added, and after addition of benzyl bromide (2.64 mL, 22.2 mmol) the mixture was stirred vigorously at 25 °C for 24 h and concentrated. The residue was chromatographed (dichloromethane–methanol) to give first benzyl 3-*O*-benzyl-β-D-mannopyranoside (**25**, 0.595 g, 14.9%): mp 112–113 °C (from EtOH), $[\alpha]_D -155°$. ^1H NMR ($CDCl_3$): δ 4.88–4.52 (4 d, 1 H each, 2 CH_2Ph), 4.36 (s, 1 H, H-1), 4.02 (t, 1 H, *J* 9.6 Hz, H-4), 3.96 (bd, 1 H, H-2), 3.90 (dd, partially overlapped, $J_{5,6a}$ 3.2, $J_{6a,6b}$ 12.1 Hz, H-6a), 3.81 (dd, partially overlapped, $J_{5,6b}$ 2.7 Hz, H-6b), 3.27 (dd, 1 H, $J_{2,3}$ 3.0, $J_{3,4}$ 9.3 Hz, H-6b), 3.15 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 98.41 (C-1, $J_{C,H}$ 158 Hz), 80.83 C-3), 75.96 (C-5), 71.28, 70.51 (2 *C*H_2Ph), 68.01 (C-2), 65.48 (C-4), 61.33 (C-6); CIMS: *m*/*z* 378. Anal. Calcd for $C_{22}H_{24}O_{64}$: C, 66.65; H, 6.71. Found: C, 66.48; H, 6.73.

Second was eluted a 1:1.2 mixture (1.2 g, 40.0%, NMR) of benzyl β-D-mannopyranoside (**26**) and 3-*O*-benzyl-D-mannose (**27**).

Methyl β-D-*mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-*D*-glucopyranoside* (**15**).—(a) A mixture of D-mannose (**2**, 0.181 g, 1.01 mmol) and dibutyltin oxide (**3**, 0.234 g, 0.94 mmol) in anhyd methanol (7 mL) was stirred at 60 °C until a clear solution was obtained (1 h). Toluene (2 mL) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd DMF (1.0 mL), molecular sieves (4 Å, 0.1 g) were added, and, after addition of methyl 2,3,6-tri-*O*-benzoyl-4-*O*-trifluromethanesulfonyl-α-D-galactopyranoside [18] (**9**, 0.1 g, 0.157 mmol), the mixture was stirred vigorously at 25 °C for 5 days. After concentration, the residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography (CH_2Cl_2–MeOH) gave **15** (0.04 g, 40.0%): mp 106–107 °C (from ethanol); $[\alpha]_D$

+104°. ^{1}H NMR ($CDCl_3 + D_2O$): δ 6.00 (t, 1 H, *J* 9.6 Hz, H-3^I), 5.23 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$10.2 Hz, H-2^I), 5.13 (d, 1 H, H-1^I), 4.70 (bd, 1 H, H-6^{I}a), 4.61 (dd, 1 H, $J_{5,6a}$ 4.2, $J_{5,6b}$ 12.3 Hz, H-6^{I}b), 4.58 (s, 1 H, H-1^{II}), 4.28 (m, 1 H, H-5^I), 4.12 (t, 1 H, *J* 9.4 Hz, H-4^I), 3.95 (d, 1 H, $J_{2,3}$ 2.5 Hz, H-2^{II}), 3.56 (t, 1 H, *J* 9.4, H-4^{II}), 3.41 (s, 3 H, OCH_3), 3.34 (dd, 1 H, $J_{3,4}$ 9.4 Hz, H-3^{II}), 3.17 (dd, 1 H, $J_{5,6a}$ 3.5, $J_{6a,6b}$ 12.3 Hz, H-6^{II}a), 3.04 (dd, 1 H, $J_{5,6b}$ 2.4 Hz, H-6^{II}b), 2.83 (dbt, 1 H, H-5^{II}); ^{13}C NMR ($CDCl_3$): δ 100.55 (C-1^{II}, $J_{C,H}$ 156.3 Hz), 96.79 (C-1^I, $J_{C,H}$ 176.1 Hz), 76.87 (C-4^I), 76.04 (C-5^{II}), 73.55 (C-3^{II}), 71.80 (C-2^I), 71.17 (C-3^I), 70.89 (C-2^{II}), 68.38 (C-5^I), 65.79 (C-4^{II}), 63.08 (C-6^I), 60.51 (C-6^{II}), 55.40 (OCH_3); CIMS: *m/z* 686 ($[M+18]^+$). Anal. Calcd for $C_{34}H_{36}O_{14}\cdot 0.5\ H_2O$: C, 60.26; H, 5.50. Found: C, 60.41; H, 5.52.

(b) A mixture of D-mannose (**2**, 0.36 g, 2.00 mmol) and dibutyltin oxide (**3**, 0.47 g, 1.88 mmol) in anhyd methanol (13 mL) was stirred at 60 °C until a clear solution was obtained (~1.5 h). Toluene (2 mL) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd DMA (1.5 mL), molecular sieves (4 Å, 0.2 g) and diisopropylethylamine (0.14 mL, 0.94 mmol) were added, and, after addition of methyl 2,3,6-tri-*O*-4-*O*-triflurometh anesulfonyl-α-D-galactopyranoside [18] (**9**, 0.2 g, 0.35 mmol), the mixture was stirred vigorously at 25 °C for 3 days and concentrated. The residue was triturated with acetonitrile, the resulting suspension was filtered through a pad of Celite, solids were washed with acetonitrile, and the combined filtrate was concentrated. Chromatography (CH_2Cl_2–MeOH) gave **15** (0.11 g, 52.6%).

(c) A mixture of D-mannose (**2**, 0.36 g, 2.00 mmol) and dibutyltin oxide (**3**, 0.47 g, 1.88 mmol) in anhyd methanol (13 mL) was stirred at 60 °C until a clear solution was obtained (1.6 h). CsF (0.29 g, 1.88 mmol) and toluene (2 mL) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.267 kPa for 2.5 h, was dissolved in anhyd Me_2SO (1.5 mL), molecular sieves (4 Å, 0.2 g) were added and, after addition of methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflurometh anesulfonyl-α-D-galactopyranoside [18] (**9**, 0.2 g, 0.35 mmol), the mixture was stirred vigorously at 25 °C for 2 days and concentrated. The residue was treated as described above, and chromatography gave **15** (0.12 g, 59.0%).

Methyl 3-O-*benzyl*-β-D-*mannopyranosyl-(1→6)-2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**14**).—A mixture of 3-*O*-benzyl-D-mannose (**25**) (0.618 g, 2.28 mmol) and dibutyltin oxide (**3**, 0.546 g, 2.197 mmol) in anhyd methanol (25 mL) was stirred at 70 °C until a clear solution was obtained (65 min). Toluene (4 mL) and tetrabutylammonium fluoride monohydrate (0.115 g, 0.439) were added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd acetonitrile (3.5 mL), and molecular sieves (4 Å, 0.2 g) were added. After addition of **7** (0.3 g, 0.439 mmol), the mixture was stirred vigorously at 20 °C for 20 h and concentrated. The residue was processed as described above, and chromatography (CH_2Cl_2–MeOH) gave **14** (0.26 g, 72.6%): $[\alpha]_D$ +16.2°; ^{1}H NMR ($CDCl_3 + D_2O$): δ 6.15 (t, 1 H, *J* 9.7, H-3^I), 5.63 (t, 1 H, *J* 9.7, H-4^I), 5.27 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 10.1, H-2^I), 5.22 (d, 1 H, H-1^I), 4.78, 4.63 (2 d, 1 H each, ^{2}J 12.3 Hz, CH_2Ph), 4.41 (s, 1 H, H-1^2), 4.27–4.20 (m, 1 H, H-5^I), 4.19 (d, 1 H, $J_{2,3}$ 3.1, H-2^{II}), 4.14 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 11.5 Hz, H-6^{I}a), 4.02 (t, 1 H, *J* 9.5 Hz, H-4^{II}), 3.83 (dd, partially overlapped, $J_{5,6a}$ 4.1, $J_{6a,6b}$ 11.8 Hz, H-6^{II}a), 3.78 (dd, partially overlapped, $J_{5,6b}$ 3.3 Hz, H-6^{II}b), 3.68 (dd, 1 H, $J_{5,6b}$ 6.4 Hz, H-6^{I}b), 3.41 (s, 3 H, OCH_3), 3.36 (dd, 1 H, H-3^{II}); ^{13}C NMR ($CDCl_3 + D_2O$): δ 100.86 (C-1^{II}, $J_{C,H}$ 158.6 Hz), 96.93 (C-1^I, $J_{C,H}$ 175.7 Hz), 80.57 (C-3^{II}), 75.88 (C-5^{II}), 71.96 (C-2^I), 71.09 (CH_2Ph), 70.41 (C-3^I), 69.18 (C-4^I), 68.76 (C-2^{II}), 67.91 (C-6^I), 67.51 (C-5^I), 65.80 (C-4^{II}), 58.64 (C-6^{II}), 55.60 (OCH_3); CIMS: *m/z* 776 ($[M+18]^+$). Anal. Calcd for $C_{41}H_{42}O_{14}$: C, 64.90; H, 5.58. Found: C, 64.85; H, 5.59.

Methyl 3-O-*benzyl*-β-D-*mannopyranosyl-(1→4)-2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**16**).—A mixture of 3-*O*-benzyl-D-mannose (**25**) (0.552 g, 2.03 mmol) and dibutyltin oxide (**3**, 0.468 g, 1.88 mmol) in anhyd MeOH (25 mL) was stirred at 70 °C until a clear solution was obtained (~60 min). Toluene (4 mL) and CsF (0.285 g, 1.88 mmol) were added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhydrous DMF (1.5 mL), and molecular sieves (4 Å, 0.2 g) were added. After addition of **9** [18] (0.2 g, 0.313 mmol), the mixture was stirred vigorously at (−5)–0 °C for 4 h, and at 20 °C for another 16 h. After concentration, the residue was processed as described above, and chromatography (CH_2Cl_2–MeOH) gave **16** (0.16 g, 67.5%): $[\alpha]_D$ +83°. ^{1}H NMR ($CDCl_3 + D_2O$): δ 5.96 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 8.6 Hz, H-3^I), 5.33 (dd, 1 H, $J_{1,2}$ 3.7, H-2^I),

5.12 (d, 1 H, H-1^{I}), 4.70, 4.48 (2 d, partially overlapped, ^{2}J 11.9 Hz, CH_2Ph), 4.67 (dd, partially overlapped, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.1 Hz, H-6^{I}a) 4.57 (dd, 1 H, $J_{5,6b}$ 3.9, H-6b), 4.49 (s, overlapped, H-1^{II}), 4.29–4.22 (m, 1 H, H-5^{I}), 4.18 (t, 1 H, J 8.6, H-4^{I}), 4.04 (d, 1 H, $J_{2,3}$ 2.9 Hz, H-2^{II}), 3.63 (t, 1 H, J 9.4, H-4^{II}), 3.45 (s, 3 H, OCH_3), 3.22–3.14 (m, 2 H, H-3^{II},6^{II}a), 2.95–2.87 (m, 2 H, H-5^{II},6^{II}b); ^{13}C NMR ($CDCl_3 + D_2O$): δ 99.29 (C-1^{II}, $J_{C,H}$ 157.7 Hz), 96.99 (C-1^{I}, $J_{C,H}$ 171 Hz), 80.84 (C-3^{II}), 75.79 (C-5^{II}), 75.34 (C-4^{I}), 71.18 (2 C, C-2^{I},3^{I}), 71.02 (CH_2Ph), 68.34 (C-5^{I}), 67.41 (C-2^{II}), 66.00 (C-4^{II}), 62.98 (C-6^{I}), 61.66 (C-6^{II}), 55.51 (OCH_3); CIMS: m/z 776 ($[M + 18]^+$). Anal. Calcd for $C_{41}H_{42}O_{14}$: C, 64.90; H, 5.58. Found: C, 64.71; H, 5.64.

Methyl 2,4,6-tri-O-*benzoyl-3*-O-*benzyl*-β-D-*mannopyranosyl-(1→4)-2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**17**).—Benzoyl chloride (0.25 mL, 2.3 mmol) was slowly added at 20 °C to a stirred solution of **16** (0.5 g, 0.66 mmol) in anhyd pyridine (5 mL). After 4 h the reaction was quenched by addition of methanol, the mixture was concentrated, and chromatography (toluene–EtOAc) gave **17** (0.6 g, 85%): mp. 101–102 °C (from ethanol); $[\alpha]_D$ −11.5°, ^{1}H NMR ($CDCl_3$): δ 6.01 (t, 1 H, J 9.0 Hz, H-3^{I}), 5.92 (bd, 1 H, H-2^{II}), 5.50 (t, 1 H, J 9.8 Hz, H-4^{II}), 5.16 (dd, partially overlapped, $J_{2,3}$ 10.3 Hz, H-2^{I}), 5.12 (d, partially overlapped, H-1^{I}), 4.82 (bs, 1 H, H-1^{II}), 4.76 (dd, 1 H, $J_{5,6a}$ 3.4, $J_{6a,6b}$ 12.7 Hz, H-6^{I}a), 4.65 (d, partially overlapped, ^{2}J 12.7 Hz, C*H*aPh), 4. 63 (dd, partially overlapped, $J_{5,6b}$ 2.0 Hz, H-6^{I}b), 4.45 (d, 1 H, C*H*b Ph), 4.29–4.19 (m, 2 H, H-5^{I}, incl t at 4.22, J 8.5, H-4^{I}), 4.14 (dd, 1 H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 12.6 Hz, H-6^{II}a), 3.94 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-6^{II}b), 3.72 (dd, 1 H, $J_{2,3}$ 3.1, H-3^{II}), 3.61 (ddd, 1 H, H-5^{II}), 3.38 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 98.57 (C-1^{II}), 96.86 (C-1^{I}), 75.95 (2 C, C-4^{I},3^{II}), 72.50 (C-5^{II}), 72.06 (C-2^{I}), 70.45 (CH_2Ph), 69.76 (C-3^{I}), 68.31 (C-5^{I}), 68.01 (C-4^{II}), 67.70 (C-2^{II}), 62.94 (C-6^{II}), 62.91 (C-6^{I}), 55.42 (OCH_3); CIMS: m/z 1089 ($[M + 18]^+$. Anal. Calcd for $C_{62}H_{54}O_{17}$: C, 69.52; H, 5.08. Found: C, 69.46; H, 5.13.

Methyl (2,3,4,6-tetra-O-*acetyl*-β-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)-(1→3)-2,4,6-tri*-O-*benzoyl*-β-D-*mannopyranosyl-(1→4)-2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranoside* (**29**). — A solution of the 3-*O*-benzyl derivative **17** (0.1 g) in ethanol (5 mL) was stirred under hydrogen at 50 °C until TLC (solvent) showed that the reaction was complete (~48 h). Conventional processing and chromatography gave the amorphous methyl 2,4,6-tri-*O*-benzoyl-β-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (**18**) (0.075 g, 82.4%): $[\alpha]_D$ +15.6°. ^{1}H NMR ($CDCl_3$): δ 5.99 (m, 1 H, H-3^{I}), 5.70 (bd, 1 H, $J_{2,3}$ ~3 Hz, H-2^{II}), 5.32 (t, J 9.8 Hz, H-4^{II}), 5.18–5.12 (m, 2 H, H-1^{I},2^{I}), 4.91 (s, 1 H, H-1^{II}), 4.67 (m, 2 H, H-6^{I}a,b), 4.25–4.17 (m, 3 H, H-4^{I},5^{I},6^{II}a), 4.10–3.95 (m, 2 H, H-3^{II},6^{II}b), 3.72 (ddd, $J_{5,6a}$ 2.8, $J_{5,6b}$ 4.9, $J_{6a,6b}$ 9.6 Hz, H-5^{II}), 3.38 (s, 3 H, OCH_3), 2.65 (d, 1 H, $J_{3,OH}$ 7.1 Hz, OH); ^{13}C NMR ($CDCl_3$): δ 98.38 (C-1^{II}), 96.86 (C-1^{I}), 75.87 (C-4^{I}), 72.37 (C-5^{II}), 72.10 (C-2^{I}), 71.80 (C-2^{II}), 71.62 (C-3^{II}), 70.20 (C-4^{II}), 69.80 (C-3^{I}), 68.34 (C-5^{I}), 62.86 (2 C, C-6^{I,II}), 55.45 (OCH_3); CIMS: m/z 998 ($[M + 18]^+$).

$BF_3{\cdot}Et_2O$ (0.029 mL, 0.23 mmol) was added at 0–+5 °C to a stirred solution of lactosyl imidate [20] **28** (0.183 g, 0.245 mmol) and **18** (0.140 g, 0.143 mmol) in anhyd CH_2Cl_2 (1 mL). The mixture was allowed to reach slowly at 20 °C within ~3.5 h, when the reaction mixture was neutralized by addition of triethylamine. After concentration, chromatography (hexane–EtOAc) gave **29** (0.16 g, 70%): $[\alpha]_D$ −9°. ^{1}H NMR ($CDCl_3$): δ 3.96 (m, 1 H, H-3^{I}), 5.79 (bd, 1 H, $J_{2,3}$ ~3 Hz, H-2^{II}), 5.41 (t, 1 H, J 9.9 Hz, H-4^{II}), 5.27 (bd, 1 H, $J_{3,4}$ ~2.9 Hz, $J_{4,5}$ < 1 Hz), 5.16–5.10 (m, 2 H, H-1^{I},2^{I}), 5.09–5.00 (m, 2 H, H-2^{IV},3^{III}), 4.85 (dd, partially overlapped, $J_{3,4}$ 3.4, $J_{2,3}$ 10.2 Hz, H-3^{IV}), 4.83 (s, partially overlapped, H-1^{II}), 4.74 (dd, 1 H, $J_{5,6a}$ 3.2, $J_{6a,6b}$ 12.2 Hz, H-6^{I}a), 4.66–4.60 (m, 3 H, H-1^{III},2^{III},6^{I}b), 4.25–4.13 (m, 6 H, H-1^{IV},3^{II},4^{I},5^{I},6^{II}a,6^{III}a), 4.03–3.95 (m, 2 H, H-6^{IV}a,b), 3.91 (dd, partially overlapped, $J_{5,6b}$ 5.6, $J_{6a,6b}$ 12.0 Hz, H-6^{II}b), 3.85 (dd, partially overlapped, $J_{5,6b}$ 4.1, $J_{6a,6b}$ 11.5 Hz, H-6^{III}b), 3.74–3.66 (m, 2 H, H-5^{II,IV}), 3.64–3.54 (m, 2 H, H-4^{III},5^{III}); ^{13}C NMR ($CDCl_3$): δ 100.96 (C-1^{IV}, $J_{C,H}$ 161.2 Hz), 98.30 (C-1^{II}, $J_{C,H}$ 155.1 Hz), 97.24 (C-1^{III}, $J_{C,H}$ 164.8 Hz), 96.86 (C-1^{I}, $J_{C,H}$ 175 Hz), 75.96 (C-4^{III}), 75.75 (C-4^{I}), 75.21 (C-3^{II}), 72.99 (C-3^{III}), 72.37 (2 C, C-5^{II},5^{III}), 72.01 (C-2^{I}), 71.17 (C-2^{III}), 70.85 (C-3^{IV}), 70.53 (C-5^{IV}), 69.68 (C-3^{I}), 68.94 (C-2^{IV}), 68.21 (C-5^{I}), 67.77 (C-2^{II}), 67.63 (C-4^{II}), 66.49 (C-4^{IV}), 63.03 (C-6^{I},6^{II}), 62.14 (C-6^{III}), 60.66 (C-6^{IV}), 54.47 (OCH_3); CIMS: m/z 1618 ($[M + 18]^+$). Anal. Calcd for $C_{81}H_{82}O_{34}$: C, 60.82; H, 5.17. Found: C, 60.76; H, 5.23.

Methyl 2,3,4,6-tetra-O-*acetyl*-α-D-*glucopyranosyl-(1→4)-1,3,6-di*-O-*acetyl-2*-O-*(methyl 2,3,6-tri*-O-*benzoyl*-α-D-*glucopyranos-2-yl)*-β-D-*glucopyranoside (methyl 2,3,6-tri*-O-*benzoyl-4*-O-*(hepta*-O-*acetyl*-β-*maltos-2-yl)*-α-D-*glucopyranoside* (**32**).—A

mixture of maltose (**30**, 1.044 g, 2.9 mmol) and dibutyltin oxide (**3**, 0.649 g, 2.6 mmol) in anhyd methanol (30 mL) was stirred at 70 °C until a clear solution was obtained (~1 h). Toluene (2 mL) and tetrabutylammonium fluoride monohydrate (0.605 g, 2.316 mmol) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhyd DMF (3.5 mL). After addition of **9** (0.27 g, 0.429 mmol), the mixture was stirred vigorously at 20 °C for 20 h, and concentrated. The residue was chromatographed (CH_2Cl_2–MeOH), to give **31** (0.261 g, 74.6%) as a mixture of anomers, CIMS: m/z 846 ($[M+18]^+$).

Acetic anhydride (1 mL) was added slowly, with stirring, at 100 °C, to a solution of the foregoing material in pyridine (2 mL). After usual processing, chromatography (toluene–EtOAc) gave **32**: $[\alpha]_D$ +115°. ^{1}H NMR ($CDCl_3$) for the β-anomer (largely predominating): δ 5.81 (bt, 1 H, J 10.1 Hz, H-3^I), 5.61 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1^{II}), 5.24 (t, partially overlapped, H-3^{III}), 5.19 (t, partially overlapped, J 9.0 Hz, H-3^{II}), 5.11–5.05 (m, 2 H, H-1^I,2^I), 5.02 (t, partially overlapped, J 9.7 Hz, H-4^{III}), 4.96 (d, partially overlapped, $J_{1,2}$ ~4 Hz, H-1^{III}), 4.80 (dd, 1 H, $J_{1,2}$ 4.0, $J_{2,3}$10.5 Hz, H-2^{III}), 4.47 (m, 2 H, H-6^{I}a,b), 4.31 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{5,6b}$ 11.8 Hz, H-6^{II}a), 4.24–4.08 (m, 4 H, H-4^I,5^I,6^{II}b,6^{III}a), 4.00–3.90 (m, 2 H, H-2^{II},6^{III}b), 3.80 (m, 1 H, H-5^{III}), 3.72 (m, 1 H, H-5^{II}), 3.42 (s, 3 H, OCH_3), 3.33 (t, 1 H, J 9.0 Hz, H-4^{II}), 2.24, 2.09, 2.08, 2.06, 2.00, 1.97, 1.94 (7 s, 3 H each, 7 COCH3); ^{13}C NMR ($CDCl_3$): δ 96.57 (C-1^I), 95.42 (C-1^{III}), 93.88 (C-1^{II}), 76.87 (C-2^{II}), 75.32 (C-4^I), 73.93 (C-3^I), 73.85 (C-3^{II}), 73.03 (C-5^{II}), 72.93 (C-4^{II}), 72.30 (C-2^I), 69.71 (C-2^{III}), 69.37 (C-3^{III}), 68.34 (C-5^{III}), 68.00 (C-5^I), 67.93 (C-4^{III}), 63.65 (C-6^I), 62.53 (C-6^{II}), 61.46 (C-6^{III}), 55.33 (OCH_3); CIMS: m/z 1142 ($[M+18]^+$). Anal. Calcd for $C_{54}H_{60}O_{26}$: C, 57.65; H, 5.38. Found: C, 57.56 ; H, 5.39.

*Methyl 4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside* (**35**).—A mixture of 4,6-*O*-benzylidene-D-glucose (**33**, 0.252 g, 0.94 mmol) and dibutyltin oxide (**3**, 0.230 g, 0.94 mmol) in anhyd methanol (10 mL) was stirred at 60 °C until a clear solution was obtained (~1 h). Toluene (2 mL) and tetrabutylammonium fluoride monohydrate (0.047 g, 0.16 mmol) was added, and the mixture was concentrated. The residue, after having been kept at 50 °C/0.2 kPa for 2.5 h, was dissolved in anhydrous acetonitrile (4 mL). After addition of **7** (0.1 g, 0.16 mmol), the mixture was stirred vigorously at 50 °C for 10 h, and concentrated. The residue was separated by column chromatography (toluene–ethyl acetate containing a little triethylamine) to give first a small amount of a byproduct, methyl 4,6-*O*-benzylidene-*β*-D-glucopyranos-2-yl-(2→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (**34**): CIMS: m/z 775 ($[M+18]^+$). The material was acetylated as described for the preparation of **32**, to give methyl 1,3-di-*O*-acetyl-4,6-*O*-benzylidene-*α*,*β*-D-glucopyranos-2-yl-(2→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (**36**). ^{1}H NMR for the predominating β-anomer ($CDCl_3$): δ 6.13 (t, 1 H, J 9.6 Hz, H-3^I), 5.74 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1^{II}), 5.45 (s, partially overlapped, C*H*Ph), 5.44 (t, partially overlapped, H-4^I), 5.34 (t, 1 H, J 9.2, H-3^{II}), 5.21 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 10.0 Hz, H-2^I), 5.16 (d, 1 H, H-1^I), 4.36 (dd, 1 H, $J_{5,6}$ 5.6, $J_{6a,6b}$ 9.6 Hz, H-6^{II}a), 4.14 (m, 1 H, H-5^I), 3.87 (dd, 1 H, $J_{5,6a}$ 6.4, $J_{6a,6b}$ 10.4 Hz, H-6^{I}a), 3.76 (dd, partially overlapped, $J_{5,6b}$ 1.6 Hz, H-6^{I}b), 3.70 (d, partially overlapped, H-6^{II}b), 3.68–3.56 (m, 2 H, H-4^{II},5^{II}), 3.49 (dd, partially overlapped, H-2^{II}), 3.43 (s, 3 H, OCH_3), 2.09, 1.95 (2 s, 3 H, each, 2 $COCH_3$) ; $\delta_{H\text{-}1_\alpha}$ 6.40, $J_{1,2}$ 3.3 Hz; ^{13}C NMR ($CDCl_3$): δ 101.44 (*C*HPh), 96.75 (C-1^I), 93.78 (C-1^{II}), 80.19 (C-2^{II}), 78.37 (C-4^{II}), 72.64 (C-3^{II}), 72.09 (C-2^I), 70.35 (C-3^I), 69.35 (C-4^I), 69.12 (C-5^I), 68.42 (2 C, C-6^{I,II}), 66.74 (C-5^{II}), 55.53 (OCH_3); CIMS: m/z 858 ($[M+18]^+$).

Second eluted was the title compound **35** (0.068 g, 57.1%): $[\alpha]_D$ +15.6°. ^{1}H NMR ($CDCl_3+D_2O$): δ 6.19 (m, 1 H, H-3^I), 5.87 (t, 1 H, J 9.8 Hz, H-4^I), 5.54 (s, 1 H, C*H*Ph), 5.32–5.28 (m, 2 H, H-1^I,2^I), 4.35 (d, partially overlapped, $J_{1,2}$ 7.5 Hz, H-1^{II}), 4.32 (dd, partially overlapped, $J_{5,6a}$ 5.0 Hz, H-6^{II}a), 4.27–4.19 (m, 2 H, H-5^I,6^{I}a), 3.87–3.80 (m, 2 H, H-3^{II},6^{II}b), 3.72–3.61 (m, 3 H, H-2^{II},6^{I}b, incl t at 3.64, J 10.0 Hz, H-4^{II}), 3.47 (s partially overlapped, OCH_3), 3.49–3.40 (m, partially overlapped, H-5^{II}); ^{13}C NMR ($CDCl_3+D_2O$): δ 103.53 (C-1^{II}, $J_{C,H}$ 159.6 Hz), 101.84 (*C*HPh), 97.30 (C-1^I, $J_{C\text{-}1,H\text{-}1}$ 175.7 Hz), 80.17 (C-4^{II}), 74.43 (C-2^{II}), 72.91 (C-3^{II}), 72.94 (C-2^I), 70.36 (C-3^I), 68.74 (C-4^I), 68.55 (C-6^{II}), 68.08 (C-5^I), 67.83 (C-6^I), 66.59 (C-5^{II}), 55.79 (OCH_3); CIMS: m/z 775, ($[M+18]^+$).

For characterization, a portion was acetylated with 1:1 pyridine–acetic anhydride to give methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (**37**) as a foam: $[\alpha]_D$ +1.7° (c 0.9). ^{1}H

NMR ($CDCl_3$): δ 6.18–6.10 (m, H-3^I), 5.47 (t, s, 2 H, partially overlapped, $J\sim10.8$ Hz, H-4^I, C*H*Ph), 5.33 (t, J 9.5 Hz, H-3^{II}), 5.28–5.22 (m, 2 H, H-1^I,2^I), 5.06 (dd, 1 H, $J_{1,2}$ 7.8, $J_{2,3}$ 9.2 Hz, H-2^{II}), 4.66 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{II}), 4.32 (dd, 1 H, $J_{5,6a}$ 5.1, $J_{6a,6b}$ 10.5 Hz, H-6^{II}a), 4.23 (ddd, 1 H, $J_{5,6a}$ 1.7, $J_{5,6b}$ 6.1, $J_{4,5}$ 9.8 Hz, H-5^I), 4.06 (dd, 1 H, $J_{6a,6b}$ 10.8 Hz, H-6^Ia), 3.78–3.64 (m, 3 H, H-6^Ib,6^{II}b, incl t, partially overlapped, J 9.5 Hz, H-4^{II}), 3.57–3.45 (m, 4 H, H-5^{II}, incl s, 3.45, OCH_3), 2.11, 2.05 (2 s, 3 H each, 2 $COCH_3$); ^{13}C NMR ($CDCl_3$): δ 101.40 (2 C, C-1^{II}, *C*HPh), 96.76 (C-1^I), 78.20 (C-4^I), 72.03 (C-2^{II}), 71.94 (C-2^I), 71.65 (C-3^{II}), 70.40 (C-3^I), 69.19 (C-4^I), 68.50 (C-5^I), 68.39, 68.34 (C-$6^{I,II}$), 66.28 (C-5^{II}), 20.76, 20.71 (2 CO*C*H_3); CIMS: m/z 858 ($[M+18]^+$). Anal. Calcd for $C_{45}H_{44}O_{16}$: C, 64.28; H, 5.27. Found: C, 64.23; H, 5.35.

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