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Synthesis of N-glycan oxazolines: donors for endohexosaminidase catalysed glycosylation

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Dedicated to Professor Steve Ley on the occasion of his 60th birthday

Abstract—Oxazoline mono-, di-, tri- and hexasaccharides, corresponding to the core components of N-linked glycoprotein high mannose glycans, are synthesised as potential glycosyl donors for endohexosaminidase catalysed glycosylation of glycopeptides and glycoprotein remodelling. The crucial β-D-Man*p*-(1→4)-D-Glc*p*NAc linkage is synthesised via epimerisation of *gluco* disaccharide substrates by sequential triflation and nucleophilic substitution. Oxazolines are formed directly from the anomeric OPMP protected *N*-acetyl glucosamine derivatives. Efficient endohexosaminidase catalysed glycosylation of a synthetic β-D-Glc*p*NAcAsn glycosyl amino acid is demonstrated with the trisaccharide oxazoline donor.

Keywords: Endoglycosidase; Endohexosaminidase; Oxazoline; N-Glycan; Transglycosylation; Protein remodelling

1. Introduction

It is now well established that oligosaccharides play a huge number of vital roles in a wide variety of fundamentally important biological systems.[1] In particular, the post-translational modification of proteins by glycosylation[2] is well known to have an important role in protein folding,[3] is able to modulate protein stability and enzymatic activity[4] and in addition can also affect other important properties, such as circulatory lifetime.[5]

As protein glycosylation is not under direct genetic control, glycoproteins are intracellularly expressed as mixtures of glycoforms. These are proteins that possess identical amino acid sequences but differ in the structures of attached oligosaccharides. In general, the separation of mixtures of glycoforms of glycoproteins is extremely difficult[4] due to extremely small differences in physical properties. As such, not only is the study of the precise effect of differential glycosylation on protein stability and function hampered, but moreover all glycoprotein therapeutics are currently administered as mixtures of glycoforms, the components which may in fact possess different biological activities.[4] This presents substantial regulatory difficulties that must be addressed in the near future and there is therefore an extreme amount of current interest in developing new technology, which will allow access to pure single glycoforms of glycoproteins,[6] both for further biological study and for glycoprotein therapeutic manufacture.

One of the recently proposed approaches, which may allow access to single glycoforms of glycoproteins, is to use enzymatic remodelling of mixtures of glycoforms produced by expression in mammalian cell lines. In this approach, an initial heterogeneous mixture of glycoforms is trimmed back to a single protein glycoform, consisting of *N*-acetyl glucosamine (GlcNAc) residues at N-linked glycosylation sites, by treatment with an endohexosaminidase enzyme, such as endo-H. In theory, subsequent enzyme-mediated glycosylation of these

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single GlcNAc residues using an endohexosaminidase catalyst,[7] together with an activated glycosyl donor substrate, which itself contains a single terminal GlcNAc unit or equivalent, will allow remodelling of the N-linked glycosylation sites of the protein so that attached oligosaccharides are now of a defined and homogeneous nature (Fig. 1).

This remodelling approach requires access to both endohexosaminidases that are capable of catalysing this desired synthetic transformation, and also to activated glycosyl donor substrates terminating in a single GlcNAc unit. Whilst several types of activated donors, such as, for example, glycosyl fluorides or *p*-nitrophenyl glycosides, are plausible substrates for such a process, we, like others,[8,9] have decided to focus our investigations on the use of GlcNAc oxazoline derivatives. This decision was largely taken because oxazolines/oxazolinium ions are postulated to be intermediates in several hexosaminidase catalysed hydrolysis processes.[10] In this paper, we therefore detail the chemical synthesis of a series of N-glycan oxazolines as potential donor substrates for such enzymatic remodelling experiments,

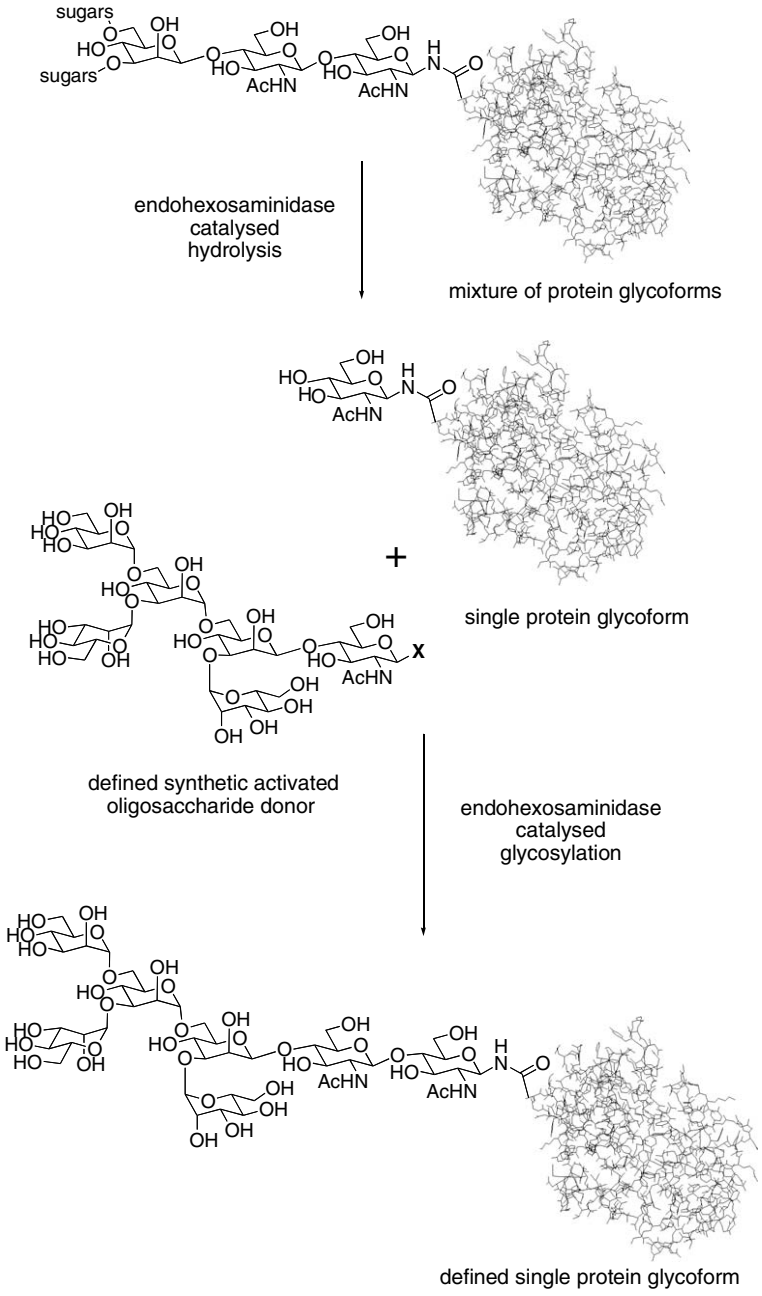


Figure 1. Glycoprotein remodelling with endohexosaminidase catalysis using synthetic activated oligosaccharide donors.

and we also outline successful endohexosaminidase catalysed glycosylation of a synthetic glycopeptide substrate with one of these donors.

2. Results and discussion

Previous studies have shown that both a β-D-Man*p*-(1→4)-D-Glc*p*NAc derived disaccharide oxazoline[9] and an α-D-Man*p*-(1→3)-[α-D-Man*p*-(1→6)]-β-D-Man*p*-(1→4)-D-Glc*p*NAc derived tetrasaccharide oxazoline[10] were good substrates for a variety of endohexosaminidase catalysed glycosylations. The following synthetic oxazoline targets were chosen to explore the substrate tolerance and glycosylation efficiency of a wider variety of endohexosaminidases: a monosaccharide oxazoline derived simply from GlcNAc, the previously accessed β-D-Man*p*-(1→4)-D-Glc*p*NAc derived disaccharide oxazoline (as a control), a trisaccharide oxazoline derived from α-D-Man*p*-(1→3)-β-D-Man*p*-(1→4)-D-Glc*p*NAc, and a hexasaccharide oxazoline derived from α-D-Man*p*(1→3)-[α-D-Man*p*-(1→6)]-α-D-Man*p*-(1→6)-[α-D-Man*p*(1→3)]-β-D-Man*p*-(1→4)-D-Glc*p*NAc; all of the parent oligosaccharides corresponding to key fragments of a typical high mannose N-glycan oligosaccharide. The key synthetic aspects involved the formation of the β-mannose linkage to the 4-hydroxyl of glucosamine; and the direct formation of oxazoline donors from their parent *N*-acetyl glucosamine derivatives, which will be discussed in turn.

The known phthalimide-protected glucosamine derivative **1**,[11] which was accessed following published procedures, was selected as the building block for the glucosamine portion of all the oxazolines synthesised. To ensure that any monosaccharide oxazoline derivative of glucosamine could act only as a glycosyl donor for endohexosaminidase catalysed glycosylation and not also act as an acceptor, it was deemed sensible to block the 4-hydroxyl group. Therefore, alcohol **1** was first methylated at position 4 by treatment with methyl iodide and sodium hydride, to yield methyl ether **2**. Removal of benzyl protection at the 3- and 6-positions by palladium catalysed hydrogenolysis gave diol **3**, the structure of which was confirmed by X-ray crystallography (Fig. 2).[12]

Subsequent removal of the phthalimide protecting group was immediately followed by peracetylation to yield acetate **4**. Direct conversion of the anomeric OPMP group into the desired oxazoline **5** was achieved by modification of a procedure originally published by Magnusson for the conversion of anomeric PMP derivatives into the corresponding glycosyl halides and thioglycosides.[13] Thus treatment of **4** with acetyl bromide, boron trifluoride diethyl etherate, and zinc iodide in chloroform, followed by heating to 50 °C directly furnished the desired oxazoline **5**. Finally, removal of the

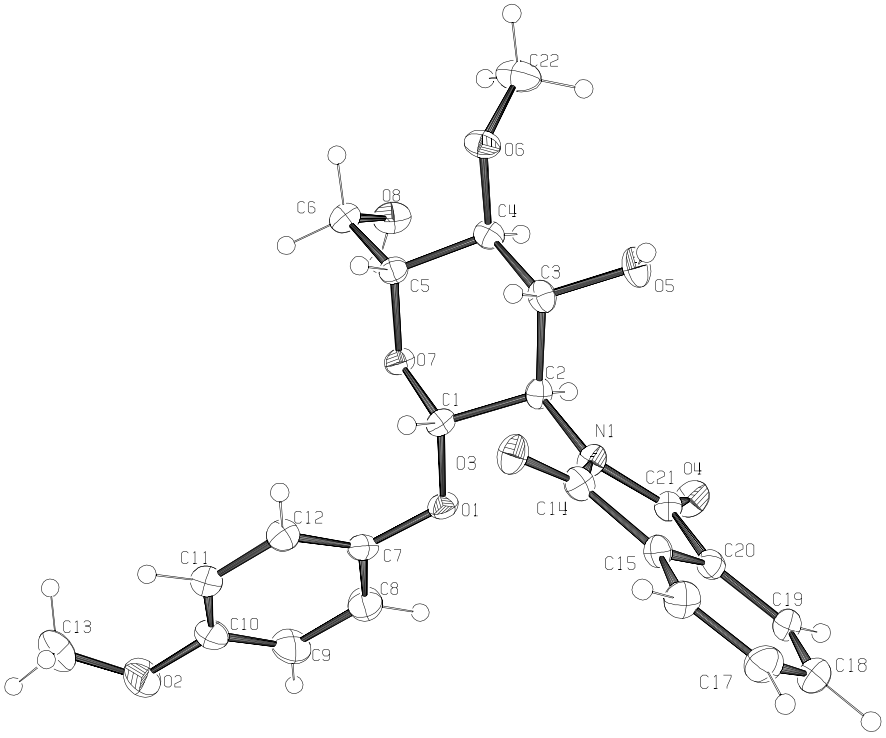
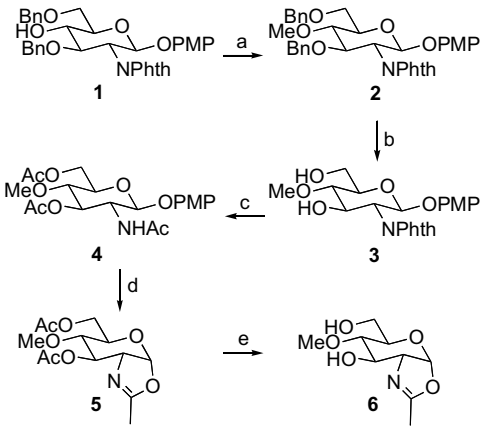


Figure 2. Crystal structure of diol **3** showing crystallographic numbering scheme [thermal ellipsoid plot (ORTEP-3) at 40% probability, solvent not shown].

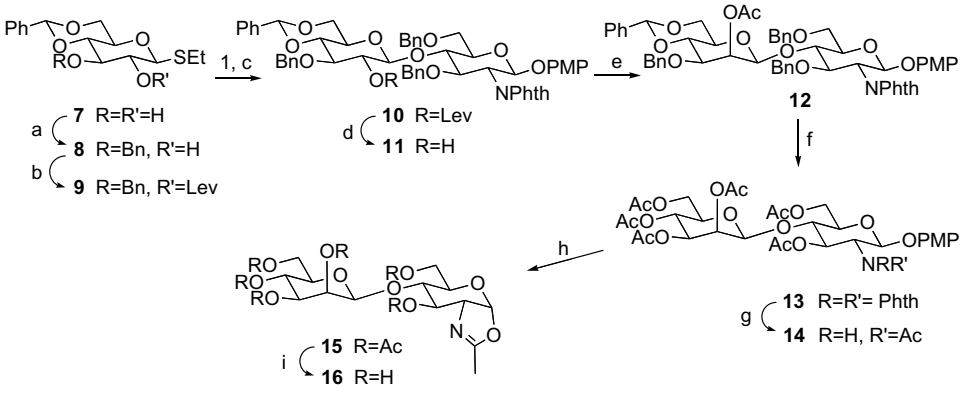


Scheme 1. Reagents and conditions: (a) NaH, MeI, DMF, 0 °C, 2.5 h, 64%; (b) H_2, Pd (10% on C), EtOAc, rt, 18 h, quant.; (c) (i) $NH_2CH_2CH_2NH_2$, MeOH, reflux; (ii) Ac_2O, py, rt, 16 h, 80% over two steps; (d) AcBr, $BF_3{\cdot}OEt_2$, ZnI_2, $CHCl_3$, 50 °C, 18 h, 57%; (e) NaOMe, MeOH, rt, 21 h, 98%.

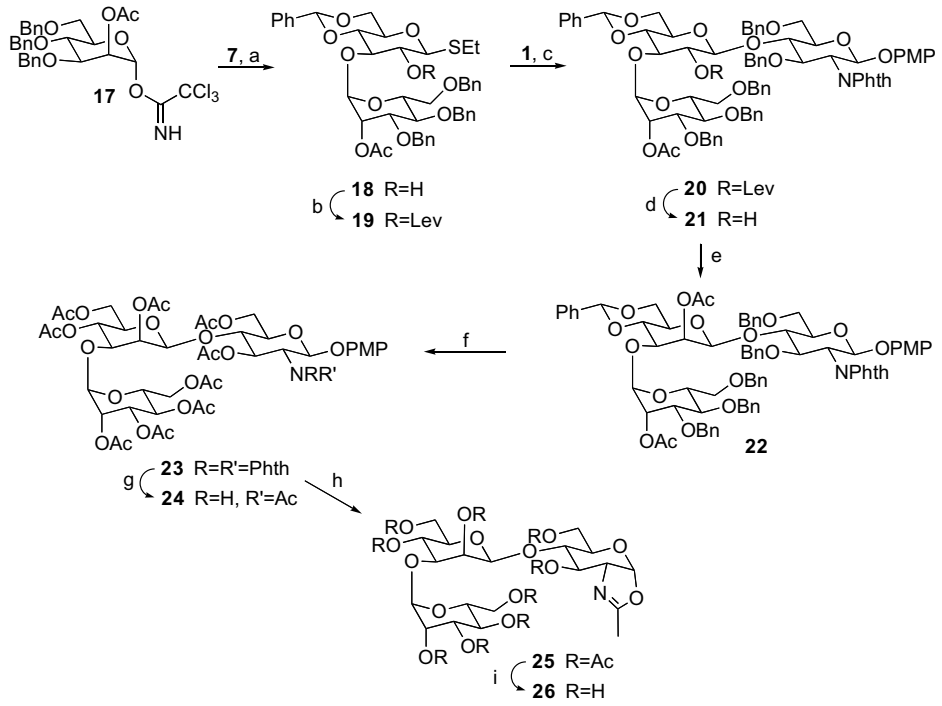
remaining acetates gave the desired deprotected monosaccharide oxazoline **6** (Scheme 1).

Amongst several possible strategies for the construction of the key β-D-Man*p*-(1→4)-D-Glc*p*NAc linkage, the recent approaches developed by Schmidt and Boons using epimerisation strategies appeared to be the most attractive and reliable.[14,15] Thus, the known *gluco* thioglycoside **7** was regioselectively benzylated by generation of the tin ether in situ by treatment with di-*n*-butyltin oxide and then subsequent exposure to benzyl bromide to yield alcohol **8**.[16,17] Orthogonal protection of the 2-position as the levulinic ester then yielded glycosyl donor **9**. Glycosylation of thioglycoside **9** with the glucosamine acceptor **1** by activation with methyl triflate yielded the β-*gluco* disaccharide **10** in excellent yield with complete control of anomeric stereochemistry due to neighbouring group participation by the 2-*O*-levulinoyl ester. Removal of the levulinoyl ester was achieved with hydrazine acetate to give alcohol **11**, which then underwent triflation and subsequent nucleophilic substitution by treatment with *n*-Bu_4NOAc in toluene under sonication (following the original sonication procedure of Fürstner and adopted by Boons)[18,15] to yield β-*manno* disaccharide **12**. Catalytic hydrogenolysis of **12** in the presence of palladium on carbon in ethyl acetate was followed by immediate acetylation to yield **13**. Removal of phthalimide protection and immediate re-acetylation was achieved by heating a solution of **13** with ethylenediamine in methanol at reflux, followed by treatment with acetic anhydride in pyridine to yield **14**. Direct conversion of the anomeric OPMP group of **14** to oxazoline **15** was again achieved using the modified Magnusson procedure and the product was then finally deacetylated to yield the desired deprotected oxazoline disaccharide **16** (Scheme 2).[9]

The trisaccharide oxazoline was synthesised following a route analogous to that of the disaccharide **16**. However, regioselective benzylation was replaced with regioselective glycosylation at the 3-position of diol **7**. Therefore, glycosylation of diol **7** with the known trichloroacetimidate **17** yielded the known disaccharide **18** with complete control of anomeric stereochemistry and good regiochemical control.[19] Once again the 2-position was protected as the levulinoyl ester to yield **19**. As expected, the methyl triflate promoted glycosylation of **19** with glucosamine acceptor **1** yielded the β-*gluco* trisaccharide **20**. Removal of the levulinoyl ester gave alcohol **21**, which underwent the sequence of triflation and nucleophilic substitution to yield β-*manno* trisaccharide **22**. Catalytic hydrogenolysis of **22** in the presence of palladium on carbon removed benzylidene and benzyl protecting groups and was followed by acetylation to yield **23**. Removal of phthalimide protection and subsequent re-acetylation furnished acetamide **24**. Finally,



Scheme 2. Reagents and conditions: (a) (i) *n*-Bu_2SnO, MeOH, reflux, 18 h; (ii) BnBr, CsF, DMF, rt, 24 h, 51% over two steps; (b) Levulinic acid, DCC, DMAP, CH_2Cl_2, rt, 18 h, 76%; (c) **1**, MeOTf, 4 Å mol. sieves, CH_2Cl_2, 0 °C, 15 h, 91%; (d) hydrazine acetate, MeOH, CH_2Cl_2, rt, 19 h, 98%; (e) (i) Tf_2O, py, CH_2Cl_2, 0 °C, 2.5 h; (ii) *n*-Bu_4NOAc, toluene, rt, sonication, 18 h, 88% over two steps; (f) (i) H_2, Pd (10% on C), EtOAc, EtOH, rt, 25 h; (ii) Ac_2O, py, rt, 22 h, 91% over two steps; (g) (i) $NH_2CH_2CH_2NH_2$, MeOH, reflux, 48 h; (ii) Ac_2O, py, rt, 72 h, 94% over two steps; (h) AcBr, $BF_3{\cdot}OEt_2$, ZnI_2, $CHCl_3$, 50 °C, 4.5 h, 65%; (i) NaOMe, MeOH, rt, 16 h, quant.

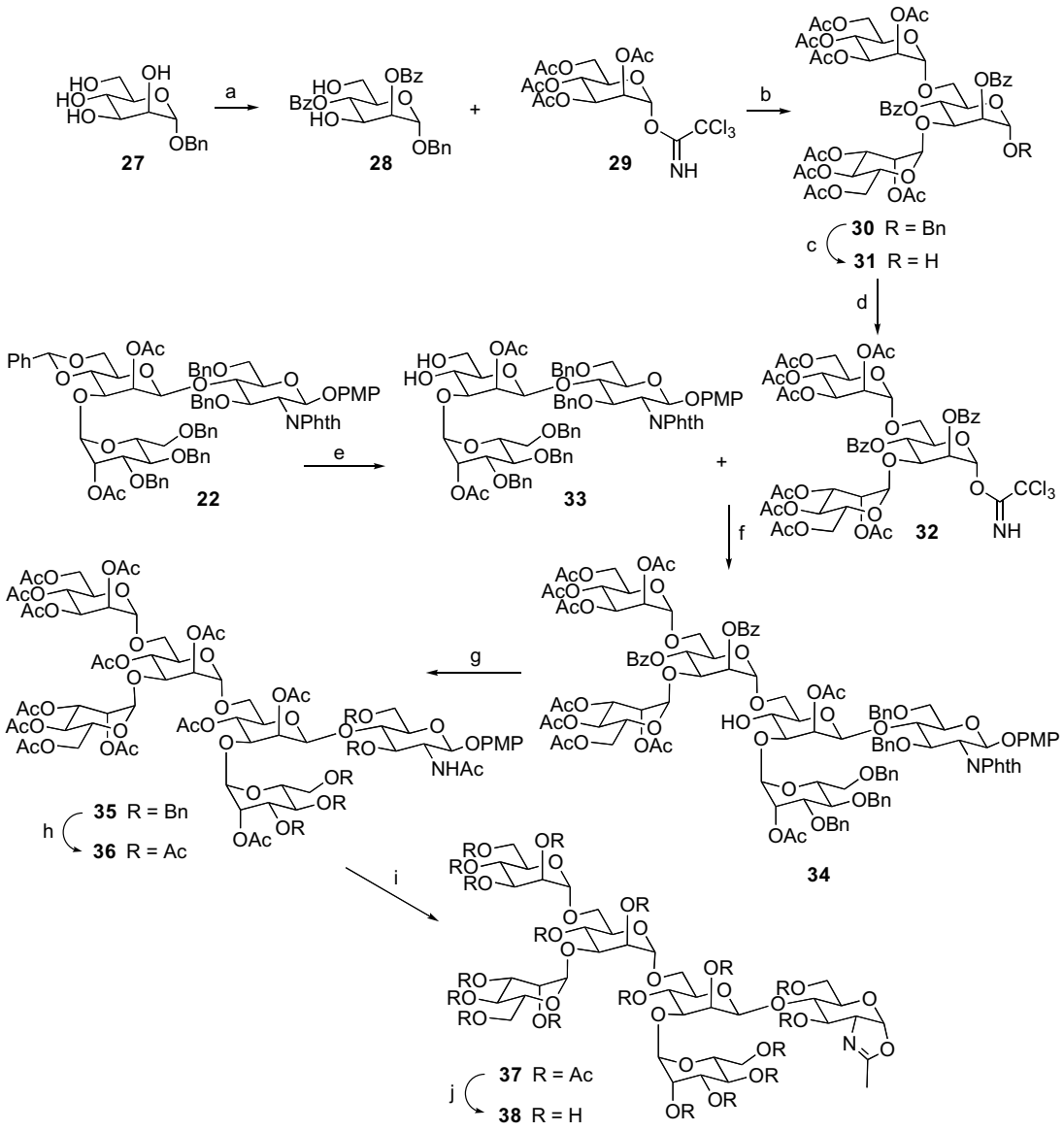


Scheme 3. Reagents and conditions: (a) **7**, TMSOTf, 4 Å mol. sieves, CH_2Cl_2, −60 to 0 °C, 17.5 h, 51%; (b) Levulinic acid, DCC, DMAP, CH_2Cl_2, rt, 20 h, quant.%; (c) **1**, MeOTf, 4 Å mol. sieves, CH_2Cl_2, 0 °C to rt, 20 h, 77%; (d) hydrazine acetate, MeOH, CH_2Cl_2, rt, 24 h, 89%; (e) (i) Tf_2O, py, CH_2Cl_2, 0 °C, 2.5 h; (ii) *n*-Bu_4NOAc, toluene, rt, sonication, 14 h, 90% over two steps; (f) (i) H_2, Pd (10% on C), EtOAc, MeOH, rt, 18 h; (ii) Ac_2O, py, rt, 24 h, 87% over two steps; (g) (i) $NH_2CH_2CH_2NH_2$, MeOH, reflux, 24 h; (ii) Ac_2O, py, rt, 120 h, 87% over two steps; (h) AcBr, $BF_3{\cdot}OEt_2$, ZnI_2, $CHCl_3$, 50 °C, 21 h, 63%; (i) NaOMe, MeOH, rt, 24 h, quant.

direct conversion of the anomeric OPMP group of **24** to the oxazoline yielded oxazoline **25**, which was then deacetylated to yield the desired deprotected oxazoline trisaccharide **26** (Scheme 3).

The hexasaccharide oxazoline containing an extended α-D-Man*p*-(1→3)[α-D-Man*p*-(1→6)]-α-D-Man*p*-(1→6)-[α-D-Man*p*(1→3)]-β-D-Man*p*-(1→4)-β-D-Glc*p*NAc structure was primarily synthesised to assess the glycosylation potential of endohexosaminidases, such as endo-H, which are known to have more specific substrate requirements. For example, endo-H is only capable of hydrolysing high mannose N-glycans containing the α-D-Man*p*-(1→3)-α-D-Man*p*-(1→6)-[α-D-Man*p*-(1→3)]-β-D-Man*p*-(1→4)-β-D-Glc*p*NAc-β-(1→4)-D-Glc*p*NAc motif.[20] The inclusion of the extra 3,6-branched mannose trisaccharide onto the core trisaccharide structure synthesised above therefore required access to a branched α-D-Man*p*-(1→3)-[α-D-Man*p*-(1→6)]-α-D-Man glycosyl donor. Although several approaches to 3,6-branched mannose trisaccharides have been published, the most convenient and efficient appeared to be the regioselective hydrolysis of mannose bis-orthoesters.[21] Thus, the known benzyl mannoside **27** was treated with trimethylorthobenzoate and *p*-toluenesulfonic acid in acetonitrile to yield a bis-orthoester, which underwent immediate hydrolysis by exposure to aqueous trifluoroacetic acid to yield the 2,4-di-*O*-benzoate **28** as the major product (46% yield over two steps).[22] Double glycosylation of diol **28** by treatment with an excess of known trichloroacetimidate **29** and boron trifluoride diethyl etherate in dichloromethane yielded trisaccharide **30**.[23] Removal of the anomeric protecting group by catalytic hydrogenolysis (10% Pd on C) yielded lactols **31** which were then converted into the trichloroacetimidate donor **32** by treatment with trichloroacetonitrile and DBU in dichloromethane. The required trisaccharide glycosyl acceptor was accessed from the previously synthesised trisaccharide **22** by removal of the 4,6-benzylidene protecting group with 80% aqueous acetic acid to yield diol **33**. Completely regioselective glycosylation of the primary hydroxyl of diol **33** with glycosyl donor **32** was achieved by activation of **32** with TMSOTf to yield hexasaccharide **34**. Removal of phthalimide protection by treatment with ethylene diamine and subsequent peracetylation gave completely protected hexasaccharide **35**. Catalytic hydrogenolysis and immediate acetylation of free hydroxyls produced **36**, which was then converted into the peracetylated oxazoline **37**, again using the modified Magnusson conditions. Finally, deacetylation with sodium methoxide in methanol produced the desired deprotected hexasaccharide oxazoline **38** (Scheme 4).

The principle of the use of N-glycan oxazolines as donors for endohexosaminidase catalysed glycosylation



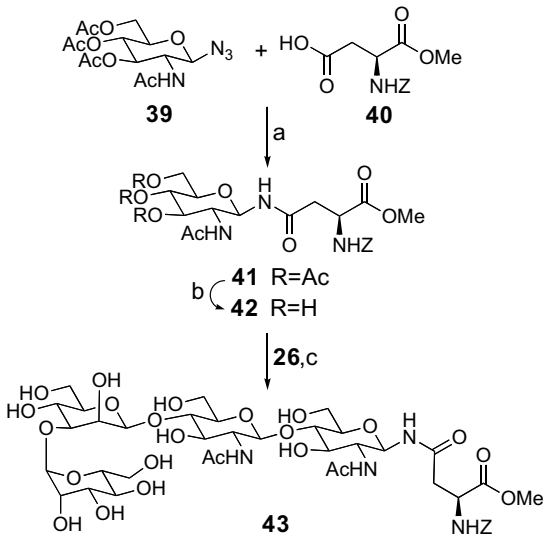
Scheme 4. Reagents and conditions: (a) (i) $PhC(OMe)_3$, TsOH, MeCN, rt, 15 min; (ii) 10% aqueous TFA, rt, 10 min, 46% over two steps; (b) **28**, **29**, $BF_3{\cdot}OEt_2$, 4 Å mol. sieves, CH_2Cl_2, rt, 18 h, 89%; (c) H_2, Pd (10% on C), EtOAc, rt, 24 h, 76%; (d) Cl_3CCN, DBU, CH_2Cl_2, 0 °C to rt, 1.5 h, 92%; (e) 80% aqueous AcOH, 50 °C, 19 h, 86%; (f) **32**, **33**, TMSOTf, 4 Å mol. sieves, CH_2Cl_2, −60 °C to rt, 20 h, 86%; (g) (i) $NH_2CH_2CH_2NH_2$, MeOH, reflux, 25 h; (ii) Ac_2O, py, rt, 72 h, 90% over two steps; (h) (i) H_2, Pd (10% on C), MeOH, rt, 18 h; (ii) Ac_2O, py, rt, 24 h, 81% over two steps; (i) AcBr, $BF_3{\cdot}OEt_2$, ZnI_2, $CHCl_3$, 50 °C, 4 h, 58%; (j) NaOMe, MeOH, rt, 21 h, quant.

was further demonstrated by a model study using trisaccharide oxazoline **26** and a synthetic glucosamine derivative linked to a protected asparagine residue. Thus, the known glycosyl azide **39** was coupled to the commercially available aspartic acid derivative **40** by treatment with tri-*n*-butylphosphine to yield protected β-D-Glc*p*NAcAsn glycosyl amino acid **41**, which was then de-acetylated to yield triol acceptor **42** (Scheme 5).[24,25]

Endo-M catalysed glycosylation of **42** was then achieved by treatment of an aqueous solution of **42** with deprotected oxazoline trisaccharide donor **26** at room temperature at pH 6.0 in the presence of Endo-M. Monitoring of the extent of reaction by HPLC revealed that the optimum length of time for efficient glycosylation was 60 min (Fig. 3) and after this time the desired tetrasaccharide glycosyl amino acid **43** could be isolated in 81% yield (based on glycosyl acceptor). Prolonged reaction times produced a lower yield of product due to Endo-M catalysed hydrolysis of the desired product.

3. Conclusions

Deprotected mono-, di-, tri- and hexasaccharide oxazolines corresponding to core fragments of high mannose



Scheme 5. Reagents and conditions: (a) *n*-Bu_3P, CH_2Cl_2, −78 °C to rt, 10 h, 67%; (b) NaOMe, MeOH, rt, 0.1 h, 90%; (c) **26**, Endo-M, Na_2HPO_4/NaH_2PO_4 (100 mM), pH 6.0, 23 °C, 1 h, 81%.

N-linked glycans have been successfully synthesised. The key synthetic challenge of the synthesis of the difficult β-D-Man*p*-(1→4)-D-Glc*p*NAc linkage was achieved with complete stereocontrol via an OH-2 epimerisation procedure using *gluco* disaccharide substrates. Other key transformations were the direct conversion of anomeric OPMP GlcNAc derivatives into their corresponding oxazolines, and the rapid efficient synthesis of a 3,6-branched mannose trisaccharide donor accessed via double glycosylation of a 2,4-protected benzoyl mannoside, itself accessed by regioselective acid catalysed hydrolysis of a *manno* bis-orthoester. The use of N-glycan oxazolines for endohexosaminidase catalysed glycosylation has been demonstrated by the high yielding glycosylation of a synthetic β-D-Glc*p*NAcAsn glycosyl amino acid with a trisaccharide oxazoline donor. Further investigations into the use of these oxazoline donors as substrates for endohexosaminidase mediated glycosylation reactions to allow the synthesis of complex glycopeptides and for the remodelling of glycoproteins are currently in progress, and the results will be reported in due course.

4. Experimental

4.1. General

Melting points were recorded on a Kofler hot block and are uncorrected. Proton and carbon nuclear magnetic resonance (δ_H, δ_C) spectra were recorded on Bruker DPX 250 (250 MHz), Bruker DPX 400 (400 MHz), Bruker DQX 400 (400 MHz), Bruker AVC 500 (500 MHz) or Bruker AMX 500 (500 MHz) spectrometers. All chemical shifts are quoted on the δ-scale in ppm using residual solvent as an internal standard. Low resolution mass spectra were recorded on a Micromass Platform 1 spectrometer using electrospray ionisation in either positive or negative polarity (ES^+ or ES^-), or using a VG Micromass spectrometer. High-resolution mass spectra were recorded on a Walters 2790-Micromass LCT electrospray ionisation mass spectrometer, using either electrospray ionisation (NH_3, Cl) techniques as stated. *m*/*z* values are reported in Daltons and are followed by their percentage abundance in parentheses. Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g/100 mL. Microanalyses were performed by the Inor-

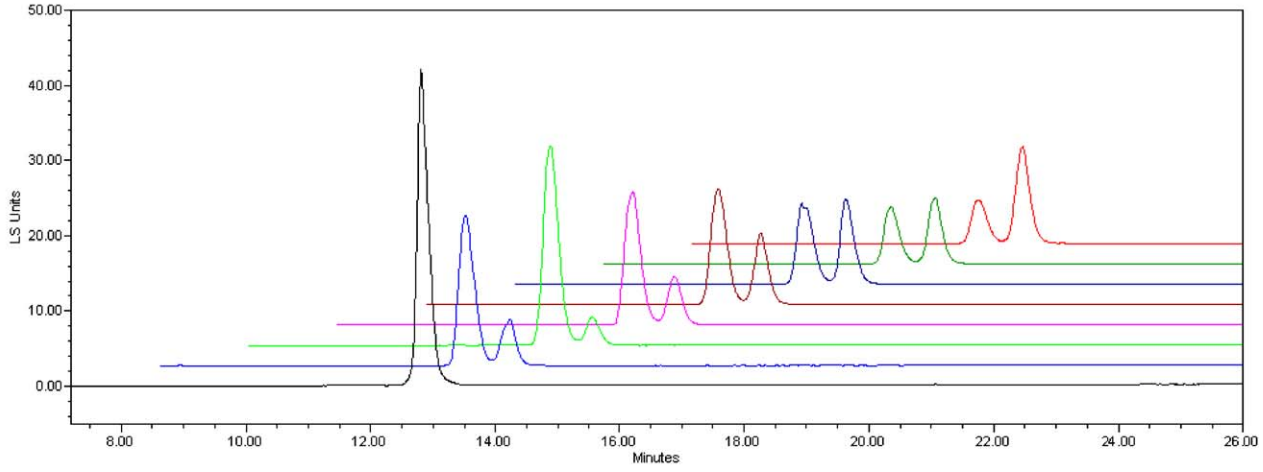


Figure 3. HPLC analysis (see general experimental) of Endo-M catalysed glycosylation of acceptor **42** with trisaccharide oxazoline donor **26**. Line traces are taken at 30 min intervals. $T = 0$ indicates only unreacted glycosyl amino acid **42** staring material (right hand peak). $T = 30$ min and $T = 60$ min traces reveal increasing formation of tetrasaccharide glycosyl amino acid product **43** (left hand peak). $T > 60$ min traces indicate reconversion to **42** by Endo-M catalysed product hydrolysis.

ganic Chemistry Laboratory Elemental Analysis service, Oxford University, UK. Thin Layer Chromatography (TLC) was carried out on Merck Kieselgel $60F_{254}$ precoated glass-backed plates. Visualisation of the plates was achieved using a UV lamp ($\lambda_{max} = 254$ or 365 nm), and/or ammonium molybdate (5% in 2 M sulfuric acid), or sulfuric acid (5% in ethanol). Flash column chromatography was carried out using Sorbsil C60 40/60 silica. Dichloromethane was distilled from calcium hydride, or dried on an alumina column. Anhydrous THF, DMF, pyridine, MeOH and toluene were purchased from Fluka over molecular sieves. 'Petrol' refers to the fraction of light petroleum ether boiling in the range of 40–60 °C. Analytical HPLC was carried out using a Waters 2795 Alliance HT HPLC instrument using Empower software (version 5.0) connected to a Waters 2996 Photodiode Array Detector and a Waters 2420 ELS Detector, using a Phenomenex Gemini™ 5μ C_{18} column (150 × 4.6 mm) at 23 °C. The column was eluted with a linear gradient of 0–90% MeCN/H_2O at a flow rate of 1 mL/min over 20 min, with a return to 100% H_2O over 2 min and with a re-equilibration at 100% H_2O for a further 8 min.

4.2. *p*-Methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-4-methoxy-2-phthalimido-β-D-glucopyranoside (2)

To a dry round-bottomed flask, alcohol **1**[11] (1.58 g, 2.65 mmol) was added. DMF (20 mL) was added via canula, and the reaction mixture cooled to 0 °C. Methyl iodide (240 μL, 3.89 mmol) was added, followed by the portion-wise addition of sodium hydride (207 mg of a 60% mineral oil dispersion, 5.18 mmol). After 2.5 h, TLC (2:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.3$) and complete consumption of starting material ($R_f = 0.15$). Isopropyl alcohol (2 mL) was added until effervescence ceased, followed by the addition of MeOH (10 mL). The reaction mixture was then poured onto ice/water (100 mL) and extracted with dichloromethane (3 × 100 mL). The organic extracts were combined, washed with brine (2 × 100 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (2:1, petrol/EtOAc) to give methyl ether **2** (1.04 g, 64%) as a white foam; $[\alpha]_D^{20}$ +94 (*c* 1.0, $CHCl_3$); IR (KBr disc) 1772, 1713 cm^{-1} (s, C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 3.51–3.56 (1H, m, H-4), 3.58 (3H, s, CHOCH_3), 3.66 (1H, ddd, $J_{4,5} = 9.9$ Hz, $J_{5,6} = 4.8$ Hz, $J_{5,6'} = 2.1$ Hz, H-5), 3.71 (3H, s, $PhOCH_3$), 3.78 (1H, dd, $J_{6,6'} = 10.9$ Hz, H-6), 3.85 (1H, dd, H-6′), 4.30 (1H, dd, $J_{2,3} = 10.8$ Hz, $J_{3,4} = 8.4$ Hz, H-3), 4.39 (1H, dd, $J_{1,2} = 8.5$ Hz, H-2), 4.48, 4.83 (2H, ABq, $J = 12.2$ Hz, $PhCH_2$), 4.60, 4.68 (2H, ABq, $J = 11.9$ Hz, $PhCH_2$), 5.62 (1H, d, H-1), 6.66–6.84 (4H, m, 4 × Ar-H), 6.88–7.06 (5H, m, 5 × Ar-H), 7.28–7.37 (5H, m, 5 × Ar-H), 7.62–7.81 (4H, m, 4 × Ar-H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5 (q, PhOCH_3), 55.6 (d, C-2), 60.7 (q, CHOCH_3), 68.7 (t, C-6), 73.5, 74.6 (2 × t, 2 × $PhCH_2$), 75.3 (d, C-5), 78.8 (d, C-3), 81.6 (d, C-4), 97.5 (d, C-1), 114.3, 118.6, 125.9, 127.4, 127.6, 127.7, 128.0, (7 × d, 18 × Ar-C), 128.1, 128.3 (2 × s, 2 × Ar-C), 137.9, 138.2 (2 × s, 2 × Ar-C), 151.5, 155.9 (2 × s, 2 × Ar-C), 175.5 (2 × s, 2 × C=O); *m*/*z* (ES^+) 668 ($[M+NH_4+MeCN]^+$, 100%). ESIMS *m*/*z* calcd for $C_{36}H_{35}NO_8Na$ $[M+Na]^+$: 632.2260. Found 632.2271.

4.3. *p*-Methoxyphenyl 2-deoxy-4-methoxy-2-phthalimido-β-D-glucopyranoside (3)

Alcohol **2** (950 mg, 1.56 mmol) was added to a dry two-necked flask and dissolved in EtOAc (15 mL). Palladium (10% on carbon, 320 mg) was then added. The flask was purged three times with argon, and then stirred under an atmosphere of hydrogen at rt. After 18 h, TLC (1:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.1$) and complete consumption of starting material ($R_f = 0.5$). The reaction mixture was poured onto Celite, washed with EtOAc (3 × 100 mL), filtered and concentrated in vacuo. The residue was recrystallised (EtOAc/petrol) to give diol **3** (669 mg, quant.) as white crystals, mp 101–102 °C (EtOAc/petrol); $[\alpha]_D^{20}$ +21 (*c* 0.4, $CHCl_3$); IR (KBr disc): 3544 (br, OH), 1772, 1703 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, CD_3OD): δ 3.33–3.35 (1H, m, H-4), 3.53 (1H, ddd, $J_{4,5} = 9.7$ Hz, $J_{5,6} = 4.5$ Hz, $J_{5,6'} = 2.0$ Hz, H-5), 3.63 (3H, s, CHOCH_3), 3.71 (3H, s, PhOCH_3) 3.78 (1H, dd, $J_{6,6'} = 12.0$ Hz, H-6), 3.93 (1H, dd, H-6′), 4.24 (1H, dd, $J_{1,2} = 8.5$ Hz, $J_{2,3} = 10.6$ Hz, H-2), 4.41 (1H, dd, $J_{3,4} = 8.5$ Hz, H-3), 5.65 (1H, d, H-1), 6.75–6.86 (4H, m, 4 × Ar-H), 7.84–7.90 (4H, m, 4 × Ar-H); ^{13}C NMR (125.7 MHz, CD_3OD): δ 55.0 (q, CHOCH_3), 57.6 (d, C-2), 60.0 (q, $PhOCH_3$), 61.1 (t, C-6), 71.8 (d, C-3), 76.6 (d, C-5), 80.4 (d, C-4), 98.1 (d, C-1), 114.5, 118.2, 123.3 (3 × d, 8 × Ar-C), 132.0, 134.6 (2 × s, 2 × Ar-C), 151.6, 155.9 (2 × s, 2 × Ar-C), 171.2 (2 × s, 2 × C=O); *m*/*z* (ES^+) 488 ($[M+NH_4+MeCN]^+$, 100%); ESIMS *m*/*z* calcd for $C_{22}H_{23}NO_8Na$ $[M+Na]^+$: 452.1321. Found 452.1339. Crystal structure data—see Supplementary data.

4.4. *p*-Methoxyphenyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-methoxy-β-D-glucopyranoside (4)

To a solution of diol **3** (1.67 g, 3.89 mmol) in MeOH (75 mL) was added ethylenediamine (80 mL). The reaction mixture was heated at reflux at 80 °C. After 20 h, TLC (EtOAc) indicated the formation of a major product ($R_f = 0$), and complete consumption of starting material ($R_f = 0.5$). The solution was concentrated in vacuo and co-evaporated with toluene (3 × 20 mL). The residue was dissolved in pyridine (40 mL) and the

reaction mixture cooled to 0 °C. Ac_2O (30 mL) was added slowly, and the reaction mixture stirred at rt. After 16 h, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.4$) and complete consumption of intermediate product ($R_f = 0$). The reaction mixture was poured onto ice/water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined and washed with aqueous hydrochloric acid (3 × 50 mL of a 1 M solution), aqueous sodium hydrogen carbonate (3 × 50 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was recrystallised (EtOAc/petrol) to give acetate **4** (1.44 g, 80%) as white crystals, mp 180–181 °C; $[\alpha]_D^{20}$ −20 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3280 (br, NH), 1743, 1663 (s, C=O), 1558 (m, NH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.98 (3H, s, NC(O)CH_3), 2.01, 2.13 (6H, 2 × s, 2 × OC(O)-CH_3), 3.43 (1H, at, $J = 8.7$ Hz, H-4), 3.46 (3H, s, CHOCH_3), 3.65 (1H, ddd, $J_{4,5} = 9.5$ Hz, $J_{5,6} = 5.6$ Hz, $J_{5,6'} = 2.3$ Hz, H-5), 3.77 (3H, s, PhOCH_3), 4.24–4.31 (2H, m, H-2, H-6), 4.41 (1H, dd, $J_{6,6'} = 11.9$ Hz, H-6′), 4.87 (1H, d, $J_{1,2} = 8.0$ Hz, H-1), 5.11 (1H, dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 9.0$ Hz, H-3), 5.68 (1H, d, $J_{NH,2} = 9.2$ Hz, NH), 6.78–6.94 (4H, m, 4 × Ar-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.8, 21.0 (2 × q, 2 × OC(O)CH_3), 23.3 (q, NC(O)CH_3), 53.9 (d, C-2), 55.6 (q, PhOCH_3), 60.4 (q, CHOCH_3), 62.9 (t, C-6), 72.9 (d, C-5), 74.7 (d, C-3), 77.4 (d, C-4), 100.5 (d, C-1), 114.4, 118.3 (2 × d, 4 × Ar-C), 151.2, 155.4 (2 × s, 2 × Ar-C), 170.2, 175.5 (2 × s, 2 × C=O); *m/z* (ES^+) 484 ($[M+NH_4+MeCN]^+$, 100%); ESIMS *m/z* calcd for $C_{20}H_{28}NO_9$ $[M+H]^+$: 426.1764. Found 426.1760.

4.5. 2-Methyl-(4-methoxy-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-oxazoline (6)

Acetate **4** (50 mg, 0.118 mmol) was dissolved in anhydrous chloroform (5 mL) and acetyl bromide (87.0 μL, 1.18 mmol), $BF_3{\cdot}OEt_2$ (45.0 μL, 0.353 mmol) and zinc(II) iodide (2.00 mg, 6.00 μmol) were added. The reaction mixture was heated and stirred at 50 °C. After 18 h, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.4$) and complete consumption of starting material ($R_f = 0.45$). The reaction mixture was allowed to cool to rt and then CH_2Cl_2 (30 mL) was added. The organic layer was washed with aqueous sodium hydrogen carbonate (20 mL of a saturated solution) and aqueous sodium thiosulfate (10 mL of a 5% w/v solution), water (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford acetylated oxazoline **5** (20 mg, 57%) as a white amorphous solid; *m/z* (ES^+) 324 ($[M+Na]^+$, 100%); ESIMS *m/z* calcd for $C_{13}H_{20}NO_7$ $[M+H]^+$: 302.1240. Found 302.1236.

A portion of the acetylated oxazoline **5** (19.0 mg, 63.1 μmol) was dissolved in dry MeOH (2 mL). NaOMe in MeOH (175 μL of a 5 mg/mL solution, 37.8 μmol) was added, and the solution stirred at rt under an atmosphere of argon. After 21 h, the solution was concentrated in vacuo to yield deprotected oxazoline **6** (15.4 mg, 98%) as a white amorphous solid; IR (KBr disc): 3343 (br, OH), 1665 (s, C=N) cm^{-1}; ^1H NMR (500 MHz, D_2O): δ 1.97 (3H, d, $J_{2,C(O)CH_3} = 1.7$ Hz, C(O)CH_3), 3.19–3.20 (2H, m, H-4, H-5), 3.35 (3H, s, OCH_3), 3.54–3.58 (1H, m, H-6), 3.68–3.71 (1H, m, H-6′), 4.15–4.18 (2H, m, H-2, H-3), 6.01 (1H, d, $J_{1,2} = 7.2$ Hz, H-1); ^{13}C NMR (125.8 MHz, D_2O): δ 12.8 (q, C(O)CH_3), 57.0 (q, OCH_3), 62.1 (t, C-6), 65.2 (d, C-2), 65.7 (d, C-3), 71.0 (d, C-4), 78.6 (d, C-5), 99.7 (d, C-1), 168.1 (s, *C*(O)CH_3); *m/z* (ES^-) 216 ($[M-H]^+$, 100%); ESIMS *m/z* calcd for $C_9H_{14}NO_5$ $[M-H]^+$: 216.0872. Found 216.0876.

4.6. Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (8)

Diol **7**[16] (5.80 g, 19.2 mmol) was dissolved in MeOH (200 mL), di-*n*-butyltin oxide (5.74 g, 23.0 mmol) added and the reaction mixture heated at reflux at 65 °C for 18 h. The reaction mixture was then cooled, concentrated in vacuo and the residue was dissolved in DMF (200 mL). Benzyl bromide (2.74 mL, 23.0 mmol) and cesium(I) fluoride (3.80 g, 25 mmol) were added and the solution stirred at rt. After 24 h, TLC (3:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.3$) and complete consumption of starting material ($R_f = 0$). The reaction mixture was concentrated in vacuo and the residue extracted with CH_2Cl_2 (200 mL). The organic layer was washed with aqueous potassium fluoride (100 mL of a 1 M solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was crystallised (diethyl ether/petrol) to give alcohol **8** (3.79 g, 51%) as white crystals, mp 139–140 °C [lit. 139 °C];[17] $[\alpha]_D^{23}$ −57 (*c* 1.0, $CHCl_3$) [lit. $[\alpha]_D$ −46.2 (*c* 0.3, $CHCl_3$)];[17] ^1H NMR (200 MHz, $CDCl_3$): δ 1.33 (3H, t, $J = 7.4$ Hz, SCH_2CH_3), 2.52 (1H, d, $J_{2,OH} = 1.7$ Hz, OH), 2.76 (2H, q, $J = 7.4$ Hz, SCH_2CH_3), 3.45–3.65 (2H, m, H-2, H-5), 3.69δ_H 3.85 (3H, m, H-3, H-4, H-6), 4.37 (1H, dd, $J_{5,6'} = 4.9$ Hz, $J_{6,6'} = 10.4$ Hz, H-6′), 4.48 (1H, d, $J_{1,2} = 9.3$ Hz, H-1), 4.82, 4.99 (2H, ABq, $J = 11.6$ Hz, $PhCH_2$), 5.59 (1H, s, PhCH), 7.28–7.53 (10H, m, 10 × Ar-H).

4.7. Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (9)

Alcohol **8** (100 mg, 0.248 mmol) was dissolved in CH_2Cl_2 (10 mL). Levulinic acid (50.9 μL, 0.497 mmol), DCC (103 mg, 0.497 mmol) and DMAP (3.03 mg, 24.8 μmol) were added and the reaction mixture stirred at rt. After 18 h, TLC (3:2, petrol/EtOAc) indicated no difference in R_f from the starting material ($R_f = 0.45$). CH_2Cl_2 (30 mL) was added to the reaction

mixture and the organic layer was separated and washed with water (20 mL), aqueous sodium hydrogen carbonate (2 × 20 mL of a saturated solution), brine (10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was crystallised (EtOAc/petrol) to give ester **9** (95.0 mg, 76%) as white crystals, mp 115–116 °C; $[\alpha]_D^{22}$ −37 (*c* 0.5, $CHCl_3$); IR (KBr disc): 1740, 1705 (s, C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.26 (3H, t, $J = 7.4$ Hz, SCH_2CH_3), 2.19 (3H, s, $C(O)CH_3$), 2.54–2.58, 2.65–2.80 (6H, m, 3 × CH_2), 3.47–3.53 (1H, m, H-5), 3.74–3.82 (3H, m, H-3, H-4, H-6), 4.38 (1H, dd, $J_{5,6'} = 4.9$ Hz, $J_{6,6'} = 10.5$ Hz, H-6′), 4.48 (1H, d, $J_{1,2} = 10.1$ Hz, H-1), 4.72, 4.88 (2H, ABq, $J = 11.9$ Hz, $PhCH_2$), 5.04–5.08 (1H, m, H-2), 5.59 (1H, s, PhCH), 7.29–7.33 (5H, m, 5 × Ar-H), 7.38–7.41 (3H, m, 3 × Ar-H), 7.49–7.51 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.8 (q, SCH_2CH_3), 24.0, 28.0 (2 × t, 2 × CH_2), 29.8 (q, $C(O)CH_3$), 37.9 (t, CH_2), 68.6 (t, C-6), 70.6 (d, C-5), 71.6 (d, C-2), 74.3 (t, $PhCH_2$), 79.5, 81.5 (2 × d, C-3, C-4), 84.2 (d, C-1), 101.2 (d, PhCH), 126.0, 127.7, 128.0, 128.3, 129.0 (5 × d, 10 × Ar-C), 137.1, 138.1 (2 × s, 2 × Ar-C), 171.4, 206.1 (2 × s, 2 × C=O); *m/z* (ES^+) 1018 ($[2M+NH_4]^+$, 100%); ESIMS *m/z* calcd for $C_{27}H_{32}O_7NaS$ $[M+Na]^+$: 523.1766. Found 523.1762. Anal. Calcd for $C_{27}H_{32}O_7S$: C, 64.78; H, 6.44. Found: C, 64.76; H, 6.46.

4.8. *p*-Methoxyphenyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (10)

Alcohol **1** (217 mg, 0.364 mmol), and thioglycoside **9** (200 mg, 0.400 mmol) were dissolved in dry CH_2Cl_2 (15 mL) and transferred via canula to a round-bottomed flask containing activated 4 Å molecular sieves (1 g), under an atmosphere of argon. The reaction mixture was cooled to 0 °C, MeOTf (206 μL, 1.82 mmol) was added and the solution stirred. After 15 h, TLC (3:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.2$) and complete consumption of alcohol **1** ($R_f = 0.25$). Et_3N (400 μL) was added, the solution was stirred for 10 min, and then filtered through Celite. The filtrate was concentrated in vacuo, and the residue purified by flash column chromatography (3:2, petrol/EtOAc) to yield disaccharide **10** (342 mg, 91%) as a white amorphous foam; $[\alpha]_D^{22}$ +31 (*c* 1.0, $CHCl_3$); IR (KBr disc): 1777, 1751, 1716 (s, C=O), 1508 (m, NH) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.26 (3H, s, $C(O)CH_3$), 2.44–2.88 (4H, m, 2 × CH_2), 3.28 (1H, dat, $J = 4.9$ Hz, $J = 9.6$ Hz, $J = 9.6$ Hz, H-5b), 3.53 (1H, at, $J = 10.3$ Hz, H-6b), 3.62 (1H, at, $J = 9.2$ Hz, H-3b), 3.70 (1H, at, $J = 9.3$ Hz, H-4b), 3.72–3.76 (1H, m, H-5a), 3.76 (3H, s, OCH_3), 3.86 (1H, br d, $J = 10.5$ Hz, H-6a), 3.93 (1H, dd, $J_{5a,6'a} = 3.2$ Hz, $J_{6a,6'a} = 11.1$ Hz, H-6′a), 4.19 (1H, at, $J = 9.2$ Hz, H-4a), 4.31–4.37 (2H, m, H-3a, H-6′b), 4.44 (1H, dd, $J_{1a,2a} = 8.5$ Hz, $J_{2a,3a} = 10.7$ Hz, H-2a), 4.49, 4.83 (2H, ABq, $J = 12.4$ Hz, $PhCH_2$), 4.52, 4.84 (2H, ABq, $J = 11.9$ Hz, $PhCH_2$), 4.65 (1H, d, $J_{1b,2b} = 8.0$ Hz, H-1b), 4.71, 4.91 (2H, ABq, $J = 12.0$ Hz, $PhCH_2$), 5.04 (1H, at, $J = 8.6$ Hz, H-2b), 5.53 (1H, s, PhCH), 5.67 (1H, d, H-1a), 6.74–6.75 (2H, m, 2 × Ar-H), 6.86–6.88 (2H, m, 2 × Ar-H), 6.92–6.97 (3H, m, 3 × Ar-H), 7.07–7.08 (2H, m, 2 × Ar-H), 7.33–7.45 (13H, m, 13 × Ar-H), 7.52–7.53 (2H, m, 2 × Ar-H), 7.72–7.89 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 27.8 (t, $CH_2CH_2C(O)CH_3$), 29.9 (q, $C(O)CH_3$), 37.7 (t, $CH_2CH_2C(O)CH_3$), 55.6 (m, C-2a, OCH_3), 65.9 (d, C-5b), 67.6 (t, C-6a), 68.6 (t, C-6b), 73.6 (d, C-2b), 73.6, 74.1, 74.6 (3 × t, 3 × $PhCH_2$), 74.9 (d, C-5a), 76.7 (d, C-3a), 77.9 (d, C-4a), 78.5 (d, C-3b), 81.7 (d, C-4b), 97.5 (d, C-1a), 100.7 (d, C-1b), 101.2 (d, PhCH), 114.3, 118.7, 123.3, 126.0, 127.1, 127.6, 127.8, 127.8, 127.9, 128.1, 128.2, 128.3, 128.5, 129.0, 133.7 (15 × d, 28 × Ar-C), 137.2, 137.9, 138.3, 138.5, 150.8, 155.3 (6 × s, 8 × Ar-C), 171.2, 206.2 (2 × s, 4 × C=O); $J_{C\text{-}1a/H\text{-}1a} = 166$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 164$ Hz (β); *m/z* (ESI^+) species observed $[M+Na]^+$ (major), $[M+NH_4]^+$; $[M+Na]^+$ peaks observed: 1056.3 (100%), 1057.3 (58%), 1058.3 (30%), 1059.3 (11%), peaks calcd: 1056.4 (100%), 1057.4 (65%), 1058.4 (30%), 1059.4 (9%). Anal. Calcd for $C_{60}H_{59}NO_{15}$: C, 69.69; N, 1.35; H, 5.75. Found: C, 69.62; N, 1.17; H, 5.81.

4.9. *p*-Methoxyphenyl 3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (11)

Levulinic ester **10** (300 mg, 0.290 mmol) was dissolved in a mixture of MeOH (10 mL) and CH_2Cl_2 (5 mL). Hydrazine acetate (52.3 mg, 0.580) was then added and the mixture stirred at rt. After 19 h, TLC (1:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.5$) and complete consumption of starting material ($R_f = 0.4$). The reaction mixture was concentrated in vacuo and the residue purified by flash column chromatography (1:1, petrol/EtOAc) to yield alcohol **11** (267 mg, 98%) as a white foam; $[\alpha]_D^{23}$ +53 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3474 (br, OH), 1777, 1715 (s, C=O), 1507 (m, NH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.00 (1H, br s, OH), 3.23 (1H, dat, $J = 4.9$ Hz, $J = 9.5$ Hz, $J = 9.5$ Hz, H-5b), 3.53–3.66 (4H, m, H-2b, H-3b, H-4b, H-6b), 3.71 (3H, s, OCH_3), 3.71–3.75 (1H, m, H-5a), 3.86 (1H, dd, $J_{5a,6a} = 1.4$ Hz, $J_{6a,6'a} = 11.4$ Hz, H-6a), 4.04 (1H, dd, $J_{5a,6'a} = 3.5$ Hz, H-6′a), 4.17–4.22 (2H, m, H-4a, H-6′b), 4.41–4.46 (3H, m, H-2a, H-3a, PhCH), 4.57, 4.74 (2H, ABq, $J = 11.9$ Hz, $PhCH_2$), 4.66 (1H, m, H-1b), 4.78, 4.96 (2H, ABq, $J = 11.8$ Hz, $PhCH_2$), 4.81 (1H, d, $J = 12.9$ Hz, PhCH), 5.49 (1H, s, PhCH), 5.60 (1H, m, H-1a), 6.69–6.71 (2H, m, 2 × Ar-H), 6.80–6.82 (2H, m, 2 × Ar-H), 6.87–6.95 (3H, m, 3 × Ar-H), 7.02–7.04 (2H, m, 2 × Ar-H), 7.29–7.39

(13H, m, 13 × Ar-H), 7.46–7.48 (2H, m, 2 × Ar-H), 7.68 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 55.6 (q, OCH_3), 55.7 (d, C-2a), 66.2 (d, C-5b), 68.0 (t, C-6a), 68.6 (t, C-6b), 73.5, 74.6, 74.7 (3 × t, 3 × $PhCH_2$), 74.9 (d, C-5a), 75.0 (d, C-2b), 77.8 (d, C-3a), 78.7 (d, C-4a), 80.4 (d, C-3b), 81.3 (d, C-4b), 97.7 (d, C-1a), 101.2 (d, PhCH), 103.4 (d, C-1b), 11.43, 118.7, 123.3, 126.0, 127.2, 127.5, 127.8, 127.8, 128.0, 128.0, 128.1, 128.2, 128.4, 128.4, 128.7, 129.0 (15 × d, 26 × Ar-C), 131.5 (s, 2 × Ar-C), 133.8 (d, 2 × Ar-C), 137.3, 137.7, 138.3, 138.4, 150.8, 155.4 (6 × s, 6 × Ar-C), 169.8 (s, C═O); $J_{C\text{-}1a/H\text{-}1a} = 166$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 164$ Hz (β); *m*/*z* (ES^+) 953 ($[M+NH_4]^+$, 100%); ESIMS *m*/*z* calcd for $C_{55}H_{53}NO_{13}Na$ $[M+Na]^+$; 958.3415. Found 958.3417. Anal. Calcd for $C_{55}H_{53}NO_{13}$: C, 70.58; N, 1.50; H, 5.71. Found: C, 70.32; N, 1.45; H, 5.83.

4.10. *p*-Methoxyphenyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (12)

Alcohol **11** (220 mg, 0.235 mmol) was dissolved in CH_2Cl_2 (20 mL), and the solution cooled to 0 °C. Triflic anhydride (316 μL, 1.88 mmol) and pyridine (342 μL, 4.23 mmol) were added and the reaction stirred. After 2.5 h, TLC (1:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.6$) and complete consumption of starting material ($R_f = 0.5$). The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with aqueous sodium hydrogen carbonate (25 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was dissolved in dry toluene (20 mL) and Bu_4NOAc (496 mg, 1.65 mmol) was added. The suspension was subjected to sonication at rt, under an atmosphere of argon. After 18 h, TLC (2:1, petrol/EtOAc) indicated the formation of one product ($R_f = 0.25$). The reaction mixture was concentrated in vacuo and purified by flash column chromatography to yield *manno* ester **12** (202 mg, 88%) as a white amorphous foam; $[\alpha]_D^{23}$ +21 (*c* 1.0, $CHCl_3$); IR (KBr disc): 1777, 1747, 1716 (s, C═O), 1508 (m, NH) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.24 (3H, s, $OCOCH_3$), 3.22 (1H, dat, $J_{5b,6'b} = 4.9$ Hz, $J = 9.7$ Hz, H-5b), 3.54 (1H, dd, $J_{2b,3b} = 3.3$ Hz, $J_{3b,4b} = 9.8$ Hz, H-3b), 3.65 (1H, at, $J = 10.3$ Hz, H-6b), 3.70–3.74 (1H, m, H-5a), 3.77 (3H, s, OCH_3), 3.84 (1H, br d, $J = 11.3$ Hz, H-6a), 3.90 (1H, dd, $J_{5a,6'a} = 3.0$ Hz, $J_{6a,6'a} = 11.3$ Hz, H-6′a), 3.95 (1H, at, $J = 9.6$ Hz, H-4b), 4.25–4.28 (2H, m, H-4a, H-6′b), 4.39 (1H, dd, $J_{2a,3a} = 10.6$ Hz, $J_{3a,4a} = 8.6$ Hz, H-3a), 4.47 (1H, dd, $J_{1a,2a} = 8.6$ Hz, H-2a), 4.51, 4.93 (2H, ABq, $J = 11.9$ Hz, $PhCH_2$), 4.53, 4.82 (2H, ABq, $J = 11.7$ Hz, $PhCH_2$), 4.62, 4.73 (2H, ABq, $J = 12.4$ Hz, $PhCH_2$), 4.75 (1H, s, H-1b), 5.54 (1H, br d, $J = 3.2$ Hz, H-2b), 5.59 (1H, s, PhCH), 5.68 (1H, d, H-1a), 6.76–6.78 (2H, m, 2 × Ar-H), 6.86–6.88 (2H, m, 2 × Ar-H), 6.96–7.00 (3H, m, 3 × Ar-H), 7.08–7.10 (2H, m, 2 × Ar-H), 7.24–7.56 (15H, m, 15 × Ar-H), 7.74–7.92 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 21.1 (q, $OCOCH_3$), 55.6 (q, OCH_3), 55.6 (d, C-2a), 66.9 (d, C-5b), 68.2 (t, C-6a), 68.4 (t, C-6b), 69.1 (d, C-2b), 71.6 (t, $PhCH_2$), 73.5 (t, $PhCH_2$), 74.5 (d, C-5a), 74.7 (t, $PhCH_2$), 75.8 (d, C-3b), 77.0 (d, C-3a), 77.8 (d, C-4b), 78.9 (d, C-4a), 97.7 (d, C-1a), 99.4 (d, C-1b), 101.4 (d, PhCH), 114.4, 118.6, 123.4, 126.1, 127.2, 127.5, 127.7, 127.8, 128.0, 128.0, 128.2, 128.4, 128.6, 128.9 (14 × d, 26 × Ar-C), 131.6 (s, 2 × Ar-C), 133.8 (d, 2 × Ar-C), 137.4, 137.8, 137.8, 138.4, 150.8, 155.4 (6 × s, 6 × Ar-C), 167.6, 168.2, 170.3 (3 × s, 3 × C═O); $J_{C\text{-}1a/H\text{-}1a} = 167$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 160$ Hz (β); *m*/*z* (ES^+) 1000 ($[M+Na]^+$, 100%); ESIMS *m*/*z* calcd for $C_{57}H_{59}N_2O_{14}$ $[M+NH_4]^+$: 995.3966. Found 995.3961. Anal. Calcd for $C_{57}H_{55}NO_{14}$: C, 70.00; N, 1.43; H, 5.67. Found: C, 69.70; N, 1.35; H, 5.84.

4.11. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (13)

Benzylated disaccharide **12** (650 mg, 665 μmol) was added to a dry two-necked flask and dissolved in EtOAc (30 mL) and ethanol (30 mL). Palladium (10% on carbon, 250 mg) was added. The flask was flushed with argon (three times) followed by hydrogen (three times) and the mixture stirred under an atmosphere of hydrogen at rt. After 25 h, TLC (1:9, MeOH/EtOAc) indicated the formation of a major product ($R_f = 0.2$) and complete consumption of starting material ($R_f = 0.8$). The reaction mixture was poured onto Celite, washed with ethanol (3 × 50 mL), filtered and concentrated in vacuo. The residue was dissolved in pyridine (25 mL), the solution cooled to 0 °C and Ac_2O (20 mL) added. The reaction mixture was stirred and allowed to warm to rt. After 22 h, TLC (1:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.2$) and complete consumption of intermediate material ($R_f = 0$). The reaction mixture was poured onto ice/water (200 mL), extracted with CH_2Cl_2 (2 × 30 mL), the organic layers combined and washed with aqueous sodium hydrogen carbonate (2 × 20 mL of a saturated solution), brine (10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:1, petrol/EtOAc) to give acetylated disaccharide **13** (501 mg, 91%) as a white amorphous solid; $[\alpha]_D^{23}$ 0 (*c* 0.5, $CHCl_3$); IR (KBr disc): 1750, 1719 (s, C═O), 1509 (m, NH) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.01, 2.04, 2.09, 2.15, 2.19 (18H, 5 × s, 6 × $OCOCH_3$), 3.70 (1H, ddd, $J_{4b,5b} = 9.7$ Hz, $J_{5b,6b} = 2.6$ Hz, $J_{5b,6'b} = 5.3$ Hz, H-5b), 3.78 (3H, s, OCH_3), 3.96 (1H, ddd, $J_{4a,5a} = 10.0$ Hz, $J_{5a,6a} = 4.5$ Hz, $J_{5a,6'a} = 2.4$ Hz, H-5a), 4.04 (1H, at, $J = 9.5$ Hz, H-4a), 4.19 (1H, dd, $J_{6b,6'b} = 12.2$ Hz, H-6b), 4.36 (1H, dd,

$J_{6a,6'a}$ = 12.0 Hz, H-6a), 4.38 (1H, dd, H-6′b), 4.48 (1H, dd, H-6′a), 4.52 (1H, dd, $J_{1a,2a}$ = 8.5 Hz, $J_{2a,3a}$ = 10.7 Hz, H-2a), 4.77 (1H, s, H-1b), 5.09 (1H, dd, $J_{2b,3b}$ = 3.3 Hz, $J_{3b,4b}$ = 9.9 Hz, H-3b), 5.25 (1H, at, J = 9.9 Hz, H-4b), 5.47 (1H, br d, J = 3.2 Hz, H-2b), 5.86 (1H, d, H-1a), 5.91 (1H, dd, $J_{3a,4a}$ = 8.9 Hz, H-3a), 6.77–6.79 (2H, m, 2 × Ar-H), 6.87–6.89 (2H, m, 2 × Ar-H), 7.77–7.81 (2H, m, 2 × Ar-H), 7.90 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.5, 20.5, 20.6, 20.7, 20.7, 20.8 (6 × q, 6 × OCO*C*H$_3$), 54.6 (d, C-2a), 55.6 (q, OCH$_3$), 62.3 (t, C-6b), 62.4 (t, C-6a), 65.8 (d, C-4b), 68.2 (d, C-2b), 69.9 (d, C-3a), 70.7 (d, C-3b), 72.5 (d, C-5b), 72.6 (d, C-5a), 75.4 (d, C-4a), 97.4, 97.4 (2 × s, C-1a, C-1b), 114.4, 118.8, 123.7 (3 × d, 6 × Ar-C), 131.3 (s, 2 × Ar-C), 134.3 (d, 2 × Ar-C), 150.5, 155.7 (2 × s, 2 × Ar-C), 169.6, 169.9, 170.0, 170.3, 170.4, 170.5 (6 × s, 8 × C=O); $J_{C\text{-}1a/H\text{-}1a}$ = 168 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ = 160 Hz (β); m/z (ES$^+$) 852.27 ([M+Na]$^+$, 100%); ESIMS m/z calcd for $C_{39}H_{43}NO_{19}$Na [M+Na]$^+$: 852.2321. Found 852.2326. Anal. Calcd for $C_{39}H_{43}NO_{19}$: C, 56.45; N, 1.69; H, 5.22. Found: C, 56.28; N, 1.81; H, 5.30.

4.12. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside (14)

Phthalimide **13** (448 mg, 0.540 mmol) was dissolved in a mixture of MeOH (20 mL) and ethylenediamine (14.4 mL, 216 mmol), and the solution was heated at reflux at 65 °C. After 2 days, the reaction mixture was concentrated in vacuo, and the residue dissolved in pyridine (15 mL). The solution was cooled to 0 °C, Ac_2O (10 mL) added and the reaction mixture stirred and allowed to warm to rt. After 3 days, TLC (EtOAc) indicated the formation of a major product (R_f = 0.05) and complete consumption of starting material (R_f = 0.35). The reaction mixture was poured onto ice/water (100 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The organic layers were washed with aqueous hydrochloric acid (2 × 50 mL of a 1 M solution), aqueous sodium hydrogen carbonate (2 × 50 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford acetamide **14** (375 mg, 94%) as a white amorphous solid; $[\alpha]_D^{23}$ −48 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3382 (br, NH), 1749, 1675 (s, C=O), 1509 (m, NH) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99, 2.00, 2.06, 2.11, 2.13, 2.16 (21H, 6 × s, 7 × COC*H*$_3$), 3.65 (1H, ddd, $J_{4b,5b}$ = 9.7 Hz, $J_{5b,6b}$ = 2.6 Hz, $J_{5b,6'b}$ = 5.3 Hz, H-5b), 3.73–3.79 (1H, m, H-5a), 3.77 (3H, s, OCH$_3$), 3.91 (1H, at, J = 8.9 Hz, H-4a), 4.11–4.23 (2H, m, H-2a, H-6b), 4.26 (1H, dd, $J_{5a,6a}$ = 4.9 Hz, $J_{6a,6'a}$ = 12.2 Hz, H-6a), 4.34 (1H, dd, $J_{6b,6'b}$ = 12.3 Hz, H-6′b), 4.40 (1H, dd, $J_{5a,6'a}$ = 3.0 Hz, H-6′a), 4.72 (1H, s, H-1b), 4.97 (1H, d, $J_{1a,2a}$ = 7.8 Hz, H-1a), 5.04 (1H, dd, $J_{2b,3b}$ = 3.3 Hz, $J_{3b,4b}$ = 9.9 Hz, H-3b), 5.21 (1H, at, J = 9.8 Hz, H-4b), 5.22 (1H, dd, $J_{2a,3a}$ = 9.9 Hz, $J_{3a,4a}$ = 8.8 Hz, H-3a), 5.42 (1H, br d, J = 3.3 Hz, H-2b), 5.56 (1H, d, $J_{2a,NH}$ = 9.1 Hz, NH), 6.79–6.81 (2H, m, 2 × Ar-H), 6.92–6.94 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.5, 20.6, 20.7, 20.7, 20.7, 23.3 (6 × q, 7 × CO*C*H$_3$), 53.8 (d, C-2a), 55.6 (q, OCH$_3$), 62.3 (t, C-6b), 62.5 (t, C-6a), 65.8 (d, C-4b), 68.3 (d, C-2b), 70.7 (d, C-3b), 71.7 (d, C-3a), 72.5 (d, C-5a), 72.6 (d, C-5b), 74.7 (d, C-4a), 97.6 (d, C-1b), 100.2 (d, C-1a), 114.5, 118.3 (2 × d, 4 × Ar-C), 151.0, 155.5 (2 × s, 2 × Ar-C), 169.6, 169.9, 170.1, 170.3, 170.4, 170.5, 170.8 (7 × s, 7 × C=O); $J_{C\text{-}1a/H\text{-}1a}$ = 168 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ = 163 Hz (β); m/z (ES$^+$) 800 ([M + MeCN/NH$_4^+$], 100%); ESIMS m/z calcd for $C_{33}H_{43}NO_{18}$Na [M+Na]$^+$: 764.2372. Found 764.2386. Anal. Calcd for $C_{33}H_{43}NO_{18}$: C, 53.44; N, 1.89; H, 5.84. Found: C, 53.15; N, 1.90; H, 5.98.

4.13. 2-Methyl-[α-D-mannopyranosyl-(1→4)-1,2-dideoxy-α-D-glucopyrano]-[2,1-*d*]-oxazoline (16)

PMP protected disaccharide **14** (50 mg, 67.4 μmol) was dissolved in chloroform (10 mL) and acetyl bromide (49.8 μL, 674 μmol), $BF_3{\cdot}OEt_2$ (25.6 μL, 202 μmol) and zinc(II) iodide (1.00 mg, 3.13 μmol) were added. The reaction mixture was stirred and heated to 50 °C. After 4.5 h, TLC (EtOAc) indicated the formation of a major product (R_f = 0.4) and complete consumption of starting material (R_f = 0.45). The reaction mixture was allowed to cool to rt and CH_2Cl_2 (20 mL) was then added. The organic layer was washed with aqueous sodium hydrogen carbonate (10 mL of a saturated solution) and aqueous sodium thiosulfate (0.5 mL of a 5% w/v solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford protected oxazoline **15** (27.0 mg, 65%) as a white amorphous solid; m/z (ES$^+$) 618 ([M+H]$^+$, 100%); ESIMS calcd for $C_{26}H_{35}NO_{16}$Na$^+$ [M+Na]$^+$: 640.1848. Found 640.1853.

A portion of the acetylated oxazoline **15** (16.0 mg, 25.9 μmol) was dissolved in dry MeOH (2 mL). NaOMe in MeOH (100 μL of a 5 mg/mL solution, 21.7 μmol) was added and the solution stirred at rt, under an atmosphere of argon. After 16 h, mass spectrometry indicated one product. The solution was concentrated in vacuo to yield deprotected disaccharide oxazoline **16**[9] (10.6 mg, quant.) as a white amorphous solid; ^{1}H NMR (500 MHz, D_2O): δ 2.01 (3H, d, J_{2a,CH_3} = 1.7 Hz, CH_3), 3.32 (1H, ddd, $J_{4b,5b}$ = 9.3 Hz, $J_{5b,6b}$ = 6.6 Hz, $J_{5b,6'b}$ = 2.2 Hz, H-5b), 3.36 (1H, ddd, $J_{4a,5a}$ = 8.7 Hz, $J_{5a,6a}$ = 6.1 Hz, $J_{5a,6'a}$ = 2.4 Hz, H-5a), 3.50 (1H, at, J = 9.6 Hz, H-4b), 3.57 (1H, dd, $J_{2b,3b}$ = 3.2 Hz, $J_{3b,4b}$ = 9.6 Hz, H-3b), 3.59 (1H, dd, $J_{6a,6'a}$ = 12.4 Hz, H-6a), 3.67–3.73 (3H, m, H-4a, H-6b, H-6′a), 3.88 (1H, dd, $J_{6b,6'b}$ = 12.2 Hz, H-6′b), 3.92 (1H, br d,

$J_{2b,3b} = 2.8$ Hz, H-2b), 4.13δ_H 4.14 (1H, m, H-2a), 4.32 (1H, m, H-3a), 4.66 (1H, br s, H-1b), 6.03 (1H, d, $J_{1a,2a} = 7.3$ Hz, H-1a).

4.14. Ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (18)

Thioglycoside **7** (2.21 g, 7.07 mmol) and 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate **17**[19] (5.41 g, 8.49 mmol) were dissolved in dry CH_2Cl_2 (125 mL) and transferred via canula to a flame-dried round-bottomed flask containing activated 4 Å molecular sieves (2.00 g). The solution was cooled to −60 °C and stirred under an atmosphere of argon. TMSOTf (77.0 μL, 420 μmol) was added and the temperature allowed to rise to 0 °C after 2 h. After 17.5 h, TLC (3:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.3$) and complete consumption of thioglycoside **7** ($R_f = 0$). Et_3N (200 μL) was added and the solution stirred for a further 10 min. The reaction mixture was then filtered through Celite, washed with aqueous sodium hydrogen carbonate (100 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was crystallised (petrol/EtOAc) to give disaccharide **18** (2.81 g, 51%) as white crystals, mp 131–132 °C; $[\alpha]_D^{18}$ −24 (*c* 0.55, $CHCl_3$); IR (KBr): 3374 (br, OH), 1745 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.32 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.12 (3H, s, OAc), 2.72–2.78 (2H, m, CH_2CH_3), 3.45–3.51 (1H, m, H-5a), 3.51 (1H, dd, $J_{1,2} = 9.6$ Hz, $J_{2,3} = 8.8$ Hz, H-2a), 3.66 (1H, at, $J = 9.6$ Hz, H-4a), 3.73 (1H, dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 10.9$ Hz, H-6b), 3.75–3.81 (2H, m, H-6a, H-6′b), 3.87–3.91 (2H, m, H-3a, H-4b), 4.03 (1H, dd, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.2$ Hz, H-3b), 4.25 (1H, ddd, $J_{4,5} = 9.9$ Hz, $J_{5,6} = 1.8$ Hz, $J_{5,6'} = 4.6$ Hz, H-5b), 4.38 (1H, dd, $J_{5,6'} = 4.9$ Hz, $J_{6,6'} = 10.5$ Hz, H-6′a), 4.42 (1H, d, $J_{1,2} = 9.9$ Hz, H-1a), 4.50, 4.86 (2H, ABq, $J = 10.8$ Hz, $PhCH_2$), 4.52, 4.89 (2H, ABq, $J = 11.4$ Hz, $PhCH_2$), 4.53, 4.72 (2H, ABq, $J = 10.8$ Hz, $PhCH_2$), 5.28 (1H, d, $J_{1,2} = 1.7$ Hz, H-1b), 5.55 (1H, dd, $J_{1,2} = 2.2$ Hz, $J_{2,3} = 3.5$ Hz, H-2b), 5.58 (1H, s, ArCH), 7.17–7.49 (20H, m, 20 × ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.1 (q, CH_2CH_3), 20.9 (q, OAc), 24.6 (t, CH_2CH_3), 68.4 (d, C-2b), 68.7 (d, C-6a, C-6b), 70.3 (d, C-5a), 71.5 (d, C-5b), 71.7 (t, $PhCH_2$), 72.0 (d, C-2a), 73.3 (t, $PhCH_2$), 74.3 (d, C-4b), 74.9 (t, $PhCH_2$), 77.9 (d, C-3b), 79.8 (d, C-3a), 80.5 (d, C-4a), 86.9 (d, C-1a), 98.6 (d, C-1b), 100.9 (d, PhCH), 125.8, 127.5, 127.6, 127.8, 127.9, 128.0, 128.2, 128.8 (8 × d, 20 × ArC), 136.8, 137.9, 138.1, 138.2 (4 × s, 4 × ArC), 169.9 (s, C=O); $J_{C\text{-}1b/H\text{-}1b} = 169$ Hz (α); *m*/*z* (ES^+) 845 ($[MMeCNNH_4]^+$, 100%); ESIMS *m*/*z* calcd for $C_{44}H_{54}NO_{11}S$ $[MNH_4]^+$: 804.3418. Found 804.3438.

4.15. Ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (19)

Alcohol **18** (400 mg, 510 μmol) was dissolved in dry CH_2Cl_2 (15 mL). Levulinic acid (100 μL, 980 μmol), DCC (202 mg, 980 μmol) and DMAP (6.00 mg, 49.0 μmol) were added, and the solution stirred at rt. After 20 h, although TLC (3:1, petrol/EtOAc) indicated no change in R_f (0.3) mass spectrometric analysis revealed complete conversion to the desired product. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with aqueous sodium hydrogen carbonate (2 × 10 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (3:1, petrol/EtOAc) to give levulinic ester **19** (449 mg, quant.) as a white foam; $[\alpha]_D^{23}$ −35 (*c* 1.0, $CHCl_3$); IR (KBr): 1746, 1719 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.27 (3H, t, $J = 7.4$ Hz, CH_2CH_3), 1.91 (3H, s, $COCH_3$Lev), 2.10 (3H, s, OAc), 2.34–2.75 (6H, m, 3 × CH_2), 3.50 (1H, dat, $J_{5,6'} = 4.9$ Hz, $J = 9.6$ Hz, H-5a), 3.71–3.80 (5H, m, H-4a, H-5b, H-6a, H-6b, H-6′b), 3.83 (1H, at, $J = 9.1$ Hz, H-4b), 3.87 (1H, dd, $J_{2,3} = 3.2$ Hz, $J_{3,4} = 8.8$ Hz, H-3b), 4.10 (1H, at, $J = 9.4$ Hz, H-3a), 4.38 (1H, dd, $J_{5,6'} = 5.3$ Hz, $J_{6,6'} = 10.4$ Hz, H-6′a), 4.42, 4.82 (2H, ABq, $J = 10.9$ Hz, $PhCH_2$), 4.48 (1H, d, $J_{1,2} = 10.0$ Hz, H-1a), 4.49, 4.67 (2H, ABq, $J = 10.9$ Hz, $PhCH_2$), 4.53, 4.68 (2H, ABq, $J = 12.1$ Hz, $PhCH_2$), 5.03 (1H, dd, $J_{1,2} = 10.2$ Hz, $J_{2,3} = 9.3$ Hz, H-2a), 5.41 (1H, d, $J_{1,2} = 1.8$ Hz, H-1b), 5.47 (1H, dd, $J_{1,2} = 1.8$ Hz, $J_{2,3} = 3.3$ Hz, H-2b), 5.58 (1H, s, ArCH), 7.09–7.46 (20H, m, 20 × ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.7 (q, CH_2CH_3), 20.9 (q, OAc), 24.1, 27.8, 37.4 (3 × t, 3 × CH_2), 29.4 (q, $COCH_3$), 67.9 (d, C-2b), 68.4 (t, C-6a), 68.7 (t, C-6b), 70.2 (d, C-2a), 70.3 (d, C-5a), 71.6 (t, $PhCH_2$), 71.7, 81.5 (2 × d, C-4a, C-5b), 73.3 (t, $PhCH_2$), 73.8 (d, C-4b), 74.7 (d, C-3a), 74.9 (t, $PhCH_2$), 77.8 (d, C-3b), 84.2 (d, C-1a), 97.3 (d, C-1b), 101.1 (d, ArCH), 125.9, 127.4, 127.6, 127.7, 128.1, 128.2, 128.3, 128.9 (8 × d, 20 × ArC), 136.6, 137.8, 138.1, 138.5 (4 × s, 4 × ArC), 170.0, 171.4, 205.9 (3 × s, 3 × C=O); *m*/*z* (ES^+) 943 ($[MMeCNNH_4]^+$, 100%); ESIMS *m*/*z* calcd for $C_{49}H_{60}NO_{13}S$ $[MNH_4]^+$: 902.3785. Found 902.3788.

4.16. *p*-Methoxyphenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-levulinoyl-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (20)

Thioglycoside **19** (2.18 g, 2.46 mmol) and alcohol 1 (1.33 g, 2.23 mmol) were dissolved in dry CH_2Cl_2 (100 mL) and transferred via canula to a flame-dried round-bottomed flask containing activated 4 Å molecular sieves (2.00 g). The solution was cooled to 0 °C.

Methyl triflate (1.26 mL) was added and the solution stirred at 0 °C under an atmosphere of argon. After 2 h, the solution was allowed to warm to rt. After a further 20 h, TLC (3:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.3$) and complete consumption of alcohol ($R_f = 0.25$). Et_3N (3 mL) was added and the reaction mixture stirred for a further 10 min. The reaction mixture was then filtered through Celite and concentrated in vacuo. The residue was purified by flash column chromatography (3:2, petrol/EtOAc) to give trisaccharide **20** (2.43 g, 77%) as a clear oil; $[\alpha]_D^{23}$ +10 (*c* 1.0, $CHCl_3$); IR (KBr disc) 1748, 1717 (s, C=O), 1508 (m, NH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.96 (3H, s, $CH_2C(O)CH_3$), 2.09 (3H, s, $OC(O)CH_3$), 2.22–2.30 (1H, m, CH_2CHH'), 2.43–2.60 (2H, m, CH_2CHH'), 2.67–2.75 (1H, m, CH_2CHH'), 3.12 (1H, dat, $J = 5.1$ Hz, $J = 9.7$ Hz, $J = 9.7$ Hz, H-5b), 3.44 (1H, at, $J = 10.3$ Hz, H-6b), 3.63 (1H, at, $J = 9.3$ Hz, H-4b), 3.68–3.74 (3H, m, H-5a, H-5c, H-6c), 3.72 (3H, s, $PhOCH_3$), 3.78 (1H, dd, $J_{5c,6'c} = 4.4$ Hz, $J_{6c,6'c} = 10.7$ Hz, H-6′c), 3.83–3.85 (3H, m, H-3c, H-4c, H-6a), 3.90 (1H, at, $J = 9.4$ Hz, H-3b), 3.93 (1H, dd, $J_{5a,6'a} = 3.3$ Hz, $J_{6a,6'a} = 11.3$ Hz, H-6′a), 4.16 (1H, at, $J = 9.2$ Hz, H-4a), 4.25 (1H, dd, $J_{5b,6'b} = 4.9$ Hz, $J_{6b,6'b} = 10.6$ Hz, H-6′b), 4.29 (1H, dd, $J = 8.5$ Hz, $J = 10.7$ Hz, H-3a), 4.37–4.42 (1H, m, H-2a), 4.40, 4.78 (2H, ABq, $J = 10.7$ Hz, $PhCH_2$), 4.41, 4.82 (2H, ABq, $J = 11.3$ Hz, $PhCH_2$), 4.42, 4.78 (2H, ABq, $J = 11.8$ Hz, $PhCH_2$), 4.45, 4.65 (2H, ABq, $J = 10.9$ Hz, $PhCH_2$), 4.53, 4.69 (2H, ABq, $J = 12.2$ Hz, $PhCH_2$), 4.58 (1H, d, $J_{1b,2b} = 8.2$ Hz, H-1b), 4.97 (1H, dd, $J_{2b,3b} = 9.4$ Hz, H-2b), 5.38 (1H, d, $J_{1c,2c} = 1.8$ Hz, H-1c), 5.44–5.45 (1H, m, H-2c), 5.45 (1H, s, PhCH), 5.62 (1H, d, $J_{1a,2a} = 8.3$ Hz, H-1a), 6.68–6.72 (2H, m, 2 × Ar-H), 6.80–6.83 (2H, m, 2 × Ar-H), 6.88–6.93 (3H, m, 3 × Ar-H), 7.07–7.10 (2H, m, 2 × Ar-H), 7.25–7.43 (23H, m, 23 × Ar-H), 7.56–7.85 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 21.1 (q, $CH_2C(O)CH_3$), 27.7 (t, CH_2CHH'), 29.7 (q, $OC(O)CH_3$), 37.4 (t, CH_2CHH'), 55.3 (d, C-2a), 55.6 (q, $PhOCH_3$), 65.5 (d, C-5b), 67.7 (t, C-6a), 68.0 (d, C-2c), 68.5 (t, C-6b), 68.8 (t, C-6c), 71.7 (t, $PhCH_2$), 71.8 (d, C-5a), 72.5 (d, C-2b), 73.6 (t, 2 × $PhCH_2$), 73.9 (d, C-4c), 73.9 (d, C-3b), 74.8 (t, $PhCH_2$), 74.9 (d, C-5c), 75.1 (t, $PhCH_2$), 76.7 (d, C-3a), 77.9 (d, C-4a), 78.0 (d, C-3c), 81.7 (d, C-4b), 97.3 (d, C-1c), 97.5 (d, C-1a), 100.5 (d, C-1b), 101.2 (d, PhCH), 114.4, 118.7, 123.4, 126.1, 127.2, 127.5, 127.6, 127.8, 127.8, 127.9, 128.0, 128.0, 128.1, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 128.6, 128.6, 129.1, 129.8, 133.8 (24 × d, 38 × Ar-C), 136.9, 137.9, 138.1, 138.5, 138.6, 150.9, 155.3 (7 × s, 10 × Ar-C), 167.6, 168.2, 170.2, 171.3, 206.3 (5 × s, 5 × C=O); $J_{C\text{-}1a/H\text{-}1a} = 169$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 168$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 180$ Hz (α); *m*/*z* (ESI^+) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks observed: 1435.6 (100%), 1436.6 (92%), 1437.6 (45%), 1438.6 (12%), peaks calculated: 1435.6 (100%), 1436.6 (90%), 1437.6 (50%), 1438.6 (20%). Anal. Calcd for $C_{82}H_{83}NO_{21}$: C, 69.43; N, 0.99; H, 5.90. Found: C, 69.36; N, 0.96; H, 5.93.

4.17. *p*-Methoxyphenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (21)

Ester **20** (7.70 g, 5.43 mmol) was dissolved in MeOH (250 mL) and CH_2Cl_2 (100 mL). Hydrazine acetate (978 mg, 10.86 mmol) was added and the solution stirred at rt. After 24 h, TLC (6:1, toluene/EtOAc) indicated the formation of a major product ($R_f = 0.25$) and complete consumption of starting material ($R_f = 0.3$). The reaction mixture was concentrated in vacuo, and the residue extracted with CH_2Cl_2 (100 mL), washed with water (3 × 20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (6:1, toluene/EtOAc) to give alcohol **21** (6.40 g, 89%) as a white foam; $[\alpha]_D^{23}$ +34 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3459 (br, OH), 1777, 1745, 1716 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.16 (3H, s, $OC(O)CH_3$), 3.21 (1H, dat, $J = 5.0$ Hz, $J = 9.6$ Hz, $J = 9.6$ Hz, H-5b), 3.45 (1H, at, $J = 8.3$ Hz, H-2b), 3.53–3.62 (3H, m, H-4b, H-6b, OH), 3.70–3.72 (1H, m, H-5a), 3.75–3.79 (2H, m, H-3b, H-6c), 3.76 (3H, s, $PhOCH_3$), 3.82 (1H, dd, $J_{5c,6'c} = 4.7$ Hz, $J_{6c,6'c} = 10.7$ Hz, H-6′c), 3.86–3.88 (1H, m, H-6a), 3.92 (1H, at, $J = 9.8$ Hz, H-4c), 4.04–4.08 (2H, m, H-3c, H-6′a), 4.18–4.25 (3H, m, H-4a, H-5c, H-6′b), 4.45–4.46 (2H, m, H-2a, H-3a), 4.48, 4.85 (2H, ABq, $J = 12.2$ Hz, $PhCH_2$), 4.52–4.57 (3H, m, 3 × PhCH), 4.57, 4.75 (2H, ABq, $J = 11.3$ Hz, $PhCH_2$), 4.64 (1H, m, H-1b), 4.74 (1H, d, $J = 11.9$ Hz, PhCH), 4.75 (1H, d, $J = 11.9$ Hz, PhCH), 4.91 (1H, d, $J = 10.4$ Hz, PhCH), 5.27 (1H, s, H-1c), 5.51 (1H, s, PhCH), 5.57 (1H, br s, H-2c), 5.64 (1H, d, $J_{1a,2a} = 7.9$ Hz, H-1a), 6.74–6.76 (2H, m, 2 × Ar-H), 6.85–6.87 (2H, m, 2 × Ar-H), 6.91–7.00 (3H, m, 3 × Ar-H), 7.06–7.10 (2H, m, 2 × Ar-H), 7.20–7.49 (25H, m, 25 × Ar-H), 7.73–7.80 (4H, m, 4 × Ar-H); IR (125.8 MHz, $CDCl_3$): δ 21.1 (q, $OC(O)CH_3$), 55.6 (q, $PhOCH_3$), 55.7 (d, C-2a), 65.9 (d, C-5b), 68.2 (t, C-6a), 68.6 (d, C-2c), 68.6 (t, C-6c), 68.9 (t, C-6b), 71.6 (d, C-5c), 71.8, 73.5, 73.7 (3 × t, 3 × $PhCH_2$), 74.2 (d, C-2b), 74.4 (d, C-4c), 74.8 (t, $PhCH_2$), 74.9 (d, C-5a), 75.1 (t, $PhCH_2$), 78.0 (d, C-3a), 78.1 (d, C-3c), 78.8 (d, C-4a), 79.6 (d, C-3b), 80.6 (d, C-4b), 97.8 (d, C-1a), 98.8 (d, C-1c), 101.0 (d, PhCH), 103.8 (d, C-1b), 114.4, 118.8, 126.0, 127.3, 127.5, 127.7, 127.8, 128.0, 128.0, 128.0, 128.1, 128.1, 128.2, 128.3, 128.4, 128.4, 128.5, 128.9, 129.1, 133.9 (20 × d, 38 × Ar-C), 137.7, 137.9, 138.0, 138.1, 138.3, 138.4, 148.9, 150.9 (8 × s, 10 × Ar-C), 168.7, 170.2 (2 × s, 3 × C=O); $J_{C\text{-}1a/H\text{-}1a} =$

167 Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 164$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 177$ Hz (α); *m/z* (ESI^+) species observed $[M+NH_4]^+$ (major); $[M+NH_4]^+$ peaks observed: 1337.3 (100%), 1338.3 (80%), 1339.3 (12%), peaks calculated: 1337.5 (100%), 1338.6 (85%), 1339.6 (45%). Anal. Calcd for $C_{77}H_{77}NO_{19}$: C, 70.04; N, 1.06; H, 5.88. Found: C, 69.65; N, 1.04; H, 5.97.

4.18. *p*-Methoxyphenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2-*O*-acetyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (22)

Alcohol **21** (128 mg, 97.0 μmol) was dissolved in dry CH_2Cl_2 (5 mL) and the solution cooled to 0 °C. Pyridine (150 μL, 1.80 mmol) and triflic anhydride (120 μL, 720 μmol) were added and the reaction mixture was allowed to stir and warm to rt. After 2.5 h, TLC (3:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.35$) and complete consumption of starting material ($R_f = 0.3$). The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with aqueous sodium hydrogen carbonate (50 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was dissolved in dry toluene (5 mL), and Bu_4NOAc (208 mg, 690 μmol) was added. The suspension was subjected to sonication at rt, under an atmosphere of argon. After 14 h, TLC (3:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.30$) and complete consumption of the intermediate material ($R_f = 0.35$). The mixture was concentrated in vacuo solution and the residue purified by flash column chromatography (3:2, petrol/EtOAc) to give *manno* acetate **22** (118 mg, 90%) as a white foam; $[\alpha]_D^{23}$ +20 (*c* 1.0, $CHCl_3$); IR (KBr disc): 1749, 1716 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.10, 2.15 (6H, 2 × s, 2 × OC(O)CH_3), 3.12–3.15 (1H, m, H-5b), 3.60 (1H, at, $J = 10.0$ Hz, H-6b), 3.64–3.66 (1H, m, H-5a), 3.72–3.78 (3H, m, H-6a, H-6c, H-6′c), 3.76 (3H, s, $PhOCH_3$), 3.81–3.83 (1H, m, H-6′a), 3.85–3.94 (5H, m, H-3b, H-3c, H-4b, H-4c, H-5c), 4.17–4.25 (2H, m, H-4a, H-6′b), 4.34 (1H, at, $J = 9.8$ Hz, H-3a), 4.42–4.46 (1H, m, H-2a), 4.45–4.56 (5H, m, 5 × PhCH), 4.69–4.77 (4H, m, H-1b, 3 × PhCH), 4.87–4.92 (2H, m, 2 × PhCH), 5.28 (1H, s, H-1c), 5.42 (1H, s, H-2b), 5.52 (1H, s, H-2c), 5.55 (1H, s, PhCH), 5.63 (1H, d, $J_{1a,2a} = 7.9$ Hz, H-1a), 6.74–6.76 (2H, m, 2 × Ar-H), 6.81–6.86 (2H, m, 2 × Ar-H), 6.94–7.00 (3H, m, 3 × Ar-H), 7.06–7.10 (2H, m, 2 × Ar-H), 7.24–7.26 (2H, m, 2 × Ar-H), 7.32–7.52 (23H, m, 23 × Ar-H), 7.69–7.86 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.9, 21.1 (2 × q, 2 × OC(O)CH_3), 55.6 (d, C-2a), 55.6 ($PhOCH_3$), 66.5 (d, C-5b), 68.0 (t, C-6c), 68.4 (t, C-6b), 68.5 (d, C-2c), 68.9 (t, C-6a), 70.7 (d, C-2b), 71.8 (t, $PhCH_2$), 72.1 (d, C-5c), 72.7 (d, C-4c), 73.5, 73.5 (2 × t, 2 × $PhCH_2$), 74.1 (d, C-4b), 74.7 (t, $PhCH_2$), 74.7 (d, C-5a), 74.8 (t, $PhCH_2$), 76.8 (d, C-3a), 77.6 (d, C-3c), 78.6 (d, C-4a), 78.7 (d, C-3b), 97.7 (d, C-1a), 98.7 (d, C-1c), 99.2 (d, C-1b), 101.2 (d, PhCH), 114.4, 118.7, 126.0, 127.3, 127.5, 127.7, 127.7, 127.8, 127.8, 127.9, 128.0, 128.0, 128.1, 128.1, 128.2, 128.3, 128.4, 128.4, 128.7, 128.9 (20 × d, 38 × Ar-C), 137.1, 137.9, 138.0, 138.2, 138.5, 138.6, 150.8, 155.4 (8 × s, 10 × Ar-C), 169.8, 170.2 (2 × s, 4 × C=O); $J_{C\text{-}1a/H\text{-}1a} = 167$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 164$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 177$ Hz (α); *m/z* (ESI^+) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks observed: 1379.5 (100%), 1380.5 (80%), 1381.5 (30%), peaks calculated: 1379.6 (100%), 1380.6 (90%), 1381.5 (45%). Anal. Calcd for $C_{79}H_{79}NO_{20}$: C, 69.64; N, 1.03; H, 5.84. Found: C, 69.45; N, 1.03; H, 5.85.

4.19. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (23)

Benzyl protected trisaccharide **22** (300 mg, 220 μmol) was added to a dry two-necked flask and dissolved in EtOAc (10 mL) and MeOH (10 mL). Palladium (10% on carbon, 100 mg) was added. The flask was flushed with argon (three times) followed by hydrogen (three times), and the mixture was then stirred under an atmosphere of hydrogen at rt. After 18 h, TLC (1:9, MeOH/EtOAc) indicated the formation of a major product ($R_f = 0.15$) and complete consumption of starting material ($R_f = 0.9$). The reaction mixture was poured onto Celite, washed with MeOH (3 × 20 mL), filtered and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL) and pyridine (3 mL) was added. The solution was cooled to 0 °C, Ac_2O (2 mL) added and the reaction mixture stirred and allowed to warm to rt. After 1 day, TLC (1:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.25$) and complete consumption of intermediate material ($R_f = 0$). The reaction mixture was poured onto ice/water (20 mL), extracted with CH_2Cl_2 (2 × 10 mL), the organic layers combined and washed with aqueous sodium hydrogen carbonate (20 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:2, petrol/EtOAc) to give acetylated trisaccharide **23** (214 mg, 87%) as a pale yellow foam; $[\alpha]_D^{23}$ +1 (*c* 0.5, $CHCl_3$); IR (KBr disc): 1749 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.00, 2.04, 2.10, 2.15, 2.17, 2.19, 2.19, 2.24 (27H, 8 × s, 9 × $OCOCH_3$), 3.59 (1H, ddd, $J_{4b,5b} = 9.6$ Hz, $J = 3.0$ Hz, $J = 5.6$ Hz, H-5b), 3.78 (3H, s, OCH_3), 3.91 (1H, dd, $J_{2b,3b} = 3.4$ Hz, $J_{3b,4b} = 9.7$ Hz, H-3b), 3.96 (1H, ddd, $J_{4a,5a} = 10.1$ Hz, $J_{5a,6a} = 2.1$ Hz, $J_{5a,6'a} = 4.2$ Hz, H-5a), 4.00 (1H, at, $J = 9.1$ Hz, H-4a), 4.12 (1H, dat, $J_{4c,5c} = 9.9$ Hz, *J* 3.1 Hz, H-5c), 4.15–4.22 (2H, m, H-6b, H-6c), 4.31–4.36 (2H, m, H-6′b, H-6′c), 4.43 (1H, dd, $J_{6a,6'a} = 12.0$ Hz, H-6a),

4.49 (1H, dd, H-6′a), 4.52 (1H, dd, $J_{1a,2a} = 8.5$ Hz, $J_{2a,3a} = 10.8$ Hz, H-2a), 4.68 (1H, s, H-1b), 5.03 (2H, br s, H-1c, H-2c), 5.22 (1H, dd, $J_{2c,3c} = 2.7$ Hz, $J_{3c,4c} = 10.1$ Hz, H-3c), 5.24 (1H, at, $J = 9.7$ Hz, H-4b), 5.36 (1H, at, $J = 10.1$ Hz, H-4c), 5.47 (1H, br d, $J = 3.2$ Hz, H-2b), 5.86 (1H, d, H-1a), 5.91 (1H, dd, $J_{3a,4a} = 8.5$ Hz, H-3a), 6.77–6.79 (2H, m, 2 × Ar-H), 6.87–6.89 (2H, m, 2 × Ar-H), 7.78–7.81 (2H, m, 2 × Ar-H), 7.91 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.5, 20.6, 20.6, 20.7, 20.7, 20.7, 20.8 (7 × q, 9 × OCO*C*H$_3$), 54.6 (d, C-2a), 55.6 (t, OCH$_3$), 62.1 (t, C-6c), 62.2 (t, C-6a), 62.4 (t, C-6b), 65.6 (d, C-4c), 67.7 (d, C-4b), 68.2 (d, C-3c), 69.3 (d, C-5c), 69.5 (d, C-2b), 69.6 (d, C-3a), 69.9 (d, C-2c), 72.4 (d, C-5b), 72.7 (d, C-5a), 75.5 (d, C-4a), 76.3 (d, C-3b), 97.4 (d, C-1a), 97.5 (d, C-1b), 98.9 (d, C-1c), 114.4, 118.8, 123.7 (3 × d, 6 × Ar-C), 131.3 (s, 2 × Ar-C), 134.4 (d, 2 × Ar-C), 150.5, 155.7 (2 × s, 2 × Ar-C), 169.5, 169.8, 169.8, 170.0, 170.1, 170.5, 170.6, 170.6 (8 × s, 11 × C═O); $J_{C\text{-}1a/H\text{-}1a} = 169$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 159$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 175$ Hz (α); *m*/*z* (ESI$^+$) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks observed: 1135.3 (100%), 1136.3 (33%), 1137.3 (7%), 1138.3 (2%), peaks calculated: 1135.4 (100%), 1136.4 (60%), 1137.4 (25%), 1138.4 (8%). Anal. Calcd for $C_{51}H_{59}NO_{27}$: C, 54.79; N, 1.25; H, 5.32. Found: C, 54.87; N, 1.22; H, 5.32.

4.20. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-β-D-mannopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside (24)

Phthalimide **23** (199 mg, 178 μmol) was dissolved in MeOH (15 mL), ethylene diamine (4.76 mL, 71.2 mmol) added and the resulting solution was heated at reflux at 65 °C. After 1 day, TLC (1:2, petrol/EtOAc) indicated formation of a major product ($R_f = 0$) and complete consumption of starting material ($R_f = 0.25$). The reaction mixture was concentrated in vacuo, and the residue dissolved in pyridine (20 mL). The solution was cooled to 0 °C, Ac_2O (15 mL) added and the reaction mixture stirred and allowed to warm to rt. After 5 days, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.4$) and complete consumption of starting material ($R_f = 0.8$). The reaction mixture was poured onto ice/water (20 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The organic layers were washed with aqueous hydrochloric acid (20 mL of a 1 M solution), aqueous sodium hydrogen carbonate (2 × 15 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (2:1, petrol/EtOAc) to afford acetamide **24** (160 mg, 87%) as a pale yellow foam; $[\alpha]_D^{22}$ −33 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3386 (br, NH), 1749 (s, C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.03, 2.04, 2.10, 2.14, 2.15, 2.17, 2.18, 2.19, 2.25 (30H, 9 × s, 10 × OCOCH_3), 3.60 (1H, m, H-5b), 3.80 (1H, m, H-5a), 3.82 (3H, s, OCH_3), 3.91 (1H, at, $J = 9.0$ Hz, H-4a), 3.93 (1H, dd, $J_{2b,3b} = 3.5$ Hz, $J_{3b,4b} = 9.5$ Hz, H-3b), 4.11 (1H, dat, $J = 3.1$ Hz, $J = 3.1$ Hz, $J = 9.9$ Hz, H-5c), 4.15–4.22 (3H, m, H-2a, H-6b, H-6c), 4.32–4.36 (2H, m, H-6′b, H-6′c), 4.41 (2H, m, H-6a, H-6′a), 4.69 (1H, s, H-1b), 5.04 (2H, br s, H-1c, H-2c), 5.06 (1H, d, $J_{1a,2a} = 7.9$ Hz, H-1a), 5.21–5.27 (2H, m, H-3c, H-4b), 5.30 (1H, dd, $J_{2a,3a} = 9.9$ Hz, $J_{3a,4a} = 8.8$ Hz, H-3a), 5.37 (1H, at, $J = 10.1$ Hz, H-4c), 5.46 (1H, br d, $J = 3.0$ Hz, H-2b), 5.62 (1H, d, $J_{2a,NH} = 9.1$ Hz, NH), 6.84–6.86 (2H, m, 2 × Ar-H), 6.97–6.98 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.6, 20.7, 20.7, 20.7, 20.8, 20.8 (6 × q, 9 × OCO*C*H$_3$), 23.3 (q, NCO*C*H$_3$), 53.9 (d, C-2a), 55.6 (t, OCH$_3$), 62.1 (t, C-6c), 62.4 (t, C-6a), 62.4 (t, C-6b), 65.7 (d, C-4c), 67.6 (d, C-4b), 68.1 (d, C-3c), 69.3 (d, C-5c), 69.6 (d, C-2b), 69.9 (d, C-2c), 71.5 (d, C-3a), 72.5 (d, C-5b), 72.6 (d, C-5a), 74.8 (d, C-4a), 76.1 (d, C-3b), 97.7 (d, C-1b), 98.8 (d, C-1c), 100.0 (d, C-1a), 114.5, 118.3 (2 × d, 4 × Ar-C), 151.0, 155.5 (2 × s, 2 × Ar-C), 169.6, 169.8, 169.8, 170.0, 170.2, 170.5, 170.6, 170.6, 170.9 (9 × s, 10 × C═O); $J_{C\text{-}1a/H\text{-}1a} = 163$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 158$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 175$ Hz (α); *m*/*z* (ESI$^+$) species observed $[M+Na]^+$ (major); $[M+Na]^+$ peaks observed: 1052.3 (100%), 1053.3 (35%), 1054.3 (5%), peaks calculated: 1052.3 (100%), 1053.3 (55%), 1054.3 (20%).

4.21. 2-Methyl-[α-D-mannopyranosyl-(1→3)-β-D-mannopyranosyl-(1→4)-α-D-glucopyrano]-[2,1-*d*]-oxazoline (26)

PMP protected trisaccharide **24** (300 mg, 291 μmol) was dissolved in anhydrous chloroform (15 mL) and acetyl bromide (215 μL, 2.91 mmol), $BF_3{\cdot}OEt_2$ (111 μL, 873 μmol) and zinc(II) iodide (4.64 mg, 14.6 μmol) were added. The reaction mixture was stirred and heated to 50 °C. After 21 h, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.35$) and complete consumption of starting material ($R_f = 0.4$). The reaction mixture was allowed to cool to rt and dichloromethane (30 mL) was then added. The organic layer was washed with aqueous sodium hydrogen carbonate (20 mL of a saturated solution) and aqueous sodium thiosulfate (5 mL of a 5% w/v solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford protected oxazoline **25** (161 mg, 63%) as a pale yellow solid; *m*/*z* (ES$^+$) 928 ($[M+Na]^+$, 100%); ESIMS *m*/*z* calcd for $C_{38}H_{51}NO_{24}Na^+$ $[M+Na]^+$: 928.2699. Found 928.2721.

A portion of the acetylated oxazoline **25** (78.0 mg, 44.2 μmol) was dissolved in dry MeOH (3 mL). NaOMe in MeOH (100 μL of a 5 mg/mL solution, 21.7 μmol) was added and the solution stirred at rt under an atmosphere of argon. After 24 h, mass spectrometry indicated

the formation of a single product. The solution was concentrated in vacuo to yield deprotected trisaccharide oxazoline **26** (46.5 mg, quant.) as a pale yellow solid; IR (KBr disc): 3386 (br, OH), 1669 (s, C=N) cm^{-1}; ^1H NMR (500 MHz, D_2O): δ 2.00 (3H, d, $J_{2,CH_3} = 1.4$ Hz, CH_3), 3.33–3.37 (2H, m, H-5a, H-5b), 3.53–3.57 (2H, m, H-4c, H-6a), 3.60 (1H, at, $J = 9.8$ Hz, H-4b), 3.64–3.72 (6H, m, H-3b, H-4a, H-5c, H-6b, H-6c, H-6′a), 3.80–3.84 (2H, m, H-3c, H-6b/c), 3.87 (1H, dd, $J_{5b/c,6'b/c} = 1.8$ Hz, $J_{6b/c,6'b/c} = 12.2$ Hz, H-6′b/c), 3.98–3.99 (1H, m, H-2c), 4.06 (1H, br d, $J = 2.8$ Hz, H-2b), 4.11–4.12 (1H, m, H-2a), 4.30 (1H, br s, H-3a), 4.66 (1H, s, H-1b), 5.02 (1H, s, H-1c), 6.01 (1H, d, $J_{1a,2a} = 7.3$ Hz, H-1a); ^{13}C NMR (125.8 MHz, D_2O): δ 12.9 (q, CH_3), 61.0, 61.0 (2 × t, C-6b, C-6c), 61.7 (t, C-6a), 65.1 (d, C-2a), 66.0 (d, C-4b), 66.8 (d, C-4c), 69.1 (d, C-3a), 70.0 (d, C-2c), 70.2 (d, C-2b), 70.3 (d, C-3c), 71.0 (d, C-5a), 73.3 (d, C-5c), 76.2 (d, C-5b), 77.3 (d, C-4a), 80.3 (d, C-3b), 99.9 (d, C-1c), 101.0 (d, C-1b), 102.4 (d, C-1a), 168.6 (s, C=N); $J_{C\text{-}1a/H\text{-}1a} = 186$ Hz (α), $J_{C\text{-}1b/H\text{-}1b} = 162$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 179$ Hz (α); *m/z* (ES^-) 526 ($[M-H]^-$, 100%); ESIMS *m/z* calcd for $C_{20}H_{32}NO_{15}$ $[M-H]^-$: 526.1772. Found 526.1787.

4.22. Benzyl 2,4-di-*O*-benzoyl-α-D-mannopyranoside (28)

p-Toluenesulfonic acid (0.5 mL of a 5% solution in MeCN) was added to a stirred suspension of benzyl α-D-mannopyranoside **27**[22] (0.50 g, 1.75 mmol) and trimethylorthobenzoate (0.78 mL, 4.53 mmol) in dry acetonitrile (33 mL). After 15 min, the solvent was removed in vacuo, and the residue dissolved in dry acetonitrile (22 mL). Trifluoroacetic acid (0.61 mL of a 10% aqueous solution) was added, and the mixture stirred at rt. After 10 min, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.8$), the complete consumption of the starting material ($R_f = 0.0$), and the formation of a minor side product ($R_f = 0.4$). The mixture was concentrated in vacuo, and then purified by flash column chromatography (2:1, petrol/EtOAc) to afford dibenzoate **28** (0.38 g, 46%) as a white amorphous solid; $[\alpha]_D^{21}$ −16 (*c* 1.2, $CHCl_3$); IR (KBr): 3485 (br, OH), 1723 (s, C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (2H, br s, 2 × OH), 3.72–3.77 (2H, m, H-6, H-6′), 3.98 (1H, ddd, $J_{4,5} = 10.0$ Hz, $J_{5,6} = 2.8$ Hz, $J_{5,6'} = 3.0$ Hz, H-5), 4.50 (1H, ddd, $J_{2,3} = 3.6$ Hz, $J_{3,4} = 10.0$ Hz, $J_{3,OH} = 6.8$ Hz, H-3), 4.64, 4.79 (2H, ABq, $J = 11.8$ Hz, $PhCH_2$), 5.18 (1H, d, $J_{1,2} = 1.2$ Hz, H-1), 5.49 (1H, dd, H-2), 5.53 (1H, at, $J = 9.9$ Hz, H-4), 7.31–7.41, 7.43–7.51, 7.60–7.64, 8.07–8.12 (15H, 4 × m, 15 × Ar-H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 61.4 (t, C-6), 68.7 (d, C-3), 70.1 (d, C-4), 70.3 (t, $PhCH_2$), 70.8 (d, C-5), 73.0 (d, C-2), 97.1 (d, C-1), 128.0, 128.2, 128.6, 129.0, 129.2, 129.9 (6 × d, 15 × Ar-C), 133.6, 133.7, 136.6 (3 × s, 3 × Ar-C), 166.0, 167.3 (2 × s, 2 × C=O); *m/z* (ESI^+) 979 ($[2M+Na]^+$, 100%), 501.20 ($[M+Na]^+$, 75%); ESIMS *m/z* calcd for $C_{27}H_{26}O_8Na$ $[MNa]^+$: 501.1501. Found 501.1501.

4.23. Benzyl 2,4-di-*O*-benzoyl-3,6-di-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (30)

Dibenzoate **28** (139 mg, 0.29 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and transferred via canula into a dried flask containing activated 4 Å molecular sieves (ca. 0.5 g) under argon. Trichloroacetimidate **29**[23] (0.57 g, 1.16 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and added via canula to the flask. The mixture was stirred for 1 h and then $BF_3{\cdot}OEt_2$ (49.1 μL, 46 mmol) was added slowly, and the solution left to stir overnight. After 18 h, TLC (4:3, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.15$) and complete consumption of the starting material ($R_f = 0.45$). The reaction was quenched by addition of Et_3N (5 mL) and the mixture was then filtered through Celite. The residue was partitioned between water (10 mL) and CH_2Cl_2 (10 mL), and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with water (2 × 10 mL), sodium hydrogen carbonate (10 mL of a satd aqueous solution), brine (10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash column chromatography (1:1, petrol/EtOAc) to yield trisaccharide **30** (293 mg, 89%) as a white amorphous solid; $[\alpha]_D^{22}$ +24 (*c* 1.3, $CHCl_3$); IR (thin film): 1751 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.87, 1.90, 1.97, 2.00, 2.03, 2.08, 2.16, 2.18 (24H, 8 × s, 8 × C(O)CH_3), 3.64 (1H, br d, $J = 9.3$ Hz, H-6a), 3.97 (1H, dd, $J_{5,6'} = 7.0$ Hz, $J_{6,6'} = 10.6$ Hz, H-6′a), 4.02 (1H, dd, $J_{5,6} = 1.2$ Hz, $J_{6,6'} = 12.0$ Hz, H-6b), 4.08 (1H, br d, $J = 11.7$ Hz, H-6′b), 4.10–4.26 (4H, m, H-5a, H-5b, H-5c, H-6c), 4.33 (1H, dd, $J_{5,6} = 5.4$ Hz, $J_{6,6'} = 12.2$ Hz, H-6′c), 4.56 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.7$ Hz, H-3a), 4.67 (1H, d, $J = 11.7$ Hz, PhCH), 4.85–4.87 (2H, m, H-1c, PhCH), 4.91 (1H, br s, H-2b), 5.03 (1H, br s, H-1b), 5.12–5.14 (2H, m, H-3b, H-4b), 5.17 (1H, br s, H-1a), 5.31–5.33 (1H, m, H-2c), 5.38–5.39 (1H, m, H-4c), 5.45 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 10.1$ Hz, H-3c), 5.60 (1H, br d, $J = 1.4$ Hz, H-2a), 5.69 (1H, at, $J = 10.0$ Hz, H-4a), 7.32–7.69 (1H, m, Ar-H), 8.07–8.09 (4H, m, 4 × Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.5, 20.5, 20.7, 20.7, 20.7, 20.8, 20.8, 21.0, (8 × q, 8 × CH_3), 62.1 (t, C-6c), 62.3 (t, C-6b), 65.6 (d, C-4b), 66.8 (t, C-6a), 68.3 (d, C-3b), 68.7 (d, C-4c) 68.7 (d, C-5b), 68.8 (d, C-2a), 6.91 (d, C-3c), 69.3 (d, C-2b) 69.3 (d, C-2c), 69.4 (d, C-5a), 69.7 (t, $PhCH_2$), 69.7 (d, C-5c), 71.8 (d, C-2a), 75.5 (d, C-3), 96.5 (d, C-1a), 97.3 (d, C-1c), 99.5 (d, C-1b), 128.4, 128.6, 128.7, 128.8, 128.9, 129.2, (6 × d, 15 × Ar-C), 130.0, 130.1 (2 × s, 3 × Ar-C), 165.0, 165.4, 169.1, 169.2, 169.6, 169.7, 169.8, 170.0, 170.7, 170.8 (10 × s, 10 × C=O); *m/z* (ESI^+) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks

observed: 1156.4 (100%), 1157.4 (67%), peaks calculated: 1156.4 (100%), 1157.4 (64%).

4.24. 2,4-Di-*O*-benzoyl-3,6-di-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-mannopyranose (31)

Benzyl ether **30** (5.47 g, 4.8 mmol) was dissolved in EtOAc (200 mL). Palladium (10% on C, 1.82 g) was added and the mixture degassed and stirred under hydrogen at rt. After 24 h, TLC (2:1, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.25$) and complete consumption of starting material ($R_f = 0.55$). The reaction mixture was poured onto Celite, which was then washed with EtOH (5 × 100 mL). The combined organic extracts were concentrated in vacuo and the residue was purified by flash column chromatography (2:1, petrol/EtOAc) to yield trisaccharide **31** (3.80 g, 76%) as a white amorphous solid; IR (KBr): 3472 (br, OH), 1753 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.88, 1.91, 1.99, 2.03, 2.04, 2.10, 2.17, 2.18 (24H, 8 × s, 8 × OAc), 3.71 (1H, dd, $J_{5,6} = 1.5$ Hz, $J_{6,6'} = 11.1$ Hz, H-6a), 3.81 (1H, d, $J_{OH,1} = 2.7$ Hz, OH), 3.95 (1H, dd, $J_{5,6'} = 7.3$ Hz, H-6′a), 4.04 (1H, dd, $J_{5,6} = 1.5$ Hz, H-6c), 4.10–4.21 (4H, m, H-5b, H-6b, H-6′b, H-5c), 4.26 (1H, dd, $J_{5,6'} = 5.0$ Hz, H-6′c), 4.43 (1H, at, $J = 7.8$ Hz, H-5a), 4.62 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.7$ Hz, H-3a), 4.86 (1H, br s, H-1c), 4.94 (1H, br s, H-2b), 5.05 (1H, d, $J_{1,2} = 0.9$ Hz, H-1b), 5.15–5.18 (2H, m, H-3b, H-4b), 5.26–5.30 (2H, m, H-2c, H-4c), 5.41 (1H, dd, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 10.1$ Hz, H-3c), 5.51 (1H, br s, H-1a), 5.60 (1H, br d, $J = 1.1$ Hz, H-2a), 5.64 (1H, at, $J = 9.9$ Hz, H-4a), 7.49–7.69 (6H, m, 6 × Ar-H), 8.14 (4H, m, 4 × Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.5, 20.5, 20.7, 20.7, 20.7, 20.8, 20.9, 21.1 (8 × q, 8 × CH_3), 62.4 (t, C-6c), 62.4 (t, C-6b), 66.1 (d, C-4b), 66.3 (d, C-4c), 67.8 (t, C-6a), 68.4 (d, C-3b), 68.5 (d, C-5b), 69.0 (d, C-3c), 69.2 (d, C-4a), 69.3 (d, C-2b), 69.4 (d, C-5a), 69.5 (d, C-5c), 69.6 (d, C-2c), 72.1 (d, C-2a), 74.8 (d, C-3a), 92.2 (d, C-1a), 97.5 (d, C-1c), 99.5 (d, C-1b), 129.3, 128.6, 128.8, 130.0, 130.1 (5 × d, 5 × Ar-C), 133.6, 133.7 (2 × s, 2 × Ar-C), 165.4, 166.0, 169.1, 169.2, 169.8, 169.9, 170.0, 170.1, 170.8, 170.9 (10 × s, 10 × C=O); *m/z* (ESI^+) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks observed: 1066.3 (100%), 1067.3 (75%), peaks calculated: 1066.3 (100%), 1067.3 (55%). The β anomer was not detected by NMR spectroscopy.

4.25. 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-]-2,4-di-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (32)

Trisaccharide **31** (150 mg, 143 μmol) was dissolved in CH_2Cl_2 (5 mL). 1,1,1-Trichloroacetonitrile (143 μL, 1.43 mmol) was added, and the reaction mixture cooled to 0 °C. DBU (4 μL, 29.0 μmol) was added and the solution stirred and allowed to warm to rt. After 80 min, TLC (1:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.35$) and complete consumption of starting material ($R_f = 0.2$). The reaction mixture was filtered through Celite and concentrated in vacuo. The residue was purified by flash column chromatography (1:2, petrol/EtOAc) to give trichloroacetimidate **32** (157 mg, 92%) as a white foam; $[\alpha]_D^{23}$ +10.4 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3324 (br, NH), 1754 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.90, 1.95, 1.98, 2.01, 2.03, 2.11, 2.14, 2.17 (24H, 8 × s, 8 × CH_3), 3.71–3.73 (1H, m, H-6a), 3.94–4.02 (3H, m, H-6b, H-6c, H-6′a), 4.11–4.14 (2H, m, H-5b, H-5c), 4.22–4.26 (2H, m, H-6′b, H-6′c), 4.36–4.39 (1H, m, H-5a), 4.58 (1H, dd, $J_{2a,3a} = 2.4$ Hz, $J_{3a,4a} = 9.2$ Hz, H-3a), 4.84 (1H, s, H-1c), 4.97 (1H, s, H-2b), 5.13 (1H, s, H-1b), 5.16 (1H, dd, $J_{2b,3b} = 2.4$ Hz, $J_{3b,4b} = 9.9$ Hz, H-3b), 5.21 (1H, at, $J = 9.7$ Hz, H-4b), 5.26 (1H, s, H-2c), 5.30 (1H, at, $J = 9.8$ Hz, H-4c), 5.34 (1H, dd, $J_{2c,3c} = 2.4$ Hz, $J_{3c,4c} = 10.1$ Hz, H-3c), 5.75 (1H, s, H-2a), 5.80 (1H, at, $J = 10.0$ Hz, H-4a), 6.51 (1H, s, H-1a), 7.51–7.54 (2H, m, 2 × Ar-H), 7.61–7.72 (4H, m, 4 × Ar-H), 8.10–8.11 (2H, m, 2 × Ar-H), 8.22–8.23 (2H, m, 2 × Ar-H), 9.00 (1H, s, NH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.6, 20.7, 20.8, 20.9, 21.0 (5 × q, 8 × CH_3), 62.0, 62.2 (2 × t, C-6b, C-6c), 65.7 (d, C-4b), 65.9 (d, C-4c), 66.3 (t, C-6a), 67.9 (d, C-4a), 68.3 (d, C-3b), 68.4 (d, C-5c), 69.0 (d, C-3c), 69.2 (d, C-2b), 69.4 (d, C-2c), 69.5 (d, C-5b), 70.4 (d, C-2a), 72.1 (d, C-5a), 75.7 (d, C-3a), 90.6 (s, CCl_3), 94.3 (d, C-1a), 97.2 (d, C-1c), 99.8 (d, C-1b), 128.5 (s, Ar-C), 128.6 (d, Ar-C), 128.7 (s, Ar-C), 129.0, 130.0, 130.2, 133.9, 134.0 (5 × d, 9 × Ar-C), 159.6 (s, *C*CCl_3), 165.3, 165.8, 169.2, 169.3, 169.6, 169.8, 169.8, 170.0, 170.7, 170.7 (10 × s, 10 × C=O); $J_{C\text{-}1a/H\text{-}1a} = 181$ Hz (α), $J_{C\text{-}1b/H\text{-}1b} = 174$ Hz (α), $J_{C\text{-}1c/H\text{-}1c} = 174$ Hz (α); *m/z* (ESI^+) species observed $[M+Na]^+$ (major), $[M+NH_4]^+$; $[M+Na]^+$ peaks observed: 1214.1 (98%), 1215.2 (30%), 1216.1 (100%), 1217.2 (27%), 1218.2 (20%), 1219.2 (5%) peaks calculated: 1214.2 (85%), 1215.2 (50%), 1216.2 (100%), 1217.2 (52%), 1218.2 (40%), 1219.2 (20%). Anal. Calcd for $C_{50}H_{56}Cl_3NO_{26}$: C, 50.32; N, 1.17; H, 4.73. Found: C, 49.98; N, 0.94; H, 4.93.

4.26. *p*-Methoxyphenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2-*O*-acetyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (33)

Benzylidene **22** (1.90 g, 1.39 mmol) was dissolved in an 80% aqueous solution of acetic acid (100 mL). The reaction mixture was stirred and heated at 50 °C. After 19 h, TLC (1:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.2$) and complete consumption of starting material ($R_f = 0.75$). The reaction mixture was cooled, and CH_2Cl_2 (150 mL) and water (50 mL)

were added. The aqueous layer was re-extracted with CH_2Cl_2 (2 × 100 mL) and the combined organic layers were washed with aqueous sodium hydrogen carbonate (2 × 200 mL of a saturated solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:2, petrol/EtOAc) to give diol **33** (1.53 g, 86%) as a white foam; $[\alpha]_D^{23}$ +40 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3476 (br, OH), 1777, 1747, 1716 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.11, 2.20 (6H, 2 × s, 2 × OC(O)CH_3), 2.92 (2H, br s, 2 × OH), 3.09–3.11 (1H, m, H-5b), 3.56–3.60 (2H, m, H-3b, H-6b), 3.67–3.68 (1H, m, H-5a), 3.73–3.83 (5H, m, H-6a, H-6c, H-6′a H-6′b H-6′c), 3.77 (3H, s, PhOCH_3), 3.83–3.89 (2H, m, H-4b, H-4c), 3.91–3.93 (1H, m, H-3c), 3.99–4.01 (1H, m, H-5c), 4.18 (1H, at, $J = 9.3$ Hz, H-4a), 4.33 (1H, at, $J = 9.6$ Hz, H-3a), 4.43–4.46 (2H, m, H-2a, PhCH), 4.50, 4.77 (2H, ABq, $J = 12.3$ Hz, PhCH_2), 4.54–4.56 (2H, m, 2 × PhCH), 4.60–4.73 (2H, ABq, $J = 11.5$ Hz, PhCH_2), 4.66–4.70 (2H, m, H-1b, PhCH), 4.89–4.92 (2H, m, 2 × PhCH), 5.29 (2H, m, H-1c, H-2c), 5.37 (1H, d, $J_{1b,2b} = 2.7$ Hz, H-2b), 5.64 (1H, d, $J_{1a,2a} = 8.8$ Hz, H-1a), 6.74–6.76 (2H, m, 2 × Ar-H), 6.84–6.86 (2H, m, 2 × Ar-H), 7.00–7.03 (3H, m, 3 × Ar-H), 7.06–7.24 (2H, m, 2 × Ar-H), 7.24–7.26 (2H, m, 2 × Ar-H), 7.32–7.42 (18H, m, 18 × Ar-H), 7.67–7.87 (4H, m, 4 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 21.1, 21.8 (2 × q, 2 × OC(O)CH_3), 55.6 (d, C-2a), 55.6 (PhOCH_3), 62.3 (t, C-6b), 66.9 (d, C-4b), 68.0 (t, C-6c), 69.1 (t, C-6a), 69.3 (d, C-2c), 71.1 (d, C-2b), 71.8 (d, C-5c), 71.9 (t, PhCH_2), 73.5 (t, PhCH_2), 73.6 (t, PhCH_2), 74.3 (d, C-4c), 74.5 (t, PhCH_2), 74.7 (d, C-5a), 74.9 (t, PhCH_2), 75.4 (d, C-5b), 76.8 (d, C-3a), 77.4 (d, C-3c), 78.2 (d, C-4a), 78.8 (d, C-3b), 97.6 (d, C-1a), 98.0 (d, C-1c), 98.4 (d, C-1b), 114.4, 118.6, 127.4, 127.7, 127.8, 127.9, 127.9, 128.0, 128.0, 128.1, 128.2, 128.4, 128.4, 128.5, 128.6, 128.7, 133.9 (17 × d, 33 × Ar-C), 137.8, 137.8, 137.9, 138.3, 138.4, 150.8, 155.4 (7 × s, 9 × Ar-C), 169.9, 170.6 (2 × s, 4 × C=O); $J_{C\text{-}1a/H\text{-}1a} = 166$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 160$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 172$ Hz (α); *m*/*z* (ESI^+) species observed $[M+NH_4]^+$ (major), $[M+Na]^+$; $[M+NH_4]^+$ peaks observed: 1291.3 (100%), 1292.3 (70%), 1293.3 (15%), peaks calculated: 1291.5 (100%), 1292.5 (80%), 1293.5 (35%). Anal. Calcd for $C_{72}H_{75}NO_{20}$: C, 67.86; N, 1.10; H, 5.93. Found: C, 67.55; N, 1.01; H, 6.02.

4.27. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-]-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-]-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (34)

Trisaccharide diol **33** (269 mg, 211 μmol) and trisaccharide trichloroacetimidate **32** (277 mg, 232 μmol) were dissolved in dry alcohol-free CH_2Cl_2 (25 mL) and added via canula to a flame-dried round-bottomed flask containing activated 4 Å molecular sieves (~200 mg). The reaction mixture was stirred, and cooled to −60 °C and TMSOTf (2.30 μL, 12.7 μmol) was then added. The reaction was then allowed to slowly warm to rt and after 20 h, TLC (1:2, petrol/EtOAc) indicated the formation of a major product ($R_f = 0.3$) and complete consumption of starting materials ($R_f = 0.4$ and $R_f = 0.25$). Et_3N (50 μL) was added and the mixture stirred for a further 10 min. The reaction mixture was filtered through Celite and the filtrate washed with aqueous sodium hydrogen carbonate (2 × 50 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:2, petrol/EtOAc) to give hexasaccharide **34** (418 mg, 86%) as an amorphous white foam; $[\alpha]_D^{22}$ +24 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3482 (br, OH), 1752 (s, C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.86, 1.89, 1.91, 2.04, 2.05, 2.08, 2.09, 2.12, 2.16, 2.19 (30H, 10 × s, 10 × OCOCH_3), 3.34–3.38 (1H, m, H-5b), 3.43 (1H, dd, $J_{5d,6d} = 1.9$ Hz, $J_{6d,6'd} = 10.4$ Hz, H-6d), 3.52–3.53 (1H, m, OH), 3.64–3.69 (2H, m, H-3b, H-5a), 3.76 (3H, s, OCH_3), 3.75–3.87 (6H, m, H-4b, H-6a, H-6b, H-6c, H-6′a, H-6′c), 3.88–3.95 (5H, m, H-3c, H-4c, H-6e, H-6′b, H-6′d), 4.00–4.02 (2H, m, H-5c, H-5e), 4.05–4.13 (4H, m, H-5d, H-5f, H-6f, H-6′e), 4.21–4.24 (2H, m, H-4a, H-6′f), 4.29 (1H, dd, $J_{2a,3a} = 10.5$ Hz, $J_{3a,4a} = 8.6$ Hz, H-3a), 4.40 (1H, dd, $J_{1a,2a} = 8.5$ Hz, H-2a), 4.50 (1H, dd, $J_{2d,3d} = 3.4$ Hz, $J_{3d,4d} = 9.9$ Hz, H-3d), 4.53–4.61 (5H, m, 5 × PhCH), 4.71–4.78 (5H, m, H-1b, H-1f, 3 × PhCH), 4.89–4.91 (2H, m, 2 × PhCH), 5.06 (1H, at, $J = 2.4$ Hz, H-2e), 5.12–5.16 (3H, m, H-1d, H-3e, H-4e), 5.19 (1H, d, $J_{1e,2e} = 1.6$ Hz, H-1e), 5.24 (1H, dd, $J_{1f,2f} = 1.7$ Hz, $J_{2f,3f} = 3.3$ Hz, H-2f), 5.28–5.32 (2H, m, H-1c, H-4f), 5.41 (1H, dd, $J_{2f,3f} = 3.4$ Hz, $J_{3f,4f} = 10.2$ Hz, H-3f), 5.44 (1H, br d, $J = 3.3$ Hz, H-2b), 5.48 (1H, m, H-2c), 5.61 (1H, dd, $J_{1d,2d} = 1.6$ Hz, $J_{2d,3d} = 3.5$ Hz, H-2d), 5.61 (1H, at, $J = 10.0$ Hz, H-4d), 5.64 (1H, d, H-1a), 6.73–6.74 (2H, m, 2 × Ar-H), 6.81–6.83 (4H, m, 4 × Ar-H), 7.02–7.04 (2H, m, 2 × Ar-H), 7.25–7.26 (2H, m, 2 × Ar-H), 7.33–7.38 (12H, m, 12 × Ar-H), 7.40–7.46 (9H, m, 9 × Ar-H), 7.52–7.69 (8H, m, 8 × Ar-H), 8.06–8.08 (2H, m, 2 × Ar-H), 8.12–8.13 (2H, m, 2 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): 20.6, 20.6, 20.6, 20.7, 20.8, 20.8, 20.8, 20.9, 21.0, 21.2 (10 × q, 10 × OCOCH_3), 55.6 (d, C-2a), 55.6 (q, OCH_3), 62.0 (t, C-6e), 62.3 (t, C-6f), 65.8 (d, C-4f), 66.0 (d, C-4e), 66.4 (t, C-6d), 66.7 (t, C-6b), 67.7 (d, C-4b), 68.2 (t, C-6a), 68.6 (d, C-5f), 68.7 (2 × d, C-3e, C-4d), 68.9 (t, C-6c), 69.0 (d, C-2c), 69.2 (d, C-2e), 69.3 (d, C-5d), 69.3 (d, C-5e), 69.3 (d, C-3f), 69.6 (d, C-2f), 71.0 (d, C-2b), 71.9 (d, C-2d), 71.9 (d, C-5c), 72.0 (t, PhCH_2), 73.4 (2 × t, 2 × PhCH_2), 74.2 (d, C-4c), 74.3 (t, PhCH_2), 74.7 (d, C-5a), 74.8 (t, PhCH_2),

74.9 (d, C-5b), 76.3 (d, C-3d), 76.5 (d, C-3a), 77.9 (d, C-3c), 78.1 (d, C-3b), 78.5 (d, C-4a), 97.1 (d, C-1f), 97.2 (d, C-1d), 97.6 (d, C-1a), 98.9 (d, C-1b), 99.3 (d, C-1c), 99.8 (d, C-1e), 114.4, 118.6, 127.1, 127.5, 127.7, 127.7, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.4, 128.6, 128.6, 128.8 (18 × d, 33 × Ar-C), 129.0, 129.2 (2 × s, 2 × Ar-C), 130.0, 130.0, 131.6, 133.4, 133.5, 133.7, 133.7, 133.8 (8 × d, 10 × Ar-C), 138.0, 138.0, 138.2, 138.5, 138.6, 150.6, 155.3 (7 × s, 9 × Ar-C), 165.6, 165.7, 169.2, 169.3, 169.7, 169.9, 170.1, 170.1, 170.4, 170.7, 170.7 (11 × s, 14 × C═O); $J_{C\text{-}1a/H\text{-}1a}$ = 169 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ = 160 Hz (β), $J_{C\text{-}1c/H\text{-}1c}$ = 175 Hz (α); $J_{C\text{-}1d/H\text{-}1d}$ = 175 Hz (α), $J_{C\text{-}1e/H\text{-}1e}$ = 175 Hz (α), $J_{C\text{-}1f/H\text{-}1f}$ = 174 Hz (α); *m*/*z* (ESI^+) species observed $[M+2Na]^{2+}$ (major); $[M+2Na]^{2+}$ peaks observed: 1174.8 (50%), 1175.3 (100%), 1175.8 (75%), 1176.3 (45%), 1176.8 (20%), peaks calculated: 1174.9 (74%), 1175.4 (100%), 1175.9 (76%), 1176.4 (40%), 1176.9 (20%).

4.28. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-]-2,4-di-*O*-acetyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-acetyl-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-]-β-D-mannopyranosyl-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (35)

Phthalimide-protected hexasaccharide **34** (260 mg, 113 μmol) was dissolved in MeOH (5 mL) and ethylenediamine (3.00 mL, 45.0 mmol) was added. The solution was then heated at reflux at 65 °C. After 25 h, TLC (MeOH) indicated the formation of a major product (R_f = 0.6) and complete consumption of starting material (R_f = 0.8). The reaction mixture was cooled to rt, concentrated in vacuo, and the residue dissolved in pyridine (15 mL). The solution was cooled to 0 °C and Ac_2O (13 mL) was added. After 3 days, TLC (1:3, petrol/EtOAc) indicated the formation of a single product (R_f = 0.3) and complete consumption of starting material (R_f = 0.5). The reaction mixture was poured onto ice/water (20 mL) and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were washed with aqueous hydrochloric acid (2 × 10 mL of a 1 M solution), aqueous sodium hydrogen carbonate (2 × 20 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:3, petrol/EtOAc) to afford acetamide protected hexasaccharide **35** (215 mg, 90%) as a white amorphous solid; $[\alpha]_D^{23}$ 27 (*c* 0.5, $CHCl_3$); IR (KBr disc): 3402 (br, NH), 1751, 1682 (s, C═O), 1508 (m, NH) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.89, 2.01, 2.01, 2.06, 2.07, 2.08, 2.09, 2.11, 2.17, 2.18, 2.19, 2.19, 2.21, 2.23 (42H, 14 × s, 14 × $COCH_3$), 3.27 (1H, dd, $J_{5d,6d}$ = 2.1 Hz, $J_{6d,6'd}$ = 11.1 Hz, H-6d), 3.36–3.39 (1H, m, H-5b), 3.41–3.46 (1H, m, H-2a), 3.56 (1H, dd, $J_{5b,6b}$ = 1.8 Hz, $J_{6b,6'b}$ = 11.3 Hz, H-6), 3.58–3.61 (1H, m, H-5a), 3.65–3.73 (5H, m, H-3b, H-6a, H-6c, H-6′a, H-6′d), 3.77 (1H, dd, $J_{5b,6'b}$ = 6.8 Hz, H-6′b), 3.81 (3H, s, OCH_3), 3.80–3.87 (3H, m, H-3c, H-5d, H-6′c), 3.88–3.91 (1H, m, H-5c), 3.94 (1H, at, *J* = 9.4 Hz, H-4c), 4.05–4.18 (7H, m, H-3a, H-3d, H-4a, H-5e, H-f, H-6e, H-6f), 4.29 (1H, dd, $J_{5e,6'e}$ = 4.6 Hz, $J_{6e,6'e}$ = 12.5 Hz, H-6′e), 4.39 (1H, dd, $J_{5f,6'f}$ = 3.9 Hz, $J_{6f,6'f}$ = 12.1 Hz, H-6′f), 4.44 (1H, d, *J* = 12.0 Hz, PhCH), 4.50–4.55 (2H, m, 2 × PhCH), 4.56–4.71 (4H, m, H-1b, 3 × PhCH), 4.75 (1H, br s, H-1f), 4.86–4.88 (3H, m, H-1d, H-1e, PhCH), 4.94 (1H, d, *J* = 11.2 Hz, PhCH), 4.98 (1H, br s, H-1c), 5.08 (1H, dd, $J_{1e,2e}$ = 1.9 Hz, $J_{2e,3e}$ = 3.2 Hz, H-2e), 5.16 (1H, dd, $J_{1c,2c}$ = 2.0 Hz, $J_{2c,3c}$ = 3.1 Hz, H-2c), 5.17 (1H, at, *J* = 9.7 Hz, H-4b), 5.23 (1H, dd, $J_{3e,4e}$ = 10.1 Hz, H-3e), 5.28 (1H, br s, H-2d), 5.30 (1H, at, *J* = 10.0 Hz, H-4e), 5.35–5.38 (4H, m, H-2f, H-3f, H-4d, H-4f), 5.39–5.44 (2H, m, H-1a, H-2b), 6.30 (1H, d, $J_{2a,NH}$ = 7.6 Hz, NH), 6.81–6.83 (2H, m, 2 × Ar-H), 6.93–6.95 (2H, m, 2 × Ar-H), 7.22–7.39 (25H, m, 25 × Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.6, 20.6, 20.7, 20.7, 20.7, 20.8, 20.8, 20.8, 20.9, 21.1, 23.4 (11 × q, 14 × $COCH_3$), 55.6 (q, OCH_3), 56.6 (d, C-2a), 62.0 (t, C-6e), 62.6 (t, C-6f), 65.5 (d, C-4e), 66.0 (d, C-4f), 66.4 (t, C-6b, C-6d), 67.3 (d, C-4d), 68.2 (t, C-6a), 68.3 (d, C-5f), 68.4 (d, C-3e), 68.6 (d, C-4b), 68.8 (t, C-6c), 69.0 (d, C-2c), 69.2 (d, C-5e), 69.3 (2 × d, C-2f, C-3f, C-5d), 69.7 (d, C-2e), 70.5 (d, C-2d), 70.6 (d, C-2b), 71.7 (t, $PhCH_2$), 72.1 (d, C-5c), 72.8 (d, C-5b), 73.2, 73.3 (2 × t, 2 × $PhCH_2$), 73.8 (d, C-4c), 74.2 (d, C-5a), 74.5, 74.7 (2 × t, 2 × $PhCH_2$), 76.0 (d, C-3d), 76.9 (d, C-4a), 77.1 (d, C-3b), 77.2 (d, C-3c), 77.7 (d, C-3a), 96.5 (d, C-1d), 97.6 (d, C-1b), 97.8 (d, C-1f), 98.9 (d, C-1a), 99.1 (d, C-1e), 100.0 (d, C-1c), 114.4, 118.4, 127.4, 127.6, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.3, 128.4, 128.5, 128.7 (14 × d, 29 × Ar-C), 137.8, 137.9, 138.2, 138.5, 138.7, 151.4, 155.2 (7 × s, 7 × Ar-C), 169.5, 169.6, 169.7, 169.9, 169.9, 170.0, 170.0, 170.1, 170.4, 170.5, 170.6, 170.9 (12 × s, 14 × C═O); $J_{C\text{-}1a/H\text{-}1a}$ = 164 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ = 161 Hz (β), $J_{C\text{-}1c/H\text{-}1c}$ = 174 Hz (α); $J_{C\text{-}1d/H\text{-}1d}$ = 175 Hz (α), $J_{C\text{-}1e/H\text{-}1e}$ = 174 Hz (α), $J_{C\text{-}1f/H\text{-}1f}$ = 174 Hz (α); *m*/*z* (ESI^+) species observed $[M+2Na]^{2+}$ (major); $[M+2Na]^{2+}$ peaks observed: 1089.9 (70%), 1090.4 (100%), 1091.0 (45%), 1091.5 (23%), 1092.0 (10%), peaks calculated: 1089.9 (80%), 1090.4 (100%), 1090.9 (65%), 1091.4 (35%), 1091.9 (12%).

4.29. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-]-2,4-di-*O*-acetyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-acetyl-[2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-]-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyranoside (36)

Benzyl ether **35** (100 mg, 46.8 μmol) was dissolved in MeOH (10 mL) and palladium (10% on carbon,

35.0 mg) was added. The flask was flushed three times with argon, and then with hydrogen. The reaction mixture was then stirred at rt under an atmosphere of hydrogen. After 18 h, TLC (1:1, EtOAc/MeOH) indicated the formation of a major product ($R_f = 0.7$) and complete consumption of starting material ($R_f = 0.9$). The reaction mixture was poured onto Celite, washed with MeOH (3×10 mL), filtered and concentrated in vacuo. The residue was dissolved in pyridine (10 mL), the solution cooled to 0 °C and Ac_2O (10 mL) added. After 1 day, TLC (EtOAc) indicated the formation of a single product ($R_f = 0.5$) and the complete consumption of starting material ($R_f = 0.7$). The reaction mixture was poured onto ice/water (20 mL) and extracted with CH_2Cl_2 (2×15 mL). The combined organic layers were washed with aqueous hydrochloric acid (2×10 mL of a 1 M solution), aqueous sodium hydrogen carbonate (2×20 mL of a satd solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford acetylated hexasaccharide **36** (72 mg, 81%) as a white amorphous solid; $[\alpha]_D^{23}$ +17 (*c* 0.5, $CHCl_3$); IR (KBr disc): 1743, 1682 (s, C=O), 1508, 1509 (m, NH) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.00, 2.02, 2.03, 2.04, 2.10, 2.11, 2.12, 2.13, 2.15, 2.17, 2.18, 2.18, 2.19, 2.20, 2.21, 2.23, 2.24, 2.28 (54H, $18 \times$ s, $18 \times C(O)CH_3$), 3.57–3.60 (2H, m, H-5b, H-6d), 3.65 (1H, dd, $J_{5b,6b} = 2.7$ Hz, $J_{6b,6'b} = 11.5$ Hz, H-6b), 3.79–3.82 (1H, m, H-5a), 3.82 (3H, s, OCH_3), 3.85–3.95 (4H, m, H-4a, H-5d, H-6′b, H-6′d), 3.95 (1H, dd, $J_{2b,3b} = 3.4$ Hz, $J_{3b,4b} = 9.4$ Hz, H-3b), 4.09–4.22 (7H, m, H-2a, H-5c, H-5e, H-5f, H-6c, H-6e, H-6f), 4.27 (1H, dd, $J_{2d,3d} = 3.4$ Hz, $J_{3d,4d} = 9.8$ Hz, H-3d), 4.31–4.44 (5H, m, H-6a, H-6′a, H-6′c, H-6′e, H-6′f), 4.74 (1H, br s, H-1b), 4.90 (1H, d, $J_{1f,2f} = 1.2$ Hz, H-1f), 4.91 (1H, d, $J_{1d,2d} = 1.6$ Hz, H-1d), 5.04–5.07 (3H, m, H-1a, H-1c, H-2c), 5.10 (1H, br d, $J_{1e,2e} = 1.8$ Hz, H-1e), 5.13 (1H, dd, $J_{2e,3e} = 3.2$ Hz, H-2e), 5.22 (1H, dd, $J_{2c,3c} = 3.2$ Hz, $J_{3c,4c} = 10.2$ Hz, H-3c), 5.23–5.39 (10H, m, H-2d, H-2f, H-3a, H-3e, H-3f, H-4b, H-4c, H-4d, H-4e, H-4f), 5.49 (1H, br d, $J = 2.5$ Hz, H-2b), 5.90 (1H, d, $J_{2a,NH} = 9.1$ Hz, NH), 6.84–6.86 (2H, m, $2 \times$ Ar-H), 6.96–6.98 (2H, m, $2 \times$ Ar-H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.7, 20.7, 20.7, 20.8, 20.8, 20.8, 20.8, 20.9, 20.9, 21.0 ($10 \times$ q, $10 \times OC(O)CH_3$), 23.3 (q, $NC(O)CH_3$), 53.9 (d, C-2a), 55.7 (q, OCH_3), 62.2 (t, C-6e), 62.2 (t, C-6c), 62.4 (t, C-6f), 62.5 (t, C-6a), 65.7 (d, C-4f), 65.7 (d, C-4c), 65.8 (d, C-4e), 66.4 (t, C-6d), 67.0 (t, C-6b), 67.7 (d, C-4b), 67.8 (d, C-4d), 68.3 (d, C-3c), 68.5 (d, C-3e), 68.7 (d, C-5f), 69.3 (d, C-5e), 69.4 ($2 \times$ d, C-2f, C-5c), 69.4 (d, C-3f), 69.6 (d, C-5d), 69.7 (d, C-2b), 69.8 (d, C-2e), 70.0 (d, C-2c), 70.7 (d, C-2d), 72.4 (d, C-3a), 72.6 (d, C-5a), 73.4 (d, C-5b), 75.0 ($2 \times$ d, C-3d, C-4a), 76.3 (d, C-3b), 97.5 (d, C-1f), 97.5 (d, C-1d), 97.9 (d, C-1b), 98.8 (d, C-1c), 99.1 (d, C-1e), 100.1 (d, C-1a), 114.5, 118.4 ($2 \times$ d, $4 \times$ Ar-C), 151.1, 155.5 ($2 \times$ s, $2 \times$ Ar-C), 169.6, 169.7, 169.8, 169.8, 169.8, 169.9, 170.0, 170.0, 170.1, 170.1, 170.4, 170.5, 170.6, 170.6, 170.7, 170.7 ($16 \times$ s, $19 \times$ C=O); $J_{C\text{-}1a/H\text{-}1a} = 164$ Hz (β), $J_{C\text{-}1b/H\text{-}1b} = 160$ Hz (β), $J_{C\text{-}1c/H\text{-}1c} = 175$ Hz (α); $J_{C\text{-}1d/H\text{-}1d} = 174$ Hz (α), $J_{C\text{-}1e/H\text{-}1e} = 174$ Hz (α), $J_{C\text{-}1f/H\text{-}1f} = 175$ Hz (α); *m*/*z* (ESI^+) species observed $[M+H]^+$, $[M+NH_4]^+$, $[M+Na]^+$ (major); $[M+Na]^+$ peaks observed: 1916.5 (100%), 1917.5 (70%), 1918.6 (25%), 1919.5 (10%), peaks calculated: 1916.6 (100%), 1917.6 (92%), 1918.6 (55%), 1919.6 (22%).

4.30. 2-Methyl-[α-D-mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→6)-]-α-D-mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→3)-]-β-D-mannopyranosyl-(1→4)-1,2-dideoxy-α-D-glucopyrano]-[2,1-*d*]-oxazoline (38)

Acetamide **36** (97 mg, 52.8 μmol) was dissolved in dry chloroform (5 mL) and acetyl bromide (39.0 μL, 528 μmol) and zinc(II) iodide (843 μg, 2.64 μmol) were added. The reaction mixture was stirred and heated to 50 °C. After 4 h, TLC (EtOAc) indicated the formation of a major product ($R_f = 0.5$) and complete consumption of starting material ($R_f = 0.55$). The reaction mixture was cooled to rt and extracted with CH_2Cl_2 (30 mL). The organic layer was washed with aqueous sodium hydrogen carbonate (2×15 mL of a satd solution), aqueous sodium thiosulfate (5 mL of a 10% w/v solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc) to afford oxazoline **37** (52.3 mg, 58%) as a white amorphous solid; *m*/*z* (ESI^+) species observed $[M+H]^+$, $[M+Na]^+$ (major); $[M+Na]^+$ peaks observed: 1792.6 (100%), 1793.6 (70%), 1794.6 (20%), 1795.5 (8%), peaks calculated: 1792.5 (100%), 1793.5 (85%), 1794.5 (50%), 1795.5 (20%).

A portion of the acetylated oxazoline **37** (11.0 mg, 5.65 μmol) was dissolved in dry MeOH (2 mL). NaOMe in MeOH (150 μL of a 5 mg/mL solution, 32.6 μmol) was added and the solution stirred at rt under an atmosphere of argon. After 21 h, mass spectrometric analysis indicated the presence of a single product. The solution was concentrated in vacuo to yield deprotected oxazoline **38** (8.10 mg, quant.) as a white amorphous solid. IR (KBr disc): 3444 (br, OH), 1651 (s, C=N) cm^{-1}; ^1H NMR (500 MHz, D_2O): δ 1.99 (3H, d, $J_{2a,CH_3} = 1.7$ Hz, CH_3), 3.32–4.29 (36H, m, H-2a,b,c,d,e,f, H-3a,b,c,d,e,f, H-4a,b,c,d,e,f, H-5a,b,c,d,e,f, H-6a,b,c,d,e,f, H-6′a,b,c,d,e,f), 4.66 (1H, s, H-1b), 4.83 (2H, br s, H-1d, H-1f), 5.01 (1H, s, H-1c), 5.06 (1H, s, H-1e), 6.01 (1H, d, $J_{1a,2a} = 7.2$ Hz, H-1a); ^{13}C NMR (125.8 MHz, D_2O): δ 12.9 (q, CH_3), 60.9, 61.0, 61.1, 61.6, 65.2, 65.7, 65.8, 66.7, 66.8, 69.3, 69.4, 69.9, 70.0, 70.1, 70.2, 70.3, 70.3, 70.6, 70.9, 70.9, 72.7, 73.3, 74.4, 77.9, 78.4, 80.6 ($29 \times$ d/t, C-2a,b,c,d,e,f, C-3a,b,c,d,e,f, C-4a,b,c,d,e,f, C-5a,b,c,d,e,f, C-6a,b,c,d,e,f), 99.3 (d, C-1f), 99.8 (d,

C-1d), 100.0 (d, C-1a), 101.3 (d, C-1b), 102.3 (d, C-1e), 102.5 (d, C-1c), 168.6 (s, C=N); *m/z* (ES^-) species observed $[M-H]^-$ (major); $[M-H]^-$ peaks observed: 1012.3 (100%), 1012.4 (20%), peaks calculated: 1012.3 (100%), 1012.3 (45%).

4.31. N^4-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-1-methyl-N^2-(benzyloxycarbonyl)-L-asparagine (41)

N-Benzyloxycarbonyl-L-aspartic acid 1-methyl ester **40** (312 mg, 1.10 mmol) and 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide **39**[24] (500 mg, 1.30 mmol) were dissolved in dry CH_2Cl_2 (10 mL) and the solution cooled to −78 °C under an atmosphere of argon. Tri-*n*-butylphosphine (224 mg, 1.10 mmol) was added, and the reaction mixture stirred at −78 °C. After 10 h, the reaction mixture was allowed to warm to rt. Petrol was then added dropwise until crystals formed, which were filtered off and washed with petrol (2 × 20 mL) to give amide **41** (453 mg, 67%) as white crystals, mp 234–236 °C; $[\alpha]_D^{21}$ +10 (*c* 1.0, $CHCl_3$); IR (KBr disc): 3316 (br, NH), 1747, 1692, 1640 (s, C=O), 1539 (m, NH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.98 (3H, s, NC(O)CH_3), 2.05, 2.08, 2.08 (9H, 3 × s, 3 × OC(O)CH_3), 2.71 (1H, dd, $J_{NCHCHH',NCHCHH'} = 16.5$ Hz, $J_{NCHCHH',NCHCHH'} = 3.9$ Hz, NCHCHH′), 2.89 (1H, dd, $J_{NCHCHH',NCHCHH'} = 4.2$ Hz, NCHCHH′), 3.70–3.77 (1H, m, H-5), 3.73 (3H, s, C(O)OCH_3), 4.08 (1H, dd, $J_{5,6} = 1.7$ Hz, $J_{6,6'} = 12.7$ Hz, H-6), 4.12–4.14 (1H, m, H-2), 4.30 (1H, dd, $J_{5,6'} = 4.3$ Hz, H-6′), 4.61–4.64 (1H, m, ZNHCH), 4.99–5.04 (2H, m, H-1, H-3), 5.13 (2H, s, $PhCH_2$), 5.13 (1H, at, $J = 9.5$ Hz, H-4), 5.98 (2H, m, ZNH, AcNH), 7.16 (1H, d, $J_{Ac_3GlcNAc\text{-}NH,1} = 8.1$ Hz, Ac_3GlcNAc-NH), 7.32–7.37 (5H, m, 5 × Ar-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.6 (3 × q, 3 × OC(O)CH_3), 23.0 (q, NC(O)CH_3), 37.5 (t, NCHCH_2), 52.6 (d, C-2), 53.4 (q, C(O)OCH_3), 61.5 (t, C-6), 67.0 (d, C-4), 67.3 (t, $PhCH_2$), 72.7 (d, C-3), 73.5 (d, C-5), 80.3 (d, C-1), 128.0 (2 × d, 2 × Ar-C), 128.0 (2 × d, 2 × Ar-C), 128.4 (2 × s, 2 × Ar-C), 169.7, 170.5, 170.6, 171.0, 171.2, 171.9, 172.4 (7 × s, 7 × C=O); *m/z* (ES^+) 669 ($[M+NH_4+MeCN]^+$, 99%); ESIMS *m/z* calcd for $C_{27}H_{36}N_3O_{13}$ $[M+H]^+$: 610.2248. Found 610.2242. Anal. Calcd for $C_{27}H_{35}N_3O_{13}$: C, 53.20; N, 6.89; H, 5.79. Found: C, 53.15; N, 6.87, H, 5.80.

4.32. N^4-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-1-methyl-N^2-(benzyloxycarbonyl)-L-asparagine (42)

To a solution of triacetate **41** (100 mg, 160 μmol) in MeOH (2 mL) and CH_2Cl_2 (2 mL), NaOMe (11.0 mg, 200 μmol) was added and the mixture stirred at rt under an atmosphere of argon. After 6 min, TLC (EtOAc) indicated the formation of a major product ($R_f = 0$) and complete consumption of starting material ($R_f = 0.3$). Ion-exchange resin (Dowex 50W-X8 H^+ form) was added to the reaction mixture until pH 7 was achieved. The resin was then filtered off, the filtrate concentrated in vacuo and the residue was purified by recrystallisation (petrol/EtOAc) to give triol **42** (71 mg, 90%) as a white solid, mp 166–168 °C; $[\alpha]_D^{21}$ +21 (*c* 1.0, H_2O); IR (KBr disc): 3409 (br, OH), 3309 (br, NH), 1701, 1722, 1669 (s, C=O), 1541 (m, NH) cm^{-1}; ^1H NMR (500 MHz, D_2O): δ 1.91 (3H, s, C(O)-CH_3), 2.72 (1H, dd, $J_{NCHCHH',NCHCHH'} = 7.9$ Hz, $J_{NCHCHH',NCHCHH'} = 16.4$ Hz, NCHCHH′), 2.83 (1H, dd, $J_{NCHCHH',NCHCHH'} = 5.3$ Hz, NCHCHH′), 3.37–3.43 (2H, m, H-4, H-5), 3.53 (1H, at, $J = 9.1$ Hz, H-3), 3.59 (3H, s, C(O)OCH_3), 3.65 (1H, dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.3$ Hz, H-6), 3.73–3.81 (2H, m, H-2, H-6′), 4.39 (1H, t, $J = 6.1$ Hz, NHCHCH_2), 4.95 (1H, d, $J_{1,2} = 9.8$ Hz, H-1), 5.06 (2H, br s, $PhCH_2$), 7.35–7.37 (5H, m, 5 × Ar-H); ^{13}C NMR (125.8 MHz, D_2O): δ 22.0 (q, C(O)CH_3), 35.3 (t, NHCH_2), 51.6 (d, NCHCH_2), 52.5 (q, C(O)OCH_3), 54.1 (d, C-2), 60.5 (t, C-6), 67.3 (t, PhCH_2), 69.5 (d, C-4), 73.9 (d, C-3), 77.6 (d, C-5), 78.8 (d, C-1), 127.7 (2 × d, 2 × Ar-C), 128.4 (d, Ar-C), 128.8 (d, Ar-C), 128.8 (s, Ar-C), 136.2 (s, Ar-C), 157.4, 172.8, 173.6, 174.9 (4 × s, 4 × C=O); *m/z* (ES^+) 543 $[M+NH_4+MeCN]^+$, 100%; ESIMS *m/z* calcd for $C_{21}H_{29}N_3O_{10}Na$ $[M+Na]^+$: 506.1751. Found 506.1762.

4.33. N^4-(α-D-mannopyranosyl)-(1→3)-β-D-mannopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-1-methyl-N^2-(benzyloxycarbonyl)-L-asparagine (43)

Oxazoline **26** (350 μg, 664 nmol) and triol **42** (106 μg, 221 nmol) were dissolved in aqueous sodium phosphate buffer (50 μL of a 100 mM solution, pH 6.0). Endo M (1 μL of a 0.01 U/μL) was added and the temperature maintained at 23 °C. The extent of reaction was monitored by HPLC, which indicated >80% conversion of triol **42** to the product after 60 min. The product was purified by direct injection of the crude reaction mixture onto the HPLC column to give **43** (180 μg, 81%) and characterised by NMR and HRMS (see Supplementary data for 2D analysis). ^1H NMR (500 MHz, D_2O): δ 1.85, 1.96 (6H, 2 × s, 2 × C(O)CH_3), 2.70 (1H, dd, $J_{NC(O)CHH',NC(O)CH_2CH} = 7.4$ Hz, $J_{NC(O)CHH',NC(O)CHH'} = 16.0$ Hz, NC(O)-CHH′), 2.76 (1H, dd, $J_{NC(O)CHH',NC(O)CH_2CH} = 4.9$ Hz, NC(O)CHH′), 3.36 (1H, ddd, $J_{4c,5c} = 9.7$ Hz, $J_{5c,6c} = 6.5$ Hz, $J_{5c,6'c} = 2.0$ Hz, H-5c), 3.46–3.84 (24H, m, CO_2CH_3, H-2a, H-2b, H-3a, H-3b, H-3c, H-3d, H-4a, H-4b, H-4c, H-4d, H-5a, H-5b, H-5d, H-6a, H-6b, H-6c, H-6d, H-6′a, H-6′b, H-6′c, H-6′d), 3.97 (1H, dd, $J_{1d,2d} = 1.6$ Hz, $J_{2d,3d} = 3.2$ Hz, H-2d), 4.13 (1H, br d, $J_{2c,3c} = 3.0$ Hz, H-2c), 4.50–4.52 (2H, m, H-1b, NC(O)CH_2CH), 4.70 (1H, br s, H-1c), 4.94 (1H, d, $J_{1a,2a} = 9.7$ Hz, H-1a), 5.01 (1H, br s, H-1d), 5.04 (2H,

s, $PhCH_2$), 7.31–7.37 (5H, m, 5 × Ar-H); *m*/*z* (ESI^+) species observed $[M+Na]^+$ (major), $[2M+Na]^+$ peaks observed: 1033.4 (100%), 1034.4 (42%), 1035.4 (10%), 1036.4 (3%), peaks calculated: 1033.4 (100%), 1034.4 (48%), 1035.4 (16%), 1036.4 (4%); ESIMS *m*/*z* calcd for $C_{41}H_{62}N_4O_{25}Na$ $[M+Na]^+$: 1033.3595. Found 1033.3604.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.03.007.

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