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L-Iduronic acid derivatives as glycosyl donors

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Abstract

O-[Methyl (2-*O*-acetyl-3-*O*-benzyl-4-*O*-levulinyl-α, and β-L-idopyranosid)uronate] trichloroacetimidate and the corresponding *n*-pentenyl glycosides are efficient L-iduronic acid glycosyl donors. Both have been used for the high-yielding synthesis of basic disaccharide blocks which are useful for the subsequent synthesis of complex oligosaccharides related to heparin/heparan sulfate, and dermatan sulfate. In contrast, the corresponding thioethyl glycosides, thiophenyl glycosides, and fluoride, did not yield the expected disaccharides.

Keywords: Iduronic acid; Glycosidation; Glycosaminoglycans; Synthesis; Glycosyl donors

1. Introduction

The biological properties of glycosaminoglycans were long believed to involve large fragments of these complex polysaccharides, but it is now well documented that rather short domains exist that have unique sequences for protein binding and are endowed with biological properties [1–8]. Only chemical synthesis can afford the great variety of pure oligosaccharides needed to explore the structure–activity relationships or to mimic the biological properties of these domains, where L-iduronic acid is frequently encountered [9]. Results of our research in this field have already been published, and we now report on the comparison of various L-iduronic acid glycosyl donors in the synthesis of heparin/heparan sulfate, and dermatan sulfate related disaccharides.

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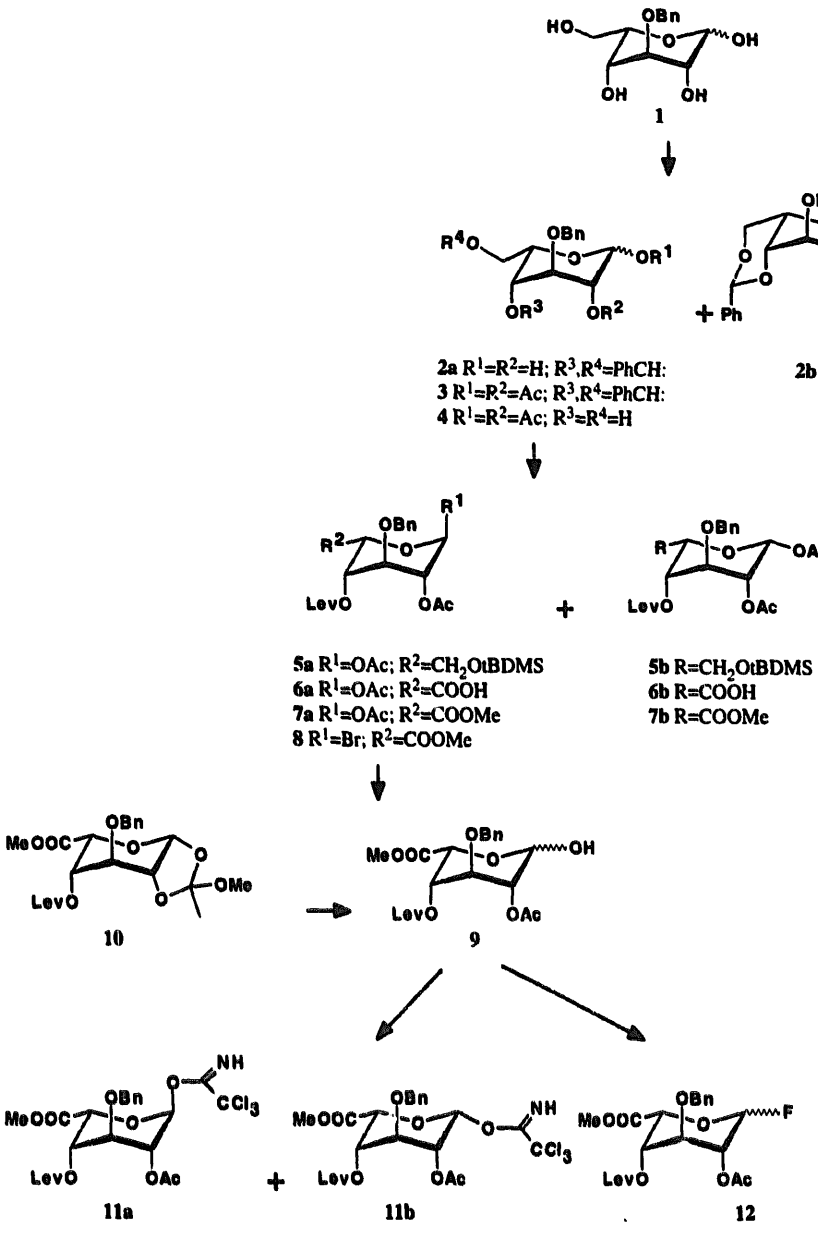
In the past, different types of iduronic acid glycosyl donors were used to prepare fragments of glycosaminoglycans: orthoesters [10–13], the bromide methyl (2,3,4-tri-*O*-acetyl-1-bromo-1-deoxy-α-L-idopyranosyl)uronate [14–16], and the imidate methyl (2,3,4-tri-*O*-acetyl-1-*O*-trichloroacetimidoyl-α,β-L-idopyranosyl)uronate [17]. In these glycosyl donors, because of its instability, the activating group was introduced on the corresponding iduronic acid derivative immediately before the glycosylation reaction. Such activation may lead to an (occasionally substantial) loss of already highly elaborated building blocks, which is not an ideal situation in a converging synthesis of oligosaccharides, particularly when hardly accessible, L-iduronic acid-containing, building blocks are involved. On the contrary, stable L-iduronic acid glycosyl donors, where activation of the anomeric center is realized via specific activation of functions that, moreover, can withstand numerous chemical modifications, are highly desired. It is the aim of the present work to investigate the glycosylation properties of such stable iduronic acid derivatives: *n*-pentenyl glycosides and thioglycosides. The imidate method was chosen as the reference for comparison. *n*-Pentenyl glycosides and thioglycosides of idose were converted into iduronic acid derivatives, and used as glycosyl donors. 1-Fluoro derivatives, which are stable enough to withstand some chemical manipulations, were also studied, due to the encouraging results obtained with idosyl fluorides in glycosylation reactions [18].

2. Results and discussion

Preparation of L-iduronic acid glycosyl donors.—As starting material for the preparation of iduronic acid derivatives 3-*O*-benzyl-L-idopyranose (**1**) [18], obtained by acid hydrolysis of 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-L-idofuranose [18], was used. Essentially, two strategies have been employed to obtain the required iduronic acid glycosyl donors from **1**: (a) the idose derivative was converted into iduronic acid before the activating group was introduced at the anomeric center; (b) the activating group was introduced first, and the idose unit was then converted into the desired iduronic acid derivative. Of course, as stated above, the latter requires the activating group being stable under a variety of experimental conditions. It can therefore only be used in the case of stable activating groups such as thioglycosides or *n*-pentenyl glycosides. The first strategy must be followed in case of reactive or labile activating groups like halides or imidates; obviously, it can also be applied to stable activating groups.

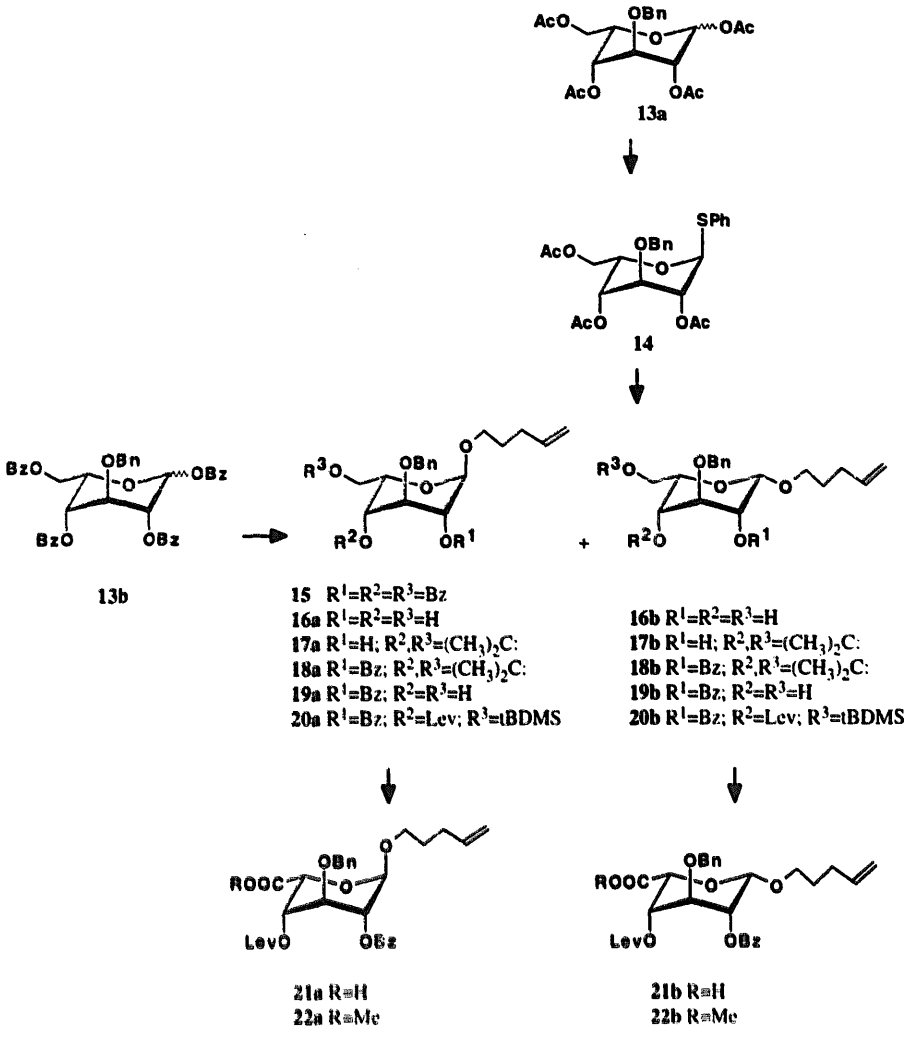
The imidates **11** and the fluorides **12** were first prepared according to strategy (a) (Scheme 1). Compound **1** was treated with benzaldehyde in the presence of trifluoroacetic acid. The monobenzylidene derivative **2a** was the major product (49%, from 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-L-idofuranose). The dibenzylidene derivative **2b** was also isolated (14%, from 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-L-idofuranose). Acetylation of **2a**, followed by removal of the benzylidene group, afforded a mixture of the two anomers of **4**. A classical sequence of reactions [9] was next used to convert **4** into the L-iduronic acid derivative **7**. After silylation and levulinoylation, the α (**5a**), and β (**5b**) anomers of **5** could be separated by silica gel



Scheme 1. Preparation of the imidates **11a** and **11b** and the fluorides **12** from **1**.

chromatography, separately oxidized, and then converted into the esters **7a** and **7b**. In preparative experiments, the reactions were carried out from **2a** to **7a** and **7b** on the mixture of anomers with an overall yield of about 50%. The mixture **7a** and **7b** was treated with titanium tetrabromide to give **8**, which was immediately hydrolyzed to **9** (80% from the mixture of **7a** and **7b**) after treatment with silver silicate in an acetone–water solution. It was quantitatively converted into the fluoride **12** by treatment with diethylaminosulfur trifluoride in tetrahydrofuran at −30 °C [19]. A mixture of anomers was obtained with $J_{H\text{-}1\alpha,F}$ 47.7 and $J_{H\text{-}1\beta,F}$ 42.1 Hz.

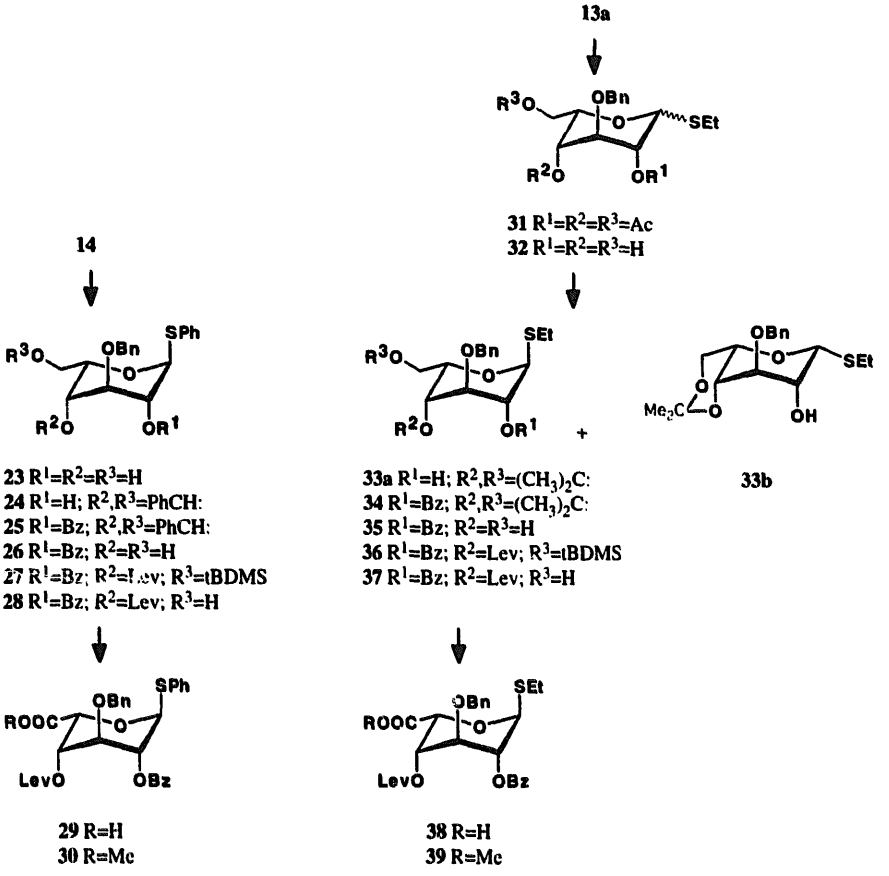
In an alternative synthesis, **9** was prepared (80%) by aqueous acetic acid treatment of



Scheme 2. Preparation of the *n*-pentenyl glycosides **22a** and **22b** from **13a**.

the orthoester **10** obtained (89%) after levulinoylation of the known methyl 3-*O*-benzyl-β-L-idopyranuronate 1,2-(methyl orthoacetate) [10]. Under anhydrous acetic acid treatment [20] the 1,2-*trans* diacetate **7a** was obtained. A mixture of the α and β trichloroacetimidates **11a** and **11b** was then easily formed (95%) from **9a** by treatment with trichloroacetonitrile in the presence of potassium carbonate [21].

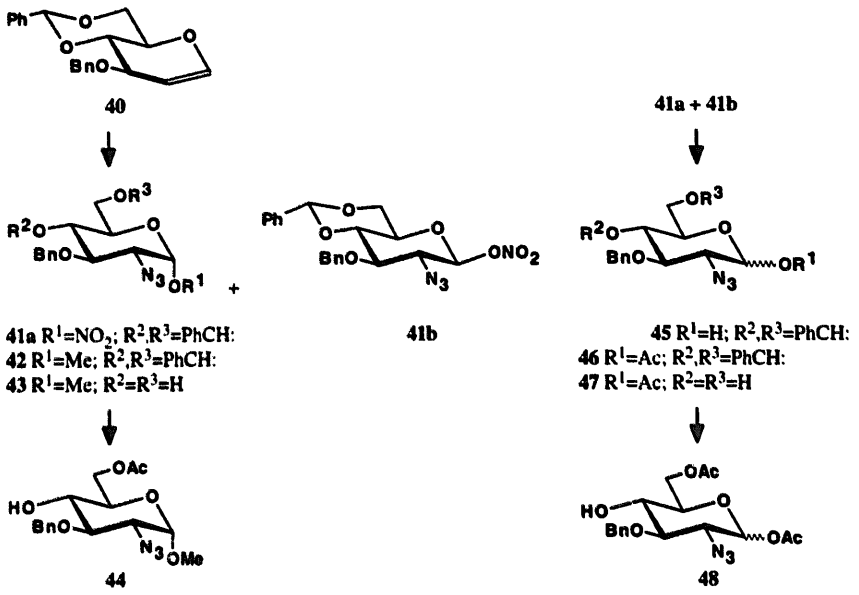
n-Pentenyl glycosides were next prepared according to strategy (b) (Scheme 2). The reaction of 4-penten-1-ol with **13a** [18], in the presence of boron trifluoride, gave the desired *n*-pentenyl glycoside in 80% yield, but this reaction proved to be very difficult to scale up (> 1 g). Other attempts using tin tetrachloride as Lewis acid resulted into debenzylation [22]. However, using the benzoylated derivative **13b** instead of **13a**, and trimethylsilyl triflate as Lewis acid, as already reported for anomeric benzoates [23], the *n*-pentenyl glycoside **15** was obtained in excellent yield (94%). Alternatively, a 4:1 mixture of α and β *n*-pentenyl isomers was obtained after prior synthesis of the thiophenylglycoside **14** (see preparation below), followed by electrochemical glycosida-



Scheme 3. Preparation of the thioglycosides **30** and **39**.

tion [24,25] in the presence of 4-penten-1-ol. Either pure **15** or a mixture of the two anomers was deacylated to give a mixture of **16a** and **16b**, which were then converted into the corresponding 4,6-*O*-isopropylidene derivatives **17a** and **17b**. Silica gel chromatography afforded pure α (**17a**) and β (**17b**) anomers. After benzoylation at C-2, they were engaged in a classical [9] reaction sequence resulting finally in the iduronic acid glycosyl donors **22a** and **22b** (54% and 50%, respectively, from **17a** and **17b**).

Thioglycosides **30** and **39** were finally prepared according to strategy (b) (Scheme 3). The reaction of **13a** with thiophenol, in the presence of $BF_3 \cdot Et_2O$, gave the glycoside **14** in 89% yield. It was then converted in five steps into the idose derivative **27** which was oxidized under Jones conditions to obtain, after methylation, the iduronic acid derivative **30**, in moderate yield (26%) because of the partial oxidation of **27** to the corresponding sulfone and sulfoxide (mass spectrometry, ~ 50%). Removal of the silyl ether protecting group followed by oxidation with pyridinium dichromate [26], and methylation, gave a substantially better yield of **30** (52%). The ethyl thioglycosides **31** were obtained from **13a** by treatment with ethanethiol in the presence of boron trifluoride etherate. In this case, at variance with the synthesis of **14**, a mixture of α and β isomers was obtained in spite of the presence of a participating group at C-2. This may be related to the high nucleophilicity of ethanethiol [27]. The reaction sequence previously described for the preparation of **30** was then applied to **31**, except that an



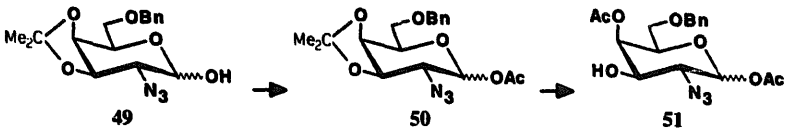
Scheme 4. Synthesis of the glucosamine derivatives **44** and **48**.

isopropylidene group was used instead of a benzylidene for temporary protection of the 4,6-diol. At the isopropylidene stage, the two isomers **33a** and **33b** could be easily separated and obtained in a 1:1 ratio. Only the α isomer **33a** was used in the remaining part of the synthesis. The glycosyl donor **39** was finally obtained in 45% yield from **33a**.

Preparation of glycosyl acceptors.—The protective groups of the different monosaccharide acceptors were selected to fit a strategy suitable for the preparation of heparin/heparan sulfate or dermatan sulfate fragments.

The first selected glycosyl acceptor was methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**44**) (Scheme 4). It was easily obtained in three steps (82%) from **41b** resulting from the selective azido-nitration of the glycal **40** [28]. In the *gluco* series, we also used, as glycosyl acceptor, the mixture of anomeric acetates **48**, which offers the possibility of elongating the chain after selective removal of the anomeric acetate, and introduction of an appropriate activating group. For the preparation of **48**, we started from the mixture of α and β nitrates **41a** and **41b**. Treatment with an excess of thiophenol in the presence of *N,N*-diisopropylethylamine at room temperature [29] afforded a nearly quantitative yield of **45**. Acetylation, acid hydrolysis of the benzylidene group, and selective acetylation by acetyl chloride in pyridine then gave **48** (63%). The pure α acetate could also be obtained from the β nitrate **41b** by treatment with acetic acid–acetic anhydride–sodium acetate for a few hours at 100 °C, followed by the above sequence of reactions.

For the preparation of the galactosamine acceptors **51** (Scheme 5), the known 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-α,β-D-galactopyranose **49** [29] was acetylated to give **50** (1:1 anomeric mixture). The isopropylidene group was then hydrolyzed, and the resulting diol was converted into **51** using the selective opening of an orthoacetate in the presence of camphorsulfonic acid [30]. The position of the acetate was confirmed by the chemical shifts observed for H-4α (5.45 ppm) and H-4β (5.37 ppm) in the corresponding ^{1}H NMR spectra.



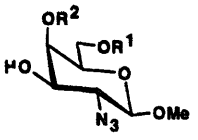
Scheme 5. Synthesis of the galactosamine derivatives **51**.

Glycosylation reactions.—The glycosylation of **44** with the fluorides **12** in the presence of boron trifluoride led to frustration, and only degradation products of **12** have been observed. We next investigated the reactivity of the phenyl thioglycoside **30** towards the acceptor **44**, using either dimethylthiomethylsulfonium triflate [31] or [tris (4-bromophenyl) ammoniumyl hexachloroantimonate] [32] as catalyst. No reaction was observed under our experimental conditions (room temperature, in dichloromethane for the former, and acetonitrile for the latter), and both the glycosyl donor and the glycosyl acceptor were recovered unchanged. Similarly, the ethyl thioglycoside **39** did not react with methyl 4-*O*-acetyl-2-azido-6-*O*-benzyl-2-deoxy-β-D-galactopyranoside (**52**) [33], the decomposition of the L-iduronic acid derivative only being observed. Among the products, the lactone **53** could be identified.

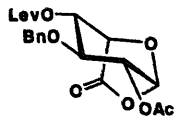
The glycosylation with *n*-pentenyl glycosides was next studied under the classical reaction conditions. Methyl [(pent-4-enyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-levulinyl-α-L-idopyranosyl)uronate] (**22a**), and its β anomer (**22b**), reacted with methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**44**) in the presence of *N*-iodosuccinimide and triflic acid [34,35] to give the disaccharide (**57**) in 80% and 83% yields, respectively. In a similar way, they reacted with alcohol **48** to provide **58** (75% and 77%, respectively). When **22a** was allowed to react with **52** in dichloromethane, in the presence of *N*-iodosuccinimide and triflic acid, the expected disaccharide **61** was obtained in very good yield (85%). Similarly, condensation of **22a** with the alcohol **51** gave the disaccharide **62** (72%), and condensation with methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranoside (**54**) [33] gave **63** in excellent yield (90%).

Glycosylation with imidates was finally studied. The two imidates **11a** and **11b** reacted in the same way with the alcohol **44**, in the presence of trimethylsilyl triflate in dichloromethane, at −20 °C, the disaccharide **55** being obtained in high yield (91–92%) whatever the anomery of the starting imidate. The four disaccharides **55**, **56**, **59**, and **60** were all prepared in good to excellent yields (91, 92, 86, and 81%, respectively) under the same experimental conditions. In an attempt to minimize silylation of the acceptor alcohol, a classical side reaction when trimethylsilyl triflate is used as a catalyst, we replaced the latter by *tert*-butyldimethylsilyl triflate. This resulted in an almost quantitative formation of the corresponding kinetic orthoesters either with a glucose (**44**) or with a galactose (**51**) derivative. ^{1}H NMR data confirmed the formation of such an orthoester (H-1′ shifted downfield 0.4 ppm compared to **55** and **60**).Scheme 6e

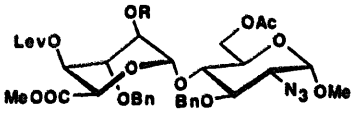
Conclusion.—Comparison of the yields in disaccharides **55–63** indicates that trichloroacetimidates and *n*-pentenyl glycosides are equally efficient in these glycosidation reactions, slightly better yields being apparently obtained with the imidates. The synthesis of the *n*-pentenyl glycosides requires one more step compared to the imidates, but the overall yield from **1** is much better (40 vs 20%). Since the *n*-pentenyl group can be introduced from the beginning of the synthesis, this advantage of the *n*-pentenyl



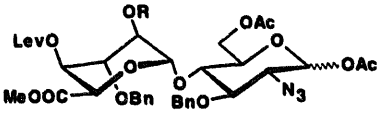
52 R^1=Bn; R^2=Ac
54 R^1,R^2=PhCH:



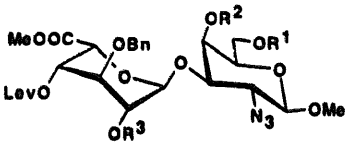
53



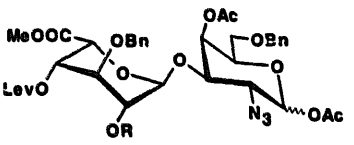
55 R=Ac
57 R=Bz



56 R=Ac
58 R=Bz



59 R^1=Bn; R^2=Ac; R^3=Ac
61 R^1=Bn; R^2=Ac; R^3=Bz
63 R^1,R^2=PhCH:; R^3=Bz



60 R=Ac
62 R=Bz

Scheme 6.

glycoside donor would be much more pronounced in a situation where the iduronic acid unit would constitute the reducing end of a disaccharide (or oligosaccharide) building block to be used as glycosyl donor. Although their interest as glycosyl donors is firmly established, in the present situation the thioglycosides did not yield the expected disaccharides. Adding the problems encountered during the oxidation steps in the synthesis, they appear as poor candidates to activate the anomeric position of iduronic acid derivatives.

3. Experimental

General.—^{1}H NMR spectra were recorded with Bruker AM100, AC 250, and AM400 instruments for solution in $CDCl_3$ (internal Me_4Si) unless otherwise stated. Melting points were determined in capillary tubes with a Mettler apparatus, and were uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter at 23 ± 3 °C. Reactions were monitored by TLC on Silica Gel 60 F_{254} (Merck) with detection by charring with H_2SO_4. Column chromatography was performed on Silica Gel 60 (Merck 63–200 μm). Elemental analyses were carried out at the Service d'Analyses Sanofi (Gentilly, France) or at the Service Central d'Analyses du C.N.R.S. (Vernaison, France).

*Crude 3-O-benzyl-*L*-idopyranose* (1).—Aqueous H_2SO_4 (0.1 M; 1 L) was added dropwise to a solution of 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-L-idofuranose (29.7 g, 0.1 mol) in dioxane (166 mL). The mixture was stirred for 1 h at 80 °C

(complete conversion of the starting material into **1** as observed by TLC in 1:9 MeOH–CH_2Cl_2). The solution was neutralized with Amberlite IR 68, filtered, and concentrated to dryness.

3-O-Benzyl-4,6-O-benzylidene-L-idopyranose (**2a**).—Crude **1** (9.2 g, 34.0 mmol) was treated with 20:1 benzaldehyde–trifluoroacetic acid (50 mL) at room temperature for 3 h. The mixture was cooled, neutralized with Et_3N, diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$), and concentrated. Column chromatography (100:1 to 50:1 CH_2Cl_2–MeOH) gave first 3-*O*-benzyl-1,2:4,6-di-*O*-benzylidene-α-L-idopyranose (**2b**) as a 1:1 *endo/exo* mixture (2.20 g, 14%); ^{1}H NMR (250 MHz): δ 7.73–7.16 (m, 10 H, Ph), 6.47 and 5.97 (2 s, 1 H, 1,2-PhCH *endo* + *exo*), 5.75 and 5.52 (2 d, 1 H, $J_{1,2}$ 2.8 Hz, H-1 *endo* + *exo*), 5.59 and 5.57 (s, 1 H, 4,6-PhCH *endo* + *exo*), 4.74 and 4.71 (2 s, 2 H, PhCH_2 *endo* + *exo*), 4.42–3.72 (m, 6 H, H-2,3,4,5,6a,6b). The elemental analysis was not in full agreement with the calcd value.

Next eluted was **2a** (α/β 1:1) (5.97 g, 49%); ^{1}H NMR (250 MHz): 7.50–7.27 (m, 20 H, Ph), 5.52 (s, 1 H, PhC*H*Oα), 5.50 (s, 1 H, PhC*H*Oβ), 5.22 (d, 1 H, $J_{1,2} < 1.0$, $J_{1,OH}$ 11 Hz, H-1α), 5.04 (d, 1 H, $J_{1,2} < 1.0$, $J_{1,OH}$ 12.8 Hz, H-1β), 4.74 and 4.64 (2 d, 2 H, *J* 12 Hz, PhCH_2), 4.63 (s, 2 H, PhCH_2), 4.38 (dd, 1 H, $J_{5,6a}$ 1.2, $J_{6a,6b}$ 12.5 Hz, H-6aβ), 4.37 (dd, 1 H, $J_{5,6b}$ 1.2, $J_{6a,6b}$ 12.5 Hz, H-6aα), 4.12 (dd, 1 H, $J_{5,6b}$ 1.9 Hz, H-6bα), 4.06 (dd, 1 H, $J_{5,6b}$ 1.6 Hz, H-6bβ), 4.20–3.90 (m, 5 H, H-3α,3β,4α,4β,5α), 3.85 (d, 1 H, H-5β), 3.75 (br d, 1 H, H-2α), 3.69 (br d, 1 H, H-2β). Anal. Calcd for $C_{20}H_{22}O_6$ (358.39): C, 66.39; H, 5.95. Found: C, 66.25; H, 5.95.

1,2-Di-O-acetyl-3-O-benzyl-4,6-O-benzylidene-α,β-L-idopyranose (**3**).—Compound **2a** (6.02 g, 16.8 mmol) was acetylated using pyridine (100 mL) and acetic anhydride (6.34 mL, 67 mmol). After 5 h at room temperature, the mixture was concentrated under reduced pressure, and traces of pyridine and acetic anhydride were coevaporated three times with toluene. Column chromatography (3:1 cyclohexane–EtOAc) gave **3** (6.98 g, 94%) as a colourless oil; ^{1}H NMR (250 MHz): δ 7.55–7.20 (m, 20 H, 2Ph), 6.25 (br s, 1 H, H-1β), 6.10 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1α), 5.40 and 5.20 (2 s, 2 H, 2 PhCH), 5.05–5.00 (m, 1 H, H-2α,2β), 4.79 and 4.66 (d, 2 H, *J* 12.8 Hz, PhCH_2), 4.78 and 4.68 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.41–4.30 (m, 2 H, H-6bα,6bβ), 4.12–4.05 (m, 4 H, H-4α,4β,6aα,6bα), 3.97–3.70 (m, 3 H, H-3α,5α,5β), 3.85–3.81 (m, 1 H, H-3β), 2.16, 2.12 and 2.10 (3 s, 12 H, 4Ac). Anal. Calcd for $C_{24}H_{26}O_8$ (442.46): C, 65.15; H, 5.92. Found: C, 65.01; H, 6.07.

1,2-Di-O-acetyl-3-O-benzyl-α,β-L-idopyranose (**4**).—A solution of **3** (6.84 g, 15 mmol) in CH_2Cl_2 (680 mL) was cooled to 0 °C, and 11:25 aq trifluoroacetic acid was added dropwise. The mixture was stirred at room temperature for 4 h and neutralized with ice-cooled satured aq $NaHCO_3$. After dilution with CH_2Cl_2, the organic phase was washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (25:1 CH_2Cl_2–MeOH) gave **4** (5.05 g, 94%) as a colourless oil; ^{1}H NMR (250 MHz): δ 7.39–7.30 (m, 10 H, Ph), 6.08 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1β), 6.06 (br s, 1 H, $J_{1,2} < 1.0$ Hz, H-1α), 5.19–5.15 (m, 1 H, H-2β), 5.04–5.01 (m, 1 H, H-2α), 4.76 and 4.63 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.72 and 4.62 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.30–4.27 (m, 1 H, H-5α), 4.17–4.13 (m, 1 H, H-5β), 3.96–3.78 (m, 6 H, H-4α,4β,6aα,6aβ,6bα,6bβ), 3.75–3.70 (m, 2 H, H-3α,3β), 2.16, 2.13, 2.11, 2.10 (4 s, 12 H, 4Ac). Anal. Calcd for $C_{24}H_{26}O_8$ (442.46): C, 65.15; H, 5.92. Found: C, 65.01; H, 6.07.

1,2-Di-O-acetyl-3-O-benzyl-4-O-levulinyl-6-O-tert-butyldimethylsilyl-α, and *β-L-idopyranose* (**5a** and **5b**).—To a solution of **4** (3.7 g, 10.4 mmol) in dry CH_2Cl_2 (50 mL), Et_3N (2.03 mL, 14.5 mmol), DMAP (51 mg, 0.42 mmol), and *tert*-butyldimethylsilyl chloride (2.04 g, 13.5 mmol) were added at room temperature. The mixture was stirred until complete conversion of the starting material. Levulinic anhydride (2.72 g, 12.7 mmol) and Et_3N (2.03 mL, 14.5 mmol) were then added. After 1 h, the mixture was diluted with CH_2Cl_2, and washed with water. The organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (60:1 CH_2Cl_2–acetone) of the crude residue gave a mixture of **5a** and **5b** (5.8 g, 98%). Pure fractions of **5a** an **5b** were isolated to characterize both compounds.

5a: $[\alpha]_D$ −16° (*c* 0.54, $CHCl_3$); ^1H NMR (250 MHz): δ 7.40–7.20 (m, 5 H, Ph), 6.10 (s, 1 H, H-1), 5.30 (d, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 4.98 (br s, 1 H, H-4), 4.70 (s, 2 H, PhCH_2), 4.35 (ddd, 1 H, $J_{4,5}$ 1.7, $J_{5,6a} = J_{5,6b} = 7.2$ Hz, H-5), 3.84 (dd, 1 H, $J_{3,4}$ 3.7 Hz, H-3), 3.72–3.73 (m, 2 H, H-6a,b), 3.00–2.50 (m, 4 H, C:OCH_2CH_2C:O), 2.20 (s, 6 H, 2Ac), 2.10 (s, 3 H, CH_2C:OCH_3), 0.85 (s, 9 H, $(CH_3)_3$C), 0.05 (s, 6 H, $(CH_3)_2$Si). Anal. Calcd for $C_{28}H_{42}O_{10}Si$ (566.605): C, 59.35; H, 7.47. Found: C, 59.40; H, 7.73.

5b: $[\alpha]_D$ +36° (*c* ..4, $CHCl_3$); ^1H NMR (250 MHz): 7.40–7.20 (m, 5 H, Ph), 6.06 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.09 (dd, 1 H, $J_{2,3}$ 2.8 Hz, H-2), 4.90 (br s, 1 H, H-4), 4.71 (s, 2 H, PhCH_2), 4.23 (ddd, 1 H, $J_{4,5}$ 1.7, $J_{5,6a} = J_{5,6b} = 7.2$ Hz, H-5), 3.90 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 3.79–3.72 (m, 2 H, H-6a,b), 2.90–2.40 (m, 4 H, C:OCH_2CH_2C:O), 2.20 (s, 6 H, 2Ac), 2.10 (s, 3 H, C:OCH_3), 0.85 (s, 9 H, $(CH_3)_3$C), 0.05 (s, 6 H, $(CH_3)_2$Si). Anal. Calcd for $C_{28}H_{42}O_{10}Si$ (566.60): C, 59.35; H, 7.47. Found: C, 59.34; H, 7.32.

Crude 1,2-di-O-acetyl-3-O-benzyl-4-O-levulinyl-α, and *β-L-idopyranosiduronic acid* (**6a** and **6b**).—A solution of chromium trioxide (1.3 g, 13 mmol) in 3.5 M H_2SO_4 (5.62 mL) was added slowly to a cooled (0 °C) solution of **5a** (2.79 g, 4.9 mmol) in acetone (36 mL). TLC analysis (9:1 CH_2Cl_2–MeOH) indicated the end of the oxidation. The reaction mixture was then poured into water at 0 °C, stirred vigorously, diluted with CH_2Cl_2, and washed with water until neutral. The organic layer was then dried ($MgSO_4$), filtered, and concentrated to give crude **6a** (2.72 g) as a light yellow oil which was used without further purification.

The same procedure was used for the preparation of **6b** from **5b**, and for the preparation of a mixture of both anomers from the mixture of **5a** and **5b**.

Methyl 1,2-di-O-acetyl-3-O-benzyl-4-O-levulinyl-α, and *β-L-idopyranosiduronate* (**7a** and **7b**).—Crude **6a** (2.72 g) was esterified in DMF (83 mL), in the presence of $KHCO_3$ (2.91 g, 29 mmol), by slow addition at 0 °C of methyl iodide (1.80 mL, 29 mmol). The reaction was monitored by TLC (25:1 CH_2Cl_2–EtOAc). After evaporation, the residue was dissolved in CH_2Cl_2. The solution was washed with water, dried ($MgSO_4$), and concentrated. Column chromatography (25:1 CH_2Cl_2–acetone) gave **7a** (1.33 g, 54% from **5a**); $[\alpha]_D$ −12° (*c* 0.56, $CHCl_3$). ^1H NMR (400 MHz): δ 7.39–7.28 (m, 5 H, Ph), 6.07 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 5.16 (ddd, 1 H, $J_{3,4}$ 3.0, $J_{4,5}$ 2.5, $J_{2,4}$ 1.0 Hz, H-4), 5.06 (ddd, 1 H, $J_{2,3}$ 3.0 Hz, H-2), 4.78 (d, 1 H, H-5), 4.75 (m, 2 H, PhCH_2), 3.95 (dd, 1 H, H-3), 3.80 (s, 3 H, CO_2CH_3), 2.90–2.40 (m, 4 H, C:OCH_2CH_2C:O), 2.18 and 2.14 (2 s, 6 H, 2Ac), 2.10 (s, 3 H, C:OCH_3). Anal. Calcd for $C_{23}H_{28}O_{11}$ (480.466): C, 57.49; H, 6.08. Found: C, 57.20; H, 5.67.

7b was similarly obtained from crude **6b**: $[\alpha]_D$ +20° (*c* 0.75, $CHCl_3$). ^1H NMR (400 MHz): 7.38–7.26 (m, 5 H, Ph), 6.24 (s, 1 H, H-1), 5.27–5.22 (m, 1 H, H-4), 4.96 (d, 1 H, $J_{4,5}$ 2.0 Hz, H-5), 4.96–4.92 (m, 1 H, H-2), 4.75 (s, 2 H, PhCH_2), 3.88–3.83 (m, 1 H, H-3), 3.80 (s, 3 H, CO_2CH_3), 2.90–2.40 (m, 4 H, C:OCH_2CH_2C:O), 2.18 and 2.12 (2 s, 6 H, 2Ac), 2.05 (s, 3 H, C:OCH_3). Anal. Calcd for $C_{23}H_{28}O_{11}$ (480.46): C, 57.49; H, 6.08. Found: C, 57.31; H, 5.88.

*Crude methyl 2-O-acetyl-3-O-benzyl-1-bromo-1-deoxy-4-O-levulinyl-α-*L*-idopyranosyluronate* (**8**).—A solution of **7b** (1.33 g, 2.76 mmol) in anhyd 20:1 CH_2Cl_2–EtOAc (29 mL) was stirred for 24 h at room temperature in the presence of $TiBr_4$ (1.13 g, 3.06 mmol). The mixture was diluted with CH_2Cl_2, washed with ice-cold water, dried ($MgSO_4$), and concentrated. The syrupy residue **8** (1.7 g) was immediately used for the next reaction.

*Methyl 2-O-acetyl-3-O-benzyl-4-O-levulinyl-α,β-*L*-idopyranosuronate* (**9a**).—(a) From **8**. A solution of **8** (1.7 g) in 20:1 acetone–water (6.3 mL) was stirred for 30 min at room temperature in the presence of silver silicate (160 mg). The reaction mixture was filtered and concentrated. Column chromatography (3:7 CH_2Cl_2–acetone) gave **9a** (928 mg, 80% from **7b**). ^1H NMR (400 MHz): δ 7.40–7.30 (m, 10 H, Ph), 5.32 (br d, 1 H, $J_{1,OH}$ 9.1 Hz, H-1α), 5.27–5.22 (m, 1 H, H-4α), 5.19 (br d, 1 H, $J_{1,OH}$ 9.6 Hz, H-1β), 5.19–5.14 (m, 1 H, H-4β), 5.01 (d, 1 H, $J_{4,5}$ 2.2 Hz, H-5α), 4.94–4.90 (m, 1 H, H-2β), 4.88–4.84 (m, 1 H, H-2α), 4.81–4.73 (m, 4 H, 2PhCH_2 α and β), 4.71 (d, 1 H, $J_{4,5}$ 1.9 Hz, H-5β), 4.29 (d, 1 H, OHα), 4.00 (dd, 1 H, $J_{2,3} = J_{3,4}$ = 2.9 Hz, H-3β), 3.99–3.93 (m, 1 H, H-3α), 3.82 and 3.80 (2 s, 6 H, $2CO_2CH_3$), 3.76 (d, 1 H, OHβ), 2.90–2.40 (m, 8 H, 2 C:OCH_2CH_2C:O α and β), 2.20 and 2.18 (2 s, 6 H, 2Ac α and β), 2.12 and 2.11 (2 s, 6 H, 2:OCH_3C:O α and β). The elemental analysis was not in full agreement with the calcd value.

(b) From **10**. A solution of **10** (1.3 g, 2.8 mmol) in 95% aq AcOH (6 mL) was left for 30 min at room temperature. After evaporation, column chromatography (5:2 toluene–EtOAc) gave **9** (0.97 g, 80%) in a 1:1 α/β ratio.

*Methyl 3-O-benzyl-4-O-levulinyl-1,2-O-[1-(exo-methoxy)ethylidene]-β-*L*-idopyranosyluronate* (**10**).—Levulinic anhydride (3 g, 14 mmol), and 4-dimethylaminopyridine (10 mg), were added to a solution of methyl 3-*O*-benzyl-1,2-*O*-[1-(*exo*-methoxy)ethylidene]-β-L-idopyranosiduronate [10] (2.5 g, 7 mmol), in CH_2Cl_2 (100 mL). After 2 h, the solution was washed with water, dried, and concentrated. Pure **10** was obtained (2.95 g, 92%) after column chromatography (4:1 toluene–EtOAc); ^1H NMR (250 MHz): δ 7.40–7.20 (m, 5 H, Ph), 5.55 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), 5.24–5.20 (m, 1 H, H-4), 4.83 and 4.75 (2 d, 2 H, *J* 11.6 Hz, PhCH_2), 4.54 (d, 1 H, $J_{4,5}$ 1.3 Hz, H-5), 4.13–4.07 (m, 2 H, H-2, H-3), 3.80 (s, 3 H, CO_2CH_3), 3.27 (s, 3 H, OCH_3), 2.80–2.72 (m, 4 H, C:OCH_2CH_2C:O), 2.20 (s, 3 H, CH_3C:O), 1.75 (s, 3 H, CCH_3).

O-*(Methyl 2-O-acetyl-3-O-benzyl-4-O-levulinyl-α,* and *β-*L*-idopyranosyluronate) trichloroacetimidate* (**11a** and **11b**).—Anhydrous Na_2CO_3 (381 mg, 3.8 mmol) was added to a solution of **9a** (928 mg, 2.1 mmol) in anhyd CH_2Cl_2 (15 mL). Trichloroacetonitrile (1.3 mL, 12.6 mmol) was added dropwise, and the mixture was stirred overnight at room temperature. Column chromatography (5:2 toluene–EtOAc) gave **11a** (amorphous powder), and **11b** (colourless syrup; total yield 1.18 g, 95%).

11a: $[\alpha]_D$ −30° (*c* 1.57, $CHCl_3$); ^1H NMR (250 MHz): δ 8.69 (s, 1 H, NH),

7.40–7.30 (m, 5 H, Ph), 6.24 (d, 1 H, $J_{1,2}$ 1.80 Hz, H-1), 5.34–5.30 (m, 1 H, H-4), 5.23–5.20 (m, 1 H, H-2), 4.82 (d, 1 H, $J_{4,5}$ 2.2 Hz, H-5), 4.77 (s, 2 H, CH_2Ph), 4.01 (dd, 1 H, $J_{2,3} = J_{3,4} = 3.1$ Hz, H-3), 3.80 (s, 3 H, OCH_3), 2.90–2.50 (m, 4 H, $C{:}OCH_2CH_2C{:}O$), 2.20 and 2.14 (2 s, 6 H, Ac and $C{:}OCH_3$). The elemental analysis was not in full agreement with the calcd value.

11b: $[\alpha]_D$ 0° (*c* 1.27, $CHCl_3$); ^1H NMR (250 MHz): δ 8.70 (s, 1 H, NH), 7.40–7.24 (m, 5 H, Ph), 6.41 (s, 1 H, H-1), 5.27–5.22 (m, 1 H, H-4), 5.14–5.12 (m, 1 H, H-2), 5.05 (d, 1 H, $J_{4,5}$ 1.6 Hz, H-5), 4.80–4.70 (2 d, 2 H, *J* 11.6 Hz, CH_2Ph), 3.92–3.86 (m, 1 H, H-3), 3.80 (s, 3 H, CO_2CH_3), 2.90–2.42 (m, 4 H, $C{:}OCH_2CH_2C{:}O$), 2.18 (s, 3 H, Ac), 2.13 (s, 3 H, $C{:}OCH_3$). The elemental analysis was not in full agreement with the calcd value.

*Methyl 2-O-acetyl-3-O-benzyl-1-deoxy-1-fluoro-4-O-levulinyl-α,β-*L*-idopyranosyluronate* (**12**).—To a cooled mixture (−30 °C) of **9a** (50 mg, 0.1 mmol) in anhyd THF (0.5 mL), diethylaminosulfur trifluoride (0.02 mL, 0.14 mmol) was added dropwise under stirring. The solution was then allowed to reach room temperature, and then stirred for 10 min. After cooling to −30 °C, MeOH (1 mL) was added, and the mixture was concentrated. Column chromatography (1:1 cyclohexane–EtOAc) gave **12** quantitatively; ^1H NMR (250 MHz): δ 7.40–7.24 (m, 5 H, 2Ph), 5.72 (dd, 1 H, $J_{1,2} < 0.5$, $J_{1,F}$ 47.7 Hz, H-1α), 5.68 (dd, 1 H, $J_{1,2}$ 1.9, $J_{1,F}$ 42.1 Hz, H-1β), 5.27–5.20 (m, 2 H, H-4α, H-4β), 5.09 (dd, 1 H, $J_{2,3}$ 5.5 Hz, H-2β), 5.04 (d, 1 H, $J_{4,5}$ 1.6 Hz, H-5α), 5.04–4.99 (m, 1 H, H-2α), 4.85–4.69 (m, 2 H, H-5b and PhCH_2 β), 4.80 and 4.72 (2 d, 2 H, *J* 11.7 Hz, PhCH_2 α), 4.14–4.07 (m, 1 H, H-3β), 3.87–3.79 (m, 1 H, H-3α), 3.84 and 3.82 (2 s, 6 H, $2CO_2CH_3$ α and β), 2.90–2.40 (m, 8 H, $2C{:}OCH_2CH_2C{:}O$ α and β), 2.20 (s, 6 H, 2Ac), 2.03 and 2.00 (2 s, 6 H, $2C{:}OCH_3$ α and β). Anal. Calcd for $C_{21}H_{25}FO_9$ (440.42): C, 57.20; H, 5.72. Found: C, 57.36; H, 5.60.

*Crude 1,2,4,6-tetra-O-benzoyl-3-O-benzyl-α,β-*L*-idopyranose* (**13b**).—To a solution of **1** (9.70 g, 36 mmol) in pyridine (50 mL), benzoic anhydride (40 g) was added, followed by 4-dimethylaminopyridine (100 mg). After 2 h at room temperature, the solvent was evaporated. Column chromatography (1:1 CH_2Cl_2–CCl_4) gave **13b** (25 g) which was used as such in the next step.

*Phenyl 2,4,6-tri-O-acetyl-3-O-benzyl-1-thio-α-*L*-idopyranoside* (**14**).—Thiophenol (0.13 mL, 1.20 mmol) was added at 0 °C to a solution of **13a** (500 mg, 1.10 mmol) and $BF_3 \cdot Et_2O$ (0.4 mL, 3.30 mmol), in anhyd CH_2Cl_2 (10 mL). After stirring for 2 h at 25 °C, aq saturated $NaHCO_3$ was introduced. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to give an oily residue which was purified by column chromatography (3:1 cyclohexane–EtOAc) to give **14** (478 mg, 89%); $[\alpha]_D$ −91° (*c* 0.56, $CHCl_3$); ^1H NMR (250 MHz): δ 7.60–7.35 (m, 10 H, Ph), 5.51 (s, 1 H, H-1), 5.20 (dd, 1 H, $J_{5,6a}$ 1.6, $J_{6a,6b}$ 7.4 Hz, H-6a), 5.05–5.00 (m, 1 H, H-5), 4.90 (dd, 1 H, $J_{5,6b}$ 1.63 Hz, H-6b), 4.90 and 4.66 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.33–4.10 (m, 2 H, H-2,4), 3.80–3.76 (m, 1 H, H-3), 2.10–2.05 (m, 9 H, 3Ac). Anal. Calcd for $C_{25}H_{28}O_8S$ (488.5): C, 69.31; H, 5.82. Found: C, 69.38; H, 5.88.

*Pent-4-enyl 2,4,6-tri-O-benzoyl-3-O-benzyl-α-*L*-idopyranoside* (**15**).—A solution of 1,2,4,6-tetra-*O*-benzoyl-3-*O*-benzyl-α,β-L-idopyranose **13b** (20 g, 0.028 mol) in dry CH_2Cl_2 (100 mL) was stirred for 30 min with 4-penten-1-ol (3.3 mL, 0.032 mol) in the presence of 4 Å molecular sieves (4 g) at room temperature under argon, then cooled to

0 °C. Trimethylsilyl triflate (5.6 mL, 0.028 mol) was added, and after 2 h at room temperature the mixture was neutralized with Et_3N, filtered on Celite, and concentrated. Column chromatography (3:1 cyclohexane–EtOAc) gave **15** (17.1 g, 94%); mp 92–93 °C (cyclohexane–EtOAc); $[\alpha]_D$ −42° (*c* 1.09, $CHCl_3$); ^1H NMR (250 MHz): δ 8.11–7.84 (m, 6 H, Ph), 7.62–7.11 (m, 14 H, Ph), 5.86–5.74 (m, 1 H, C*H*=CH_2), 5.30 (s, 1 H, H-4), 5.08 (s, 1 H, H-1), 5.03–4.96 (m, 3 H, H-2, CH_2=CH), 4.96–4.76 (m, 3 H, *J* 12 Hz, PhCH_2, H-5), 4.68 (dd, 1 H, $J_{5,6a}$ 5, $J_{6a,6b}$ 11.5 Hz, H-6a), 4.49 (dd, 1 H, $J_{5,6b}$ 4.4 Hz, H-6b), 4.08 (s, 1 H, H-3), 3.88–3.82 (m, 1 H, OC$H_aH_bCH_2$), 3.58–3.52 (m, 1 H, $OCH_aH_bCH_2$), 2.19–2.10 (m, 2 H, CH_2=CH_2CH_2), 1.80–1.75 (m, 2 H, CH_2–CH_2–CH_2). Anal. Calcd for $C_{39}H_{38}O_9$ (650.73): C, 71.99; H, 5.89. Found: C, 71.83; H, 5.92.

Crude pent-4-enyl 3-O-benzyl-α,β-L-idopyranoside (**16a** and **16b**).—A few mg of sodium were added to a solution of **15** (5.7 g, 12.3 mmol) in dry MeOH (10 mL). When TLC (1:1 cyclohexane–EtOAc) showed the reaction to be complete, the mixture was neutralized with Amberlite IR 120 (H^+), filtered, and concentrated to give **16a** (4.7 g) which was used as such in the next step.

A mixture of α and β anomers of pent-4-enyl 3-*O*-benzyl-L-idopyranoside (**16a** and **16b**) was also obtained when the same procedure was applied to pent-4-enyl 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-α,β-L-idopyranoside, itself resulting from electrochemical glycosidation of phenyl 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-1-thio-α,β-L-idopyranoside [25b].

Pent-4-enyl 3-O-benzyl-4,6-O-isopropylidene-α, and *β-L-idopyranoside* (**17a** and **17b**).—A solution of **16a** and **16b** (mixture of α and β anomers resulting from electroglycosidation, 3.2 g, 8.3 mmol) in 2,2-dimethoxypropane (50 mL), and camphorsulfonic acid (77 mg, 0.332 mmol), was stirred for 30 min at 25 °C, neutralized with Et_3N, and concentrated. Chromatography (10:1 then 5:1 cyclohexane–EtOAc) first gave **17a** (2.6 g, 73%); $[\alpha]_D$ −62° (*c* 0.88, $CHCl_3$); ^1H NMR (400 MHz): δ 7.39–7.27 (m, 5 H, Ph), 5.86–5.75 (m, 1 H, C*H*=CH_2), 5.02–4.96 (m, 2 H, CH=CH_2), 4.93 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.78 and 4.57 (2 d, 2 H, *J* 11.0 Hz, CH_2Ph), 4.06 (dd, 2 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 13.1 Hz, H-6a), 4.05 (dd, 1 H, $J_{3,4} = J_{4,5} = 2.5$ Hz, H-4), 3.92 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.92–3.90 (m, 1 H, H-5), 3.82 (dd, 1 H, H-2), 3.80–3.73 (m, 1 H, OC$H_aH_bCH_2$), 3.67 (dd, 1 H, H-3), 3.52–3.47 (m, 1 H, $OCH_aCH_bCH_2$), 2.20–2.06 (m, 2 H, CH_2CH=CH_2), 1.77–1.67 (m, 2 H, $CH_2CH_2CH_2$), 1.47–1.44 (2 s, 6 H, 2 $(CH_3)_2C$). Anal. Calcd for $C_{21}H_{30}O_6$ (378.46): C, 66.65; H, 7.99. Found: C, 66.43; H, 7.77.

Next was eluted **17b** (723 mg, 20%), mp 94–95 °C (EtOAc–cyclohexane); $[\alpha]_D$ +49° (*c* 0.57, $CHCl_3$). ^1H NMR (400 MHz): δ 7.43–7.33 (m, 5 H, Ph), 5.91–5.80 (m, 1 H, C*H*=CH_2), 5.09–4.97 (m, 1 H, CH_2=CH), 4.73 (s, 1 H, H-1), 4.70 and 4.63 (2 d, 2 H, *J* 11.5 Hz, CH_2Ph), 4.11–3.99 (m, 3 H, H-6a, 6b and OC$H_aH_bCH_2$), 3.95–3.92 (m, 1 H, H-4), 3.80–3.74 (m, 2 H, H-2,3), 3.67–3.63 (m, 1 H, H-5), 3.58–3.50 (m, 1 H, $OCH_aH_bCH_2$), 3.45 (br d, 1 H, $J_{1,OH}$ 12.0 Hz, OH), 2.20–2.13 (m, 2 H, CH_2CH=CH_2), 1.86–1.73 (m, 2 H, CH_2–CH_2–CH_2), 1.47 and 1.45 (2 s, 6 H, $(CH_3)_2C$). Anal. Calcd for $C_{21}H_{30}O_6$ (378.46): C, 66.65; H, 7.99. Found: C, 66.68; H, 7.95.

Pent-4-enyl 2-O-benzoyl-3-O-benzyl-4,6-O-isopropylidene-α, and *β-L-idopyranoside* (**18a** and **18b**).—A solution of **17a** (1.1 g, 2.9 mmol), Et_3N (0.808 mL, 5.8 mmol), and

benzoyl chloride (0.438 mL, 3.8 mmol), in dry CH_2Cl_2 (20 mL) was stirred for 30 min at 20 °C, then diluted with MeOH (10 mL), stirred during 30 min, and concentrated. Column chromatography (7:1 cyclohexane–EtOAc) gave **18a** (1.4 g, 100%); $[\alpha]_D$ −35° (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz): δ 8.17–8.14 (m, 2 H, Ph), 7.62–7.27 (m, 8 H, Ph), 5.89–5.78 (m, 1 H, C*H*=CH$_2$), 5.31 (dd, 1 H, $J_{1,2}$ 2.0, $J_{2,3}$ 3.5 Hz, H-2), 5.06 (d, 1 H, H-1), 5.05–4.96 (m, 2 H, CH=C*H*$_2$), 4.93 and 4.66 (2 d, 2 H, *J* 12.0 Hz, CH$_2$Ph), 4.13 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 7.2 Hz, H-6a), 4.08–4.05 (m, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 3.99–3.96 (m, 1 H, H-5), 3.96 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6b), 3.84–3.77 (m, 1 H, OC*H*$_a$H$_b$CH$_2$), 3.76 (dd, 1 H, H-3), 3.55–3.49 (m, 1 H, OCH$_a$*H*$_b$CH$_2$), 2.21–2.11 (m, 2 H, CH$_2$=CHC*H*$_2$), 1.80–1.71 (m, 2 H, CH$_2$C*H*$_2$CH$_2$), 1.53–1.47 (2 s, 6 H, (CH$_3$)$_2$C). Anal. Calcd for $C_{28}H_{34}O_7$ (482.58): C, 69.69; H, 7.10. Found: C, 69.65; H, 6.81.

Under the same conditions, **17b** (4.80 g, 12 mmol) gave **18b** quantitatively, $[\alpha]_D$ +65° (*c* 0.42, $CHCl_3$). ^{1}H NMR (400 MHz): δ 8.23 (m, 2 H, Bz), 7.60–7.33 (m, 8 H, Ph), 5.87–5.76 (m, 1 H, C*H*=CH$_2$), 5.30 (dd, 1 H, $J_{1,2}$ 1.0, $J_{2,3}$ 1.5 Hz, H-2), 5.02–4.93 (m, 2 H, C*H*$_2$=CH), 4.92 (d, 1 H, H-1), 4.90 and 4.70 (2 d, 2 H, *J* 11.0 Hz, CH$_2$Ph), 4.17 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.0 Hz, H-6a) 4.11 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 4.05–3.98 (m, 1 H, OC*H*$_a$H$_b$CH$_2$), 3.93–3.88 (m, 2 H, H-3,4), 3.70–3.69 (m, 1 H, H-5), 3.58–3.52 (m, 1 H, OCH$_a$*H*$_b$CH$_2$), 2.15–2.07 (m, 2 H, C*H*$_2$CH=CH$_2$), 1.76–1.66 (m, 2 H, CH$_2$C*H*$_2$CH$_2$), 1.50 (s, 3 H, CH$_3$C), 1.47 (s, 3 H, CH$_3$C). Anal. Calcd for $C_{28}H_{34}O_7$ (482.58): C, 69.69; H, 7.10. Found: C, 69.59; H, 6.87.

Crude pent-4-enyl 2-O-benzoyl-3-O-benzyl-α, and *β-*L*-idopyranoside* (**19a** and **19b**).—Compound **18a** (1.45 g, 3 mmol) was dissolved in 80% aq AcOH. The mixture was heated for 15 min at 100 °C, cooled to room temperature, neutralized with Et_3N, and concentrated to give **19a** which was immediately used for the next reaction. The same reaction was applied to **18b** (0.63 g, 1.20 mmol) to give **19b**.

*Pent-4-enyl 2-O-benzoyl-3-O-benzyl-6-O-*tert*-butyldimethylsilyl-4-O-levulinyl-α,* and *β-*L*-idopyranoside* (**20a** and **20b**).—Compounds **19a** (1.33 g, 3 mmol) or **19b** (1.33 g, 3 mmol) were treated as described for the synthesis of **6a** and **6b** until TLC analysis (4:1 cyclohexane–EtOAc) indicated complete conversion into **20a** or **20b**. They were obtained (**20a**, 1.96 g, 98%; **20b**, 1.95 g, 97%) in pure form after column chromatography (4:1 cyclohexane–EtOAc).

20a: $[\alpha]_D$ −32° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz): δ 8.09–8.02 (m, 2 H, Ph), 7.61–7.20 (m, 8 H, Ph), 5.87–5.71 (m, 1 H, C*H*=CH$_2$), 5.19 (d, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 5.01 (s, 1 H, H-2), 4.88 (s, 1 H, H-1), 4.96–4.89 (m, 2 H, CH=C*H*$_2$), 4.85 and 4.65 (2 d, 2 H, *J* 11.8 Hz, PhC*H*$_2$), 4.35 (ddd, 1 H, $J_{5,6a} = J_{5,6b} = 6.2$ Hz, H-5), 3.89–3.66 (m, 4 H, H-3, 6a, 6b and OC*H*$_a$H$_b$CH$_2$), 3.52–3.39 (m, 1 H, OCH$_a$*H*$_b$CH$_2$), 2.75–2.39 (m, 4 H, C:OCH$_2$CH$_2$:CO), 2.19–2.05 (m, 5 H, C*H*$_2$CH=CH$_2$ and CH$_3$C:O), 1.79–1.65 (m, 2 H, CH$_2$–C*H*$_2$–CH$_2$), 0.95 (s, 9 H, (CH$_3$)$_3$C), 0.15 (s, 6 H, (CH$_3$)$_2$Si). Anal. Calcd for $C_{36}H_{50}O_9Si$ (654.88): C, 66.03; H, 7.70. Found: C, 66.26; H, 7.94.

20b: $[\alpha]_D$ +58° (*c* 1, $CHCl_3$). ^{1}H NMR (250 MHz): δ 8.09–8.07 (m, 2 H, Bz), 7.61–7.20 (m, 8 H, Ph), 5.70–5.62 (m, 1 H, C*H*=CH$_2$), 5.16 (s, 1 H, H-2), 4.94–4.80 (m, 4 H, C*H*$_2$=CH and H-1,4), 4.70 (s, 2 H, PhC*H*$_2$), 4.04 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.92–3.74 (m, 3 H, H-3,5,6b), 3.52–3.39 (m, 2 H, OC*H*$_2$CH$_2$), 2.75–2.39 (m, 4 H, C:OCH$_2$CH$_2$C:O), 2.19–2.05 (m, 5 H, C*H*$_2$CH=CH$_2$ and CH$_3$C:O),

1.79–1.65 (m, 2 H, $CH_2CH_2CH_2$), 0.90 (s, 9 H, $C(CH_3)_3$), 0.15 (s, 6 H, $2(CH_3)_3Si$). Anal. Calcd for $C_{36}H_{50}O_9Si$ (654.88): C, 66.03; H, 7.69. Found C, 65.81; H, 7.64.

Crude (pent-4-enyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α, and β-L-idopyranosid)uronic acid (**21a** and **21b**).—Compounds **20a** (1.90 g, 3 mmol) and **20b** (1.90 g, 3 mmol) were oxidized as described for the preparation of **7**, until TLC analysis (20:1 CH_2Cl_2–acetone) indicated complete conversion into **21a** and **21b**, which were immediately used in the next step, and were not characterized.

Methyl (pent-4-enyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α, and β-L-idopyranosid)-uronate (**22a** and **22b**).—Compounds **21a** and **21b** were methylated as described for the preparation of **7a** and **7b**, until TLC analysis (20:1 CH_2Cl_2–acetone) indicated complete conversion into **22a** and **22b**. The latter were obtained (**22a**, 3.34 g, 55% from **20a**; **22b**, 0.831 g, 52% from **20b**) after column chromatography (3:1 cyclohexane–EtOAc).

22a: $[\alpha]_D$ −69° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz): δ 8.12–8.09 (m, 2 H, Ph), 7.66–7.30 (m, 8 H, Ph), 5.89–5.76 (m, 1 H, $CH{=}CH_2$), 5.30 (br s, 1 H, H-4), 5.21 (br s, 1 H, H-2), 5.18 (s, 1 H, H-1), 5.05–4.96 (m, 2 H, $CH{=}CH_2$), 5.00 (d, 1 H, $J_{4,5}$ 2.0 Hz, H-5), 4.91 and 4.75 (2 d, 2 H, *J* 11.0 Hz, CH_2Ph), 3.95–3.91 (m, 1 H, H-3), 3.88–3.81 (m, 4 H, OCH_3 and $OCH_aH_bCH_2$), 3.62–3.54 (m, 1 H, $OCH_aH_bCH_2$), 2.68–2.38 (m, 4 H, $C{:}OCH_2CH_2C{:}O$), 2.24–2.21 (m, 5 H, $CH_2CH{=}CH_2$ and $CH_3C{:}O$), 1.83–1.72 (m, 2 H, $CH_2CH_2CH_2$). Anal. Calcd for $C_{31}H_{36}O_{10}$ (568.62): C, 65.48; H, 6.38. Found: C, 65.31; H, 6.04.

22b: $[\alpha]_D$ +71° (*c* 0.42, $CHCl_3$); ^{1}H NMR (400 MHz): δ 8.14–8.11 (m, 2 H, Ph), 7.59–7.31 (m, 8 H, Ph), 5.83–5.67 (m, 1 H, $CH{=}CH_2$), 5.22–5.20 (m, 2 H, H-2,4), 5.00–4.90 (m, 3 H, $J_{1,2}$ 2.5 Hz, $CH_2{=}CH$, H-1), 4.80 (s, 2 H, $PhCH_2$), 4.69 (d, 1 H, $J_{4,5}$ 2.5 Hz, H-5), 4.17 (dd, 1 H, $J_{2,3} = J_{3,4} = 2.5$ Hz, H-3), 4.05–3.94 (m, 1 H, $OCH_aH_bCH_2$), 3.82 (s, 3 H, CO_2CH_3), 3.57–3.48 (m, 1 H, $OCH_aH_bCH_2$), 2.60–2.50 (m, 2 H, $CH_2CH{=}CH_2$), 2.50–2.10 (m, 4 H, $C{:}OCH_2CH_2C{:}O$), 2.08 (s, 3 H, $CH_3C{:}O$), 1.75–1.60 (m, 2 H, $CH_2CH_2CH_2$). Anal. Calcd for $C_{31}H_{36}O_{10}$ (568.62): C, 65.48; H, 6.38. Found: C, 65.49; H, 6.36.

Crude phenyl 3-O-benzyl-1-thio-α-L-idopyranoside (**23**).—Compound **14** was treated with NaOMe as described for the preparation of **16a** and **16b**. After work-up, compound **23** was immediately used in the next step, and was not characterized.

Phenyl 3-O-benzyl-4,6-O-benzylidene-1-thio-α-L-idopyranoside (**24**).—Crude **23** (337 mg, 0.9 mmol) was treated as described for preparation of **2a** until TLC analysis (1:1 cyclohexane–EtOAc) indicated complete conversion into **24**. Column chromatography (9:1 hexane–EtOAc) gave **24** (256 mg, 61%), $[\alpha]_D$ −91° (*c* 0.56, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.60–7.10 (m, 15 H, Ph), 5.67 (s, 1 H, H-1), 5.55 (s, 1 H, $PhCH$), 4.55 and 4.48 (2 d, 2 H, *J* 12.0 Hz, $PhCH_2$), 4.46 (s, 1 H, H-5), 4.35 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12.6 Hz, H-6a), 4.13–4.08 (m, 3 H, H-2,4,6b) 3.87 (d, 1 H, $J_{3,OH}$ 11.6 Hz, OH), 3.83 (s, 1 H, H-3). Anal. Calcd for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.82. Found: C, 69.38; H, 5.88.

Phenyl 2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-1-thio-α-L-idopyranoside (**25**).—Compound **24** (205 mg, 0.48 mmol) was benzoylated, as described for the synthesis of **18b**, to give **25** (250 mg, 96%) after work-up and purification by column chromatography (10:1 hexane–EtOAc); mp 137–138 °C (hexane–EtOAc), $[\alpha]_D$ −80° (*c* 1.1, $CHCl_3$); ^{1}H NMR (250 MHz): δ 8.05–7.95 (m, 2 H, Ph), 7.60–7.10 (m, 18 H, Ph),

5.83 (s, 1 H, H-1), 5.60 (s, 1 H, PhCH), 5.56–5.52 (m, 1 H, H-2), 5.02 and 4.69 (2 d, 2 H, J 11.0 Hz, PhCH_2), 4.53 (d, 1 H, H-5), 4.35 (dd, 1 H, $J_{6a,6b}$ 12.7 Hz, H-6a), 4.24–4.18 (dd, 1 H, $J_{5,6a}$ 1.8 Hz, H-6b), 4.12 (s, 1 H, H-4), 3.92 (s, 1 H, H-3). Anal. Calcd for $C_{33}H_{30}O_6S$: C, 71.46; H, 5.45. Found: C, 71.21; H, 5.53.

Crude phenyl 2-O-benzoyl-3-O-benzyl-1-thio-α-L-idopyranoside (**26**).—Compound **25** (50 mg) was treated, as described for preparation of **19a** and **19b**, until TLC analysis (1:1 cyclohexane–EtOAc) indicated complete conversion into **26**, which was directly used for the next step, and was not characterized.

Phenyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-6-O-tert-butyldimethylsilyl-1-thio-α-L-idopyranoside (**27**).—Crude compound **26** (702 mg, 1.21 mmol) was treated as described for the synthesis of **5a** and **5b**. Pure **27** (1.00 g, 98%) was obtained after column chromatography (3:1 cyclohexane–EtOAc), $[\alpha]_D$ −36° (*c* 0.46, $CHCl_3$); ^{1}H NMR (250 MHz): δ 8.07–8.00 (m, 2 H, Ph), 7.57–7.15 (m, 13 H, Ph), 5.63 (s, 1 H, H-1), 5.47–5.42 (m, 1 H, H-4), 5.15 (br s, 1 H, H-2), 4.90 and 4.77 (2 d, 2 H, J 11.9 Hz, PhCH_2), 3.98–3.92 (m, 1 H, H-3), 3.87–3.74 (m, 3 H, H-5,6a,6b), 2.70–2.33 (m, 4 H, C:OCH_2CH_2C:O), 2.08 (s, 3 H, CH_3C:O), 0.90 (s, 9 H, $(CH_3)_3$C), 0.10 (s, 6 H, $(CH_3)_2$Si). Anal. Calcd for $C_{37}H_{47}O_8SiS$ (679.842): C, 65.46; H, 6.83. Found: C, 65.30; H, 6.63.

Crude phenyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-L-idopyranoside (**28**).—Dowex 50 resin, (H^+), was added to a vigorously stirred solution of **27** (100 mg, 0.15 mmol) in anhyd MeOH (1 mL). After one night at room temperature the solution was filtered and concentrated. The residue was immediately used in the next step, and was not characterized.

Crude (phenyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-L-idopyranosid)uronic acid (**29**).—Crude **28** was oxidized at room temperature with pyridinium dichromate (226 mg, 4 eq) in DMF (0.5 mL). When the reaction was complete (TLC, 9:1 CH_2Cl_2–MeOH), the reaction mixture was poured into Et_2O. After filtration, the solution was concentrated to dryness. Esterification was performed directly on this crude product.

Methyl (phenyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-L-idopyranosid)-uronate (**30**).—Crude **29** was treated as for **7**. Ester **30** (46.3 mg, 52% from **27**) was obtained after Silica gel column chromatography (3:2 cyclohexane–EtOAc), $[\alpha]_D$ −46° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz): δ 8.10–8.04 (m, 2 H, Ph), 7.60–7.23 (m, 13 H, Ph), 5.78 (s, 1 H, $J_{1,2}$ < 0.5 Hz, H-1), 5.48 (d, 1 H, $J_{4,5}$ 2.0 Hz, H-5), 5.44–5.41 (m, 1 H, H-4), 5.33–5.30 (m, 1 H, H-2), 4.90 and 4.80 (2 d, 2 H, J 11.8 Hz, CH_2Ph), 4.00–3.96 (m, 1 H, H-3), 3.82 (s, 3 H, OCH_3), 2.65–2.10 (m, 4 H, C:OCH_2CH_2C:O), 2.08 (s, 3 H, CH_3C:O).

Ethyl 2,4,6-tri-O-acetyl-3-O-benzyl-1-thio-α,β-L-idopyranoside (**31**).—Ethanethiol (0.652 mL, 8.8 mmol) and $BF_3 \cdot Et_2O$ (0.216 mL, 1.76 mmol) were added at 0 °C to a solution of **13a** (3.5 g, 8 mmol) in anhyd CH_2Cl_2 (20 mL). After stirring for 2 h at room temperature, aq saturated $NaHCO_3$ was introduced. The organic layer was washed with water, dried ($MgSO_4$), and concentrated to give an oily residue which was purified by column chromatography (3:1 hexane–EtOAc) to give **31** (3.35 g, 92%) as a 1:1 mixture of α and β compounds; ^{1}H NMR (250 MHz): δ 7.42–7.25 (m, 5 H, Ph), 5.61 (d, 0.5 H, $J_{1,2}$ 5.0 Hz, H-1β), 5.45–5.37 (m, 1 H, H-2β and H-5β), 5.30 (s, 0.5 H, H-1α),

5.00 (s, 0.5 H, H-2α), 4.87–4.80 (m, 1 H, H-5α,4α), 4.80 and 4.60 (2 d, 1 H, PhCH_2), 4.70 and 4.50 (2 d, 1 H, PhCH_2), 4.35 (dd, 0.5 H, $J_{3,4} = J_{4,5} = 5.6$ Hz, H-4β), 4.27 (dd, 0.5 H, $J_{5,6a}$ 3.5, $J_{6a,6b}$ 12 Hz, H-6aβ), 4.22–4.18 (m, 1 H, H-6aα,6bβ), 4.12–4.05 (m, 1 H, H-3β,6bβ), 3.70 (s, 0.5 H, H-3α), 2.80–2.55 (m, 2 H, 2CH_2CH$_3$), 2.15 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.39 (t, 1.5 H, CH_3CH$_2$), 1.30 (t, 1.5 H, CH_3CH$_2$). Anal. Calcd for $C_{21}H_{28}O_8S$ (440.45): C, 57.25; H, 6.42. Found: C, 57.32; H, 6.57.

Crude ethyl 3-O-benzyl-1-thio-α,β-L-idopyranoside (**32**).—Deacetylation of **31** (3.35 g) with NaOMe (100 mg) in MeOH (5 mL) gave a quantitative yield of **32** which was directly used in the next step, and was not characterized.

Ethyl 3-O-benzyl-4,6-O-isopropylidene-1-thio-α, and *β-L-idopyranoside* (**33a** and **33b**).—Compounds **33a** and **33b** were prepared from **32** as described for the synthesis of **17a** and **17b**. After column chromatography (6:1 cyclohexane–EtOAc), a 1:1 α/β mixture of the two anomers was obtained (97%). A fraction of the pure anomers was collected in order to get their physicochemical characteristics.

33a: $[\alpha]_D$ −31° (*c* 0.69, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.40–7.20 (m, 5 H, Ph), 5.36 (s, 1 H, H-1), 4.80 and 4.48 (2 d, 2 H, *J* 12 Hz, CH_2Ph), 4.20 (s, 1 H, H-5), 4.08 (dd, 1 H, $J_{5,6a}$ 1.8, $J_{6a,6b}$ 13 Hz, H-6a), 3.98–3.92 (m, 3 H, H-2,4 and OH), 3.89 (dd, 1 H, $J_{5,6b}$ 1.7 Hz, H-6b), 3.60 (s, 1 H, H-3), 2.72–2.57 (m, 2 H, CH_2CH$_3$), 1.70 (s, 3 H, C(CH$_3$)), 1.60 (s, 3 H, C(CH$_3$)), 1.30 (t, 3 H, CH_3CH$_2$). Anal. Calcd for $C_{18}H_{26}O_5S$ (354.5): C, 60.98; H, 7.41. Found: C, 61.03; H, 7.59.

33b: $[\alpha]_D$ +137° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.40–7.30 (m, 5 H, Ph), 4.94 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.70 and 4.60 (2 d, 2 H, *J* 12 Hz, PhCH_2), 4.05–3.95 (m, 3 H, H-2,4,5), 3.88 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 13 Hz, H-6a), 3.71 (s, 1 H, H-3), 3.60–3.50 (m, 2 H, H-6b and OH), 2.80–2.70 (m, 2 H, CH_2CH$_3$), 1.50 (s, 3 H, C(CH$_3$)), 1.40 (s, 3 H, C(CH$_3$)), 1.30 (t, 3 H, CH_3CH$_2$). Anal. Calcd for $C_{18}H_{26}O_5S$ (354.5): C, 60.98; H, 7.41. Found: C, 61.01; H, 7.58.

Ethyl 2-O-benzoyl-3-O-benzyl-4,6-O-isopropylidene-1-thio-α-L-idopyranoside (**34**).—Compound **34** was prepared from **33a** as described for the synthesis of **18a** and **18b**. After column chromatography (8:1 cyclohexane–EtOAc), **34** was obtained (97%), mp 77–78 °C (hexane–EtOAc); $[\alpha]_D$ −73° (*c* 0.39, $CHCl_3$); ^{1}H NMR (250 MHz): δ 8.20–8.10 (m, 2 H, Ph), 7.60–7.20 (m, 8 H, Ph), 5.50 (s, 1 H, H-1), 5.34 (s, 1 H, H-2), 4.92 and 4.58 (2 d, 2 H, *J* 12 Hz, PhCH_2), 4.25 (s, 1 H, H-5), 4.15 (dd, 1 H, $J_{5,6a}$ 2.2, $J_{6a,6b}$ 13 Hz, H-6a), 3.97–3.90 (m, 2 H, H-4,6b), 3.70 (s, 1 H, H-3), 2.75–2.60 (m, 2 H, CH_2CH$_3$), 1.50 (s, 3 H, C(CH$_3$)), 1.40 (s, 3 H, C(CH$_3$)), 1.30 (t, 3 H, CH_3CH$_2$). Anal. Calcd for $C_{25}H_{30}O_6S$ (458.6): C, 65.47; H, 6.61. Found: C, 65.49; H, 6.65.

Ethyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-L-idopyranoside (**35**).—Compound **35** was prepared from **34** as described for the synthesis of **19a** and **19b**. After column chromatography (1:1 hexane–EtOAc) **35** was obtained (92%). It was used as such in the next step. ^{1}H NMR (250 MHz): δ 8.07–8.04 (m, 2 H, Ph) 7.62–7.26 (m, 8 H, Ph), 5.30 (s, 1 H, H-1), 5.16 (s, 1 H, H-2), 4.82 and 4.70 (2 d, 2 H, *J* 12 Hz, PhCH_2), 4.09–3.93 (m, 4 H, H-3,4,5,6a), 3.84–3.68 (m, 2 H, H-6b and OH), 2.84–2.75 (m, 2 H, CH_2CH$_3$), 2.67 (d, 1 H, OH), 1.30 (t, 3 H, CH_3CH$_2$).

Ethyl 2-O-benzoyl-3-O-benzyl-6-O-tert-butyldimethylsilyl-4-O-levulinyl-1-thio-α-L-idopyranoside (**36**).—Compound **35** (64.5 mg, 0.15 mmol) was treated as described for

the synthesis of **5a** and **5b** resulting in **36** (91.5 mg, 94%) after column chromatography (3:2 hexane–EtOAc); $[\alpha]_D$ −52° (*c* 0.39, $CHCl_3$); ^1H NMR (250 MHz): δ 8.11–8.07 (m, 2 H, Ph), 7.39–7.28 (m, 8 H, Ph), 5.14 (s, 1 H, H-1), 5.05 (s, 1 H, H-2), 4.95 (s, 1 H, H-4), 4.74 (s, 2 H, PhCH_2), 4.10–4.03 (m, 1 H, H-6a), 3.94 (s, 1 H, H-5), 3.74–3.70 (m, 2 H, H-3,6b), 2.75–2.60 (m, 2 H, CH_2CH$_3$), 2.56–2.50 (m, 2 H, CH_2 lev), 2.38–2.32 (m, 2 H, CH_2 lev), 1.90 (s, 3 H, CH_3 lev), 1.30 (t, 3 H, CH_3CH$_2$), 0.90 (s, 9 H, SiC$(CH_3)_3$), 0.05 (s, 6 H, Si$(CH_3)_2$). Anal. Calcd for $C_{33}H_{46}O_8SSi$ (630.79): C, 62.83; H, 7.35. Found: C, 62.67; H, 7.32.

*Crude ethyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-*L*-idopyranoside* (**37**).—Compound **36** (80 mg, 0.13 mmol) was treated as described for the synthesis of **28** resulting in **37** (62 mg), which was used as such in the next step.

*Crude (ethyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-*L*-idopyranosid)uronic acid* (**38**).—Compound **37** (62 mg, 0.12 mmol) was treated as described for the synthesis of **29**, yielding **38** which was used directly for the preparation of **39**, and was not characterized

*Methyl (ethyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-1-thio-α-*L*-idopyranosid)uronate* (**39**).—Crude **38** was treated as described for the synthesis of **8** until TLC analysis (3:2 hexane–EtOAc) indicated its complete conversion. Compound **39** was obtained (36 mg, 52% from **36**) as a colourless syrup after column chromatography (3:2 hexane–EtOAc); ^1H NMR (250 MHz): δ 8.09–8.07 (m, 2 H, Ph), 7.32–7.30 (m, 8 H, Ph), 5.22–5.10 (m, 2 H, H-1,4), 5.07 (s, 1 H, H-2), 4.75 (s, 2 H, PhCH_2), 4.60 (d, 1 H, $J_{4,5}$ 2.5 Hz, H-5), 3.88 (s, 1 H, H-3), 3.73 (s, 3 H, $COOCH_3$), 2.74–2.69 (m, 2 H, CH_2CH$_3$), 2.55–2.45 (m, 2 H, CH_2 lev), 2.13–2.05 (m, 2 H, CH_2 lev), 1.94 (s, 3 H, CH_3 lev), 1.30 (t, 3 H, CH_3CH$_2$).

2-Azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-α, and *β-*D*-glucopyranosyl nitrate* (**41a** and **41b**).—A solution of **40** (9.77 g, 22 mmol) in anhyd MeCN (300 mL) was added dropwise to a stirred, cooled (−20 °C) mixture of NaN_3 (2.92 g, 45 mmol), and dry cerium (IV) ammonium nitrate (36 g, 66 mmol). The suspension was stirred vigorously at −10 °C for 3 h, then diluted with ice-cold Et_2O, neutralized with cold, saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography of the residue (8:1 cyclohexane–EtOAc; containing 0.1% of Et_3N) gave the pure anomeric nitrates (α/β 1:15; 5.65 g, 60%).

A small amount (3%) of the D-*manno* α-nitrate isomer (^1H NMR) was also detected, but was not further characterized.

41a: (3%); mp 111–112 °C (hexane–EtOAc); $[\alpha]_D$ +16° (*c* 0.54, $CHCl_3$); ^1H NMR (250 MHz): δ 7.50–7.22 (m, 10 H, Ph), 6.22 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1), 5.60 (s, 1 H, PhC*H*O), 4.96 and 4.80 (2 d, 2 H, *J* 10.9 Hz, CH_2Ph), 4.35 (dd, 1 H, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 10.5 Hz, H-6a), 4.05–3.96 (m, 2 H, H-5,6b), 3.83–3.71 (m, 3 H, H-2,3,4). Anal. Calcd for $C_{20}H_{20}N_4O_7$ (428.40): C, 56.07; H, 4.70; N, 13.08. Found: C 56.39; H, 4.68; N, 12.93.

41b: (57%); mp 107–108 °C (from hexane–EtOAc); $[\alpha]_D$ −96° (*c* 0.75, $CHCl_3$); ^1H NMR (250 MHz): δ 7.50–7.22 (m, 10 H, Ph), 5.58 (s, 1 H, PhC*H*O), 5.57 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 4.95 and 4.81 (2 d, 2 H, *J* 11.2 Hz, PhCH_2), 4.35 (dd, 1 H, $J_{5,6a}$ 4.9, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.81–3.65 (m, 3 H, H-2,4,6b), 3.65–3.50 (m, 2 H, H-3,5). Anal. Calcd for $C_{20}H_{20}N_4O_7$ (428.40): C, 56.07; H, 4.70; N, 13.08. Found: C, 56.06; H, 4.73; N, 13.11.

Methyl 2-azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**42**).—Compound **41b** (1.20 g, 2.8 mmol) in anhyd MeCN (5 mL), and anhyd MeOH (12 mL), was treated at 60 °C with cesium fluoride (1.28 g, 10.4 mmol). After 2 h, the mixture was concentrated, the residue was diluted with CH_2Cl_2, washed with water, dried, and concentrated. Column chromatography (6:1 cyclohexane–EtOAc) gave **42** (0.870 g, 76%); mp 121 °C (cyclohexane–EtOAc); $[\alpha]_D$ +34° (*c* 0.6, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.72–7.28 (m, 10 H, Ph), 5.59 (s, 1 H, PhC*H*O), 4.95 and 4.80 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.78 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.30 (dd, 1 H, $J_{5,6a}$ 4.2, $J_{6a,6b}$ 9.6 Hz, H-6a), 4.06 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 3.92–3.84 (m, 1 H, H-5), 3.78 (dd, 1 H, $J_{5,6b}$ 9.0 Hz, H-6b), 3.72 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.45 (dd, 1 H, H-2), 3.44 (s, 3 H, CH_3). Anal. Calcd for $C_{21}H_{23}N_3O_5$ (397.43): C, 63.46; H, 5.83; N, 10.57. Found: C, 63.00; H, 5.69; N, 10.94.

Methyl 2-azido-3-O-benzyl-2-deoxy-α-D-glucopyranoside (**43**).—Compound **42** (0.828 g, 2.08 mmol) was treated as described for the preparation of **4**. Column chromatography (3:1 CH_2Cl_2–acetone) gave quantitatively **43** as a colourless foam; $[\alpha]_D$ +64° (*c* 1.05, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.43–7.30 (m, 5 H, Ph), 4.98 and 4.73 (2 d, 2 H, *J* 11.3 Hz, PhCH_2), 4.80 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.86–3.77 (m, 3 H, H-3,4,6a), 3.66–3.60 (m, 2 H, H-5,6b), 3.44 (s, 3 H, CH_3), 3.35 (dd, 1 H, $J_{2,3}$ 10.1 Hz, H-2). Anal. Calcd for $C_{14}H_{19}N_3O_5$ (309.32): C, 54.36; H, 6.19; N, 13.58. Found: C, 54.49; H, 6.16; N, 13.34.

Methyl 6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-α-D-glucopyranoside (**44**).—To a solution of **43** (702 mg, 2.27 mmol) in anhyd pyridine (1.5 mL), acetyl chloride (0.165 mL, 2.28 mmol) was added at 0 °C. After stirring overnight, MeOH was added at 0 °C. After evaporation, the residue was dissolved in CH_2Cl_2, washed with water, and dried ($MgSO_4$). Column chromatography (5:1 toluene–EtOAc) gave **44** (726 mg, 92%) as a syrup; $[\alpha]_D$ +28° (*c* 0.66, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.40–7.30 (m, 5 H, Ph), 4.93 and 4.82 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.80 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.53 (dd, 1 H, $J_{5,6a}$ 4.1, $J_{6a,6b}$ 12.3 Hz, H-6a), 4.20 (dd, 1 H, $J_{5,6b}$ 2.2 Hz, H-6b), 3.84 (dd, 1 H, $J_{2,3} = J_{3,4} = 10.1$ Hz, H-3), 3.80–3.71 (m, 1 H, H-5), 3.50 (dd, 1 H, $J_{4,OH}$ 3.3, $J_{4,5}$ 9.8 Hz, H-4), 3.44 (s, 3 H, CH_3), 3.36 (dd, 1 H, H-2), 2.70 (d, 1 H, OH), 2.21 (s, 3 H, Ac). Anal. Calcd for $C_{16}H_{21}N_3O_6$ (351.36): C, 54.69; H, 6.02; N, 11.96. Found: C, 54.92; H, 5.89; N, 11.81.

2-Azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-α,β-D-glucopyranose (**45**).—A mixture of **41a** and **41b** (214 mg, 0.5 mmol), and thiophenol (0.15 mL, 1.5 mmol), in MeCN (3 mL), was treated at room temperature with *N,N*-diisopropylethylamine (0.09 mL, 0.5 mmol). After 5 min, the mixture was concentrated and column chromatography (20:1 CH_2Cl_2–acetone) gave **45** (178 mg, 93%); ^{1}H NMR (250 MHz): δ 5.60 (s, 0.4 H, PhC*H*α), 5.58 (s, 0.6 H, PhC*H*β), 5.28 (d, 0.4 H, $J_{1,2}$ 3.5 Hz, H-1α), 4.64 (d, 0.6 H, $J_{1,2}$ 8 Hz, H-1β), 4.97 and 4.81; 4.94 and 4.80 (4 d, 4 H, *J* 11.2 Hz, 2PhCH_2 α and β), 4.35 (dd, 1 H, $J_{5,6a}$ 4.9, $J_{6a,6b}$ 10.5 Hz, H-6a), 4.05–3.96 (m, 2 H, H-4,6b), 3.83–3.71 (m, 3 H, H-2,3,5). Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.65; H, 5.52; N, 10.96. Found: C, 62.48; H, 5.50; N, 11.01.

1-O-Acetyl-2-azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-α,β-D-glucopyranose (**46**).—Compound **45** (0.55 g, 1.4 mmol) was treated as described for preparation of **3**. Column chromatography (6:1 cyclohexane–EtOAc) gave **46** (1:1 α/β, 0.505 g, 86%)

as a crystalline powder; mp 100–103 °C (from hexane–EtOAc); $[\alpha]_D$ +2° (*c* 0.39, $CHCl_3$); ^1H NMR (250 MHz): δ 7.53–7.29 (m, 10 H, Ph), 6.20 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.51 (s, 1 H, PhC*H*O), 5.00–4.82 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.30 (dd, 1 H, $J_{5,6a}$ 9.8 Hz, H-6a), 4.06 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 3.92 (ddd, 1 H, $J_{5,6b}$ 9.8 Hz, H-5), 3.78 (dd, 1 H, H-6b), 3.75 (dd, 1 H, H-4), 3.63 (dd, 1 H, H-2), 2.17 (s, 3 H, Ac). Anal. Calcd for $C_{22}H_{23}N_3O_6$ (425.44): C, 62.11; H, 5.45; N, 9.87. Found: C, 62.04; H, 5.45; N, 9.70.

Crude 1-O-acetyl-2-azido-3-O-benzyl-2-deoxy-α,β-D-glucopyranose (**47**).—Compound **46** (505 mg) was treated as for the preparation of **4** to give **47** (368 mg, 92%) which was used directly and was not characterized.

1,6-Di-O-acetyl-2-azido-3-O-benzyl-2-deoxy-α,β-D-glucopyranose (**48**).—Compound **47** (400 mg, 1.10 mmol) was treated as described for preparation of **44**. Column chromatography (5:1 to 1:1 toluene–EtOAc) gave **48** (1:1 α/β; 388 mg, 76%) as a colourless oil; ^1H NMR (250 MHz): δ 7.43–7.30 (m, 10 H, 2Ph), 6.23 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1α), 5.44 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1β), 4.95 and 4.90 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.94 and 4.84 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.60 (dd, 1 H, $J_{5,6a}$ 3.3, $J_{6a,6b}$ 12.4 Hz, H-6aα), 4.54 (dd, 1 H, $J_{5,6a}$ 3.1, $J_{6a,6b}$ 12.3 Hz, H-6aβ), 4.33 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6bα), 4.21 (dd, 1 H, $J_{5,6a}$ 3.1 Hz, H-6bβ), 3.89–3.78 (m, 1 H, H-5α), 3.83 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 8.9 Hz, H-3α), 3.60–3.50 (m, 6 H, H-2α,2β,3β,4α,4β,5β), 3.03–3.00 (m, 1 H, OH), 2.93–2.00 (m, 1 H, OH), 2.20, 2.19 and 2.13 (4 s, 12 H, 4Ac). Anal. Calcd for $C_{17}H_{21}N_3O_7$ (379.37): C, 53.82; H, 5.63; N, 10.93. Found: C, 53.69; H, 5.58; N, 10.94.

1-O-Acetyl-2-azido-6-O-benzyl-2-deoxy-3,4-O-isopropylidene-α,β-D-galactopyranose (**50**).—2-Azido-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-α,β-D-galactopyranose [30] (**49**, 250 mg, 0.65 mmol) was treated as described for preparation of **3** until TLC analysis (2:1 cyclohexane–EtOAc) indicated its complete conversion into **49** (70:30 α/β; 206 mg, 100%); ^1H NMR (250 MHz): δ 7.35–7.31 (m, 5 H, Ph), 6.19 (d, 0.7 H, $J_{1,2}$ 3.5 Hz, H-1α), 5.44 (d, 0.3 H, $J_{1,2}$ 9.1 Hz, H-1β), 4.65 and 4.51 (2 d, 2 H, *J* 12.0 Hz, 2PhCH_2), 4.38–4.62 (m, 3 H, H-4α,β,6α,6β), 3.80–3.54 (m, 3 H, H-2,3,5), 2.13 (s, 3 H, 2Ac), 1.42 (s, 3 H, C$(CH_3)_2$), 1.37 (s, 3 H, C$(CH_3)_2$). Anal. Calcd for $C_{18}H_{23}O_6N_3$: C, 57.28; H, 6.14. Found: C, 57.09; H, 5.96.

1,4-Di-O-acetyl-2-azido-6-O-benzyl-2-deoxy-α,β-D-galactopyranose (**51**).—Compound **50** (287 mg, 0.76 mmol) was treated as described for preparation of **19**. The residue (256 mg, 0.76 mmol) was dissolved in a mixture of triethylorthoacetate (10 mL) and camphorsulfonic acid (100 mg). After complete conversion of the starting material into orthoester (1 h, TLC anal. 3:1 cyclohexane–EtOAc), 80% aq AcOH (5 mL) was added, and the mixture was allowed to stand for 10 min at room temperature. The solution was concentrated, and toluene (40 mL) was co-evaporated several times from the residue. Column chromatography (3:1 cyclohexane–EtOAc) gave **51** (60:40 α/β) (2.76 g, 91%) as a colorless oil; ^1H NMR (250 MHz): δ 7.36–7.29 (m, 5 H, Ph), 6.28 (d, 0.6 H, $J_{1,2}$ 3.7 Hz, H-1α), 5.50 (d, 0.4 H, $J_{1,2}$ 7.5 Hz, H-1β), 5.45 (dd, 0.6 H, $J_{3,4}$ 3.2, $J_{4,5}$ 1 Hz, H-4α), 5.37 (d, 0.4 H, $J_{3,4}$ 3.7 Hz, H-4β), 4.60–4.36 (dd, 2 H, *J* 13 Hz, 2PhCH_2), 4.27–4.10 (m, 1 H, H-6α), 3.92–3.40 (m, 4 H, H-2,3,5,6β), 2.52 (m, 0.4 H, OHβ), 2.40 (m, 0.6 H, OHα), 2.15 (s, 3 H, Ac), 2.09 (s, 3 H, Ac). Anal. Calcd for $C_{17}H_{21}O_7N_3$: C, 53.82; H, 5.57. Found: C, 54.03; H, 5.76.

Methyl 6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(methyl 2-O-acetyl-3-O-benzyl-4-O-levulinyl-α-L-idopyranosyluronate)-D-glucopyranoside (**55**).—A mixture of **11a** (601 mg, 1.03 mmol), **44** (300 mg, 0.80 mmol), and activated 4 Å powdered molecular sieves in anhyd CH_2Cl_2 (10 mL) was stirred for 15 min at room temperature, then cooled to −20 °C. Trimethylsilyl triflate (0.1 M in CH_2Cl_2, 0.309 mL) was added, and stirring continued for 10 min at −20 °C. An excess of diisopropylethylamine was added, and after concentration the residue was dissolved in CH_2Cl_2. After filtration through a bed of Celite, and evaporation, column chromatography (5:3 toluene–EtOAc) gave **55** (601 mg, 91%) as a colorless oil, $[\alpha]_D$ +35° (*c* 0.6, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.45–7.20 (m, 10 H, Ph), 5.16 (s, 1 H, $J_{1',2'}$ 2.0 Hz, H-1'), 5.10 (dd, 1 H, $J_{3',4'} = J_{4',5'} =$ 4.0 Hz, H-4'), 4.95 (d, 1 H, H-5'), 4.92 (dd, 1 H, $J_{2',3'}$ 4.0 Hz, H-2'), 4.83 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.87 and 4.68 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.76 and 4.71 (2 d, 2 H, *J* 10.0 Hz, PhCH_2), 4.50 (d, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.27 (dd, 1 H, $J_{5,6b}$ 4.0 Hz, H-6b), 3.95 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.91–3.86 (m, 1 H, H-5), 3.86–3.79 (m, 2 H, H-3,3'), 3.48 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 3.48 (s, 3 H, CO_2CH_3), 3.47 (s, 3 H, OCH_3), 2.84–2.45 (m, 4 H, C:OCH_2CH_2C:O), 2.21 and 2.15 (2 s, 6 H, 2Ac), 2.10 (s, 3 H, CH_3C:O). Anal. Calcd for $C_{37}H_{45}N_3O_{15}$ (771.782): C, 57.58; H, 5.88. Found: C, 57.55; H, 5.84.

1,6-Di-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(methyl 2-O-acetyl-3-O-benzyl-4-O-levulinyl-α-L-idopyranosyluronate)-α,β-D-glucopyranose (**56**).—Glycosidation of **11a** (738 mg, 1.26 mmol) and **48** (400 mg, 1.05 mmol), as described for preparation of **55**, gave **56** (761 mg, 92%) after column chromatography (5:3 toluene–EtOAc); ^{1}H NMR (250 MHz): δ 7.34–7.25 (m, 20 H, Ph), 6.26 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1α), 5.50 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1β), 5.19 (d, 1 H, $J_{1',2'}$ 2.0 Hz, H-1'α), 5.15–5.11 (m, 3 H, H-1'β,4'α,4'β), 4.97 (d, 1 H, $J_{4',5'}$ 3.0 Hz, H-5'β), 4.96–4.91 (m, 2 H, H-2'α,5'α), 4.90 (dd, 1 H, $J_{1',2'} = J_{2',3'} = 2.0$ Hz, H-2'β), 4.84–4.70 (m, 8 H, 4CH_2Ph), 4.47 (dd, 1 H, $J_{5,6a}$ 2.2, $J_{6a,6b}$ 12 Hz, H-6aβ), 4.43 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12 Hz, H-6aα), 4.26 (dd, 1 H, $J_{5,6b}$ 3.5 Hz, H-6bα), 4.24 (dd, 1 H, $J_{5,6b}$ 4.0 Hz, H-6bβ), 4.04 (ddd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4α), 3.98 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4β), 3.97–3.91 (m, 1 H, H-5α), 3.87–3.83 (m, 2 H, H-3'α,3'β), 3.80 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-3α), 3.66 (dd, 1 H, H-2α), 3.66–3.60 (m, 1 H, H-5β), 3.59 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2β), 3.53 and 3.52 (2 s, 6 H, 2CO_2CH_3 α and β), 3.42 (dd, 1 H, H-3β), 2.84–2.46 (m, 4 H, COCH_2CH_2C:O α and β), 2.23 and 2.21 (2 s, 12 H, 4Ac α and β), 2.14 and 2.11 (2 s, 6 H, 2CH_3C:O α and β). Anal. Calcd for $C_{38}H_{45}N_3O_{16}$ (799.79): C, 57.05; H, 5.67; N, 5.26. Found: C, 57.07; H, 5.85; N, 5.10.

Methyl 6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(methyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α-L-idopyranosyluronate)-α-D-glucopyranoside (**57**).—A mixture of **22a** (392 mg, 0.69 mmol), **44** (200 mg, 0.57 mmol), and activated 4 Å powdered molecular sieves, in anhyd CH_2Cl_2 (10 mL) was stirred for 30 min at room temperature, then cooled to 0 °C. *N*-Iodosuccinimide (409 mg, 1.80 mmol) was added, followed by a solution of trifluoromethanesulfonic acid (0.12 M in CH_2Cl_2 (1.21 mL, 0.12 mmol)). Stirring was continued at room temperature for 15 min, and aq 10% $NaHCO_3$ was added. After dilution with CH_2Cl_2, and filtration through a bed of Celite, the filtrate was washed with water, dried (Na_2SO_4), filtered, and concentrated. Column chromatography (5:2 to 5:3 toluene–EtOAc) gave **57** (378 mg, 80%) as a colorless foam; $[\alpha]_D$

+44° (*c* 1.40, $CHCl_3$); ^1H NMR (250 MHz): δ 8.10–8.07 (m, 2 H, Ph), 7.50–7.24 (m, 13 H, Ph), 5.45 (d, 1 H, $J_{1',2'}$ 2.5 Hz, H-1'), 5.22 (dd, 1 H, $J_{3',4'} = J_{4',5'} = 3.0$ Hz, H-4'), 5.20 (dd, 1 H, $J_{2',3'}$ 2.5 Hz, H-2'), 5.11 (d, 1 H, H-5'), 4.84 and 4.78 (2 d, 2 H, *J* 11.5 Hz, PhCH_2), 4.82 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.81 and 4.72 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 4.45 (dd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.37 (dd, 1 H, $J_{5,6b}$ 4.0 Hz, H-6b), 4.10 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.97 (dd, 1 H, H-3'), 3.88 (m, 1 H, H-5), 3.87 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-3), 3.52 (s, 3 H, $COOCH_3$), 3.49 (dd, 1 H, H-2), 3.47 (s, 3 H, OCH_3), 2.70–2.49 (m, 4 H, C:OCH_2CH_2C:O), 2.15 (s, 3 H, Ac), 2.12 (s, 3 H, CH_3C:O). The elemental analysis was not in full agreement with the calcd value.

*1,6-Di-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-4-*O*-(methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-levulinyl-α-*L*-idopyranosyluronate)-α,β-*D*-glucopyranose* (**58**).—Reaction of **22a** (202 mg, 0.35 mmol) and **48** (110 mg, 0.29 mmol), as described for preparation of **57**, afforded **58** (185 mg, 75%) as a colourless foam, after column chromatography (5:2 to 5:3 toluene–EtOAc); ^1H NMR (250 MHz): δ 8.12–8.06 (m, 4 H, Ph), 7.51–7.26 (m, 26 H, Ph), 6.25 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1α), 5.49 (dd, 1 H, $J_{1,2}$ 8.5 Hz, H-1β), 5.38 (d, 1 H, $J_{1',2'}$ 3.0 Hz, H-1'α), 5.33 (d, 1 H, $J_{1',2'}$ 3.0 Hz, H-1'β), 5.27–5.23 (m, 2 H, H-4'α,4'β), 5.19 (dd, 1 H, $J_{2',3'}$ 3.0 Hz, H-2'α), 5.14 (dd, 1 H, $J_{2',3'}$ 3.0 Hz, H-2'β), 5.03 (d, 1 H, $J_{4',5'}$ 3.0 Hz, H-5'β), 4.98 (d, 1 H, $J_{4',5'}$ 3.0 Hz, H-5'α), 4.92–4.72 (m, 8 H, 4PhCH_2), 4.46–4.31 (m, 4 H, H-6aα,6bα,6aβ,6bβ), 4.11 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4α), 4.04 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.0$ Hz, H-4β), 4.00–3.95 (m, 2 H, H-3'α,3'β), 3.95–3.89 (m, 1 H, H-5α), 3.84 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-3α), 3.66 (dd, 1 H, H-2α), 3.64–3.59 (m, 2 H, H-2β,5β), 3.59 and 3.58 (2 s, 6 H, 2 CO_2CH_3), 3.44 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-3β), 2.72–2.67 (m, 4 H, 2 C:CH_2CH_2C:O), 2.55–2.45 (m, 4 H, 2 C:OCH_2CH_2C:O), 2.21–2.20 and 2.16 (3 s, 9 H, 3Ac), 2.12 and 2.11 (2 s, 6 H, CH_3C:O). The elemental analysis was not in full agreement with the calcd value.

*Methyl 4-*O*-acetyl-2-azido-6-*O*-benzyl-2-deoxy-3-*O*-(methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-levulinyl-α-*L*-idopyranosyluronate)-β-*D*-galactopyranoside* (**59**).—Reaction of **52** (30.1 mg) and **11a** (60 mg, 0.1 mmol), as described for preparation of **55**, gave **59** (56 mg, 86%) after column chromatography (5:4 toluene–EtOAc), $[\alpha]_D$ −28° (*c* 0.6, $CHCl_3$); ^1H NMR (250 MHz): δ 7.37–7.27 (m, 10 H, Ph), 5.33 (s, 1 H, H-4'), 5.25–5.20 (m, 2 H, H-1',4), 5.04 (d, 1 H, $J_{4',5'}$ 2.1 Hz, H-5'), 4.97 (s, 1 H, H-2'), 4.70 (s, 2 H, $PhCH_2$), 4.52 and 4.44 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.19 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 3.80 (s, 3 H, CO_2CH_3), 3.75–3.46 (m, 9 H, H-2,3,3',5,6 and OCH_3), 2.79–2.53 (m, 4 H, C:OCH_2CH_2C:O), 2.19 (s, 3 H, CH_3C:O), 2.11 (s, 3 H, Ac), 1.70 (s, 3 H, Ac). Anal. Calcd for $C_{37}H_{45}N_3O_{15}$ (771.78): C, 57.58; H, 5.87. Found: C, 57.72; H, 5.95.

*1,4-Di-*O*-acetyl-2-azido-6-*O*-benzyl-2-deoxy-(methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-levulinyl-α-*L*-idopyranosyluronate)-α,β-*D*-galactopyranoside* (**60**).—Reaction of **51** (54.0 mg, 0.14 mmol) and **11a** (100 mg, 0.17 mmol), as described for preparation of **55**, gave **60** (1:1 α/β; 93.2 mg, 83%) after column chromatography (5:4 toluene–EtOAc); ^1H NMR (400 MHz): δ 7.37–7.27 (m, 10 H, Ph), 6.33 (d, 0.5 H, $J_{1,2}$ 3.5 Hz, H-1α), 5.50 (d, 0.5 H, $J_{1,2}$ 8.0 Hz, H-1β), 5.47 (s, 0.5 H, H-4'α), 5.40 (d, 1 H, H-4'β), 5.30–5.23 (m, 2 H, H-1',4), 5.08 (d, 0.5 H, $J_{4',5'}$ 2.0 Hz, H-5'α), 5.05 (s, 0.5 H, H-5'β), 5.00–4.97 (m, 1 H, H-2'), 4.69 (s, 2 H, 2PhCH_2), 4.48 and 4.39 (2 d, 2 H, 2PhCH_2), 4.15–4.11 (m, 0.5 H, H-5β), 3.95–3.38 (m, 8.5 H, H-3α,3β,5a,2',6a,6b, 2OMe),

2.79–2.45 (m, 4 H, C:OCH$_2$CH$_2$C:O), 2.20 (s, 1.5 H, CH$_3$C:O), 2.19 (s, 1.5 H, CH$_3$C:O), 2.13 (s, 3 H, 2Ac), 2.11 (s, 3 H, 2Ac), 1.67 (s, 1.5 H, Ac), 1.66 (s, 1.5 H, Ac). Anal. Calcd for $C_{38}H_{45}N_3O_{16}$ (799.79): C, 57.07; H, 5.67. Found: C, 57.34; H, 5.67.

*Methyl 4-O-acetyl-2-azido-6-O-benzyl-2-deoxy-3-O-(methyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α-*L*-idopyranosiduronate)-β-*D*-galactopyranoside* (**61**).—Reaction of **22a** (398 mg, 0.7 mmol) and **52** (211 mg, 0.6 mmol), as described for preparation of **57**, afforded **61** (452 mg, 85%) as a colourless foam after column chromatography (1:1 cyclohexane–EtOAc); $[\alpha]_D$ −4° (*c* 1.03, CHCl$_3$); ^{1}H NMR (400 MHz): δ 8.12–8.09 (m, 2 H, Ph), 7.50–7.30 (m, 13 H, Ph), 5.40 (s, 1 H, H-1′), 5.39 (d, 1 H, $J_{3,4}$ 2.5 Hz, H-4), 5.37 (dd, 1 H, $J_{4',5'}$ 2.0 Hz, H-4′), 5.27 (s, 1 H, H-2′), 5.12 (d, 1 H, H-5′), 4.79 (s, 2 H, CH$_2$Ph), 4.55 and 4.47 (2 d, 2 H, *J* 12 Hz, CH$_2$Ph), 4.23 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.92–3.90 (m, 1 H, H-3′), 3.85 (s, 3 H, COOCH$_3$), 3.78–3.74 (m, 1 H, H-5), 3.69–3.65 (m, 2 H, $J_{2,3}$ 7.5 Hz, H-2,3), 3.63 (s, 3 H, OMe), 3.55–3.49 (m, 2 H, H-6), 2.68–2.63 (m, 2 H, CH$_2$CH$_2$), 2.50–2.43 (m, 2 H, CH$_2$), 2.15 (s, 3 H, CH$_3$), 1.82 (s, 3 H, OAc). Anal. Calcd for $C_{42}H_{47}O_{15}N_3$ (833.84): C, 60.50; H, 5.68. Found: C, 60.54; H, 5.78.

*1,4-Di-O-acetyl-2-azido-6-O-benzyl-2-deoxy-3-O-(methyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α-*L*-idopyranosiduronate)-α,β-*D*-galactopyranoside* (**62**).—Reaction of **22a** (360 mg, 0.6 mmol) and **51** (200 mg, 0.5 mmol), as described for **57**, afforded **62** as a colourless foam (310 mg, 72%) after column chromatography (1:1 cyclohexane–EtOAc); ^{1}H NMR (250 MHz): δ 8.12–8.07 (m, 2 H, Ph), 7.50–7.30 (m, 13 H, Ph), 6.29 (d, 0.5 H, $J_{1,2}$ 4.0 Hz, H-1α), 5.50 (d, 0.5 H, $J_{1,2}$ 9.0 Hz, H-1β), 5.47 (dd, 0.5 H, $J_{3,4}$ 4.0 Hz, H-4α), 5.40 (dd, 0.5 H, $J_{3,4}$ 4.0 Hz, H-4β), 5.30–5.27 (m, 1 H, H-4′α,4′β), 5.21–5.18 (m, 2 H, H-1′,2′), 5.05 (d, 1 H, $J_{4',5'}$ 2.0 Hz, H-5′), 4.89 and 4.77 (2 d, 2 H, *J* 12.0 Hz, 2PhC*H*$_2$), 4.24 (dd, 0.5 H, $J_{2,3}$ 10.5 Hz, H-3α), 4.20–4.13 (m, 0.5 H, H-5α), 3.93–3.87 (m, 1 H, H-3′α,3′β), 3.86–3.84 (m, 0.5 H, H-5β), 3.84 (s, 3 H, 2COOCH$_3$), 3.80 (dd, 0.5 H, $J_{2,3}$ 10.5 Hz, H-3β), 3.74 (dd, 0.5 H, H-2α), 3.64 (dd, 0.5 H, H-2β), 3.53–3.43 (m, 2 H, H-6a,6b), 2.70–2.61 (m, 2 H, C:CH$_2$CH$_2$C:O), 2.50–2.42 (m, 2 H, C:OCH$_2$CH$_2$C:O), 2.21 (s, 1.5 H, CH$_3$C:O), 2.16 (s, 1.5 H, CH$_3$C:O), 2.12 (s, 3 H, 2Ac), 2.10 (s, 3 H, 2Ac). Anal. Calcd for $C_{43}H_{47}N_3O_{16}$ (861.86): C, 59.93; H, 5.50. Found: C, 59.81; H, 5.67.

*Methyl 2-azido-4,6-O-benzylidene-2-deoxy-3-O-(methyl 2-O-benzoyl-3-O-benzyl-4-O-levulinyl-α-*L*-idopyranosiduronate)-β-*D*-galactopyranoside* (**63**).—Reaction of **22a** (500 mg, 0.88 mmol) and **54** (225 mg, 0.73 mmol), as described for preparation of **57**, gave **63** (520 mg, 90%) after column chromatography (3:1 cyclohexane–EtOAc); $[\alpha]_D$ +28° (*c* 0.32, CHCl$_3$); ^{1}H NMR (400 MHz): δ 8.10–8.07 (m, 2 H, Ph), 7.64–7.26 (m, 13 H, Ph), 5.49 (s, 1 H, PhC*H*), 5.41 (s, 1 H, H-4′), 5.33 (s, 2 H, H-1′,5′), 5.24 (s, 1 H, H-2′), 4.93 and 4.74 (2 d, 2 H, *J* 12.0 Hz, PhC*H*$_2$), 4.56 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 4.33 (dd, 1 H, $J_{5,6a}$ 1, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.22 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.11 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 3.94 (s, 1 H, H-3′), 3.90 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 3.70 (dd, 1 H, H-3), 3.60 (s, 3 H, CO$_2$CH$_3$), 3.45 (s, 4 H, H-5, OMe), 2.64–2.34 (m, 4 H, C:OCH$_2$CH$_2$C:O), 2.10 (s, 3 H, CH$_3$C:O). Anal. Calcd for $C_{40}H_{43}O_{14}N_3$ (789.79): C, 60.83; H, 5.49. Found: C, 60.67; H, 5.58.

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