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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 1721–1734

Propargyl mediated intramolecular aglycon delivery (IAD): applications to the synthesis of core *N*-glycan oligosaccharides

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Received 19 June 2007; accepted 28 June 2007
Available online 25 July 2007

Abstract—The use of propargyl mediated intramolecular aglycon delivery (IAD) for the synthesis of the key Manβ(1→4)GlcNAc linkage of *N*-glycan oligosaccharides, including the core *N*-glycan pentasaccharide, is investigated. Isomerisation of a 2-*O*-progargyl group of *manno* thioglycoside donors to an allene is followed by iodonium ion mediated mixed acetal formation with the 4-OH of protected GlcNAc acceptors, and subsequent intramolecular glycosylation occurs with complete control of anomeric stereochemistry to form the Manβ(1→4)GlcNAc linkage. A variety of linear and convergent approaches (1+2, 3+1, 3+2) to the core pentasaccharide are investigated as means of probing the generality and limitations of this type of intramolecular aglycon delivery for the formation of β-mannoside linkages in complex oligosaccharides.

1. Introduction

The control of anomeric stereochemistry during the course of a glycosylation reaction is a key consideration during the synthesis of any oligosaccharide. Whilst much work has been done to facilitate the speed of assembly of oligosaccharide structures, the issue of absolute control of anomeric stereochemistry still remains unanswered. Whilst 1,2-*trans* glycosidic linkages can usually be synthesised with high levels of stereocontrol by taking advantage of the neighbouring group participation of 2-*O*-acyl protected glycosyl donors,[1] the synthesis of 1,2-*cis* glycosidic linkages is considerably more difficult. One of the early focuses for synthetic development was construction of the difficult to synthesise β-mannoside linkage, which appears in all *N*-glycan oligosaccharides as the somewhat notorious Manβ(1→4)GlcAc disaccharide. Considerable effort has since led to the development of several elegant approaches to the construction of β-mannosides,[2] and a selection of these methods have been applied to the synthesis of the Manβ(1→4)GlcAc disaccharide and larger *N*-glycan oligosaccharides, which are generally the most difficult β-mannosides to make. However, the majority of these approaches, efficient as some of them are, are limited to the formation of β-mannosides and cannot be applied similarly for the synthesis of other 1,2-*cis* glycosidic linkages. The current situation is therefore one in which there is still no generally applicable method available for the formation of all 1,2-*cis* glycosidic bonds.[3]

Conceptually a potentially elegant solution to this ongoing '1,2-*cis* glycoside problem' is to apply the technique of intramolecular aglycon delivery, or IAD, which is a particular type of intramolecular glycosylation strategy,[4] wherein the glycosyl acceptor is temporarily appended to the 2-hydroxyl group of a glycosyl donor through a short linker. The first so-called 'tethering' step, that is, the linking of donor and acceptor, is followed by the activation of the glycosyl donor, which subsequently furnishes the 1,2-*cis* glycoside in a completely stereoselective fashion. The two key advantages of the IAD approach over other intramolecular glycosylation reactions in which the donor and acceptor are either connected by other hydroxyl groups, through longer linkers, or other remote positions, are the predictability and strict control of the anomeric stereochemistry of the product. However, even when using the IAD approach, one has to be careful to avoid problems of regiochemical control, that is, to ensure that only the desired hydroxyl is glycosylated,[5] and also to avoid the use of slightly longer linkers, which can lead to undesired non-stereoselective reactions.[6]

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doi:10.1016/j.tetasy.2007.06.026

Amongst several of the IAD methodologies that have been reported,[7–9] the approach developed by Ogawa, based on the use of 2-*O*-*para*-methoxybenzyl (PMB) protected glycosyl donors,[10] is the only methodology that has been really successfully applied to the synthesis of complex targets, such as the core *N*-glycan pentasaccharide. This pentasaccharide, which contains the crucial Manβ(1→4)GlcNAc linkage, can be considered a benchmark test for potential widespread utility of any 1,2-*cis* glycosylation procedure. Although the Ogawa approach has also been applied to the synthesis of a selection of other 1,2-*cis* glycosides, with varying degrees of success[11] it is notable that for whatever reason, it has not yet found routine applicability.

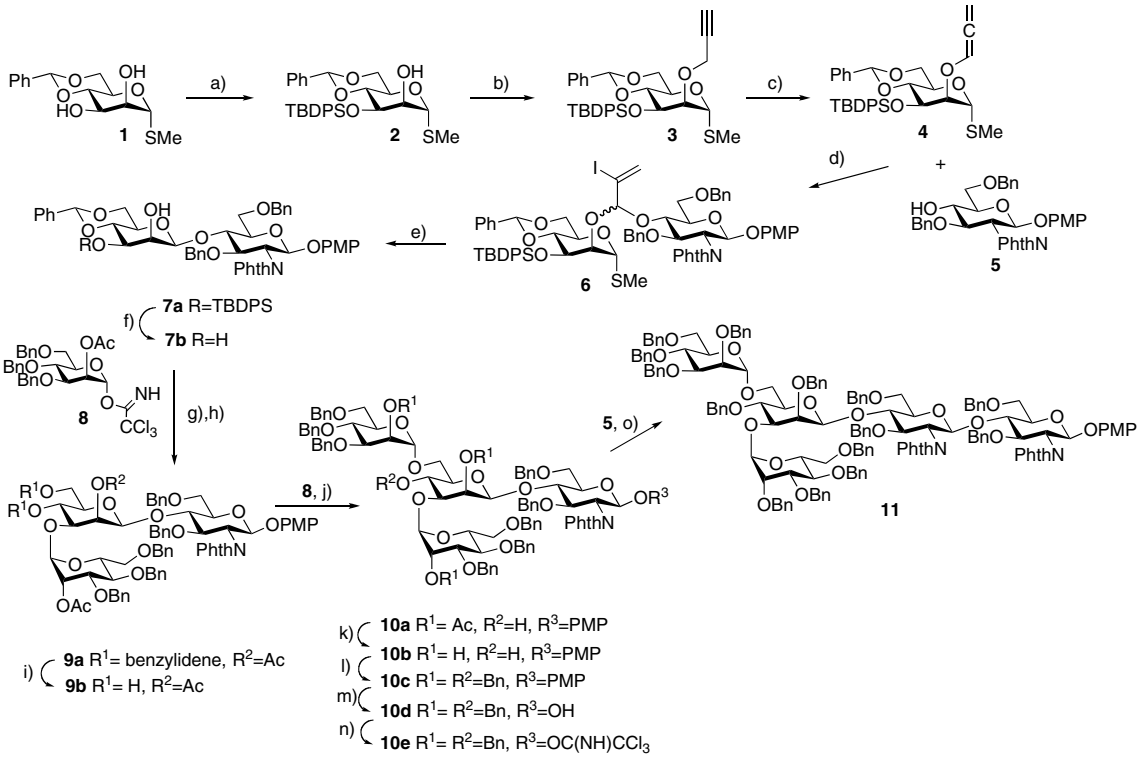
We recently reported the development of an allyl protecting group mediated IAD approach (allyl IAD),[12] based on either thioglycoside[13] or glycosyl fluoride donors.[14] This methodology relied on iodonium ion mediated formation of a mixed acetal between a glycosyl acceptor alcohol and an enol ether, itself derived from a 2-*O*-allyl protected glycosyl donor by Wilkinson's catalyst mediated isomerisation[15] of the double bond. However the attempted application of this methodology to the synthesis of complex oligosaccharides, such as the core *N*-glycan pentasaccharide, met with frustration. With the reasoning that an increase in stability of the oxonium ion produced subsequent to the intramolecular glycosylation step would facilitate the glycosylation process the use of 2-*O*-propargyl ethers for a similar intramolecular glycosylation strategy was therefore investigated, and this applied to the synthesis of the key Manβ(1→4)GlcNAc disaccharide.[16] Following on from these initial studies, it was decided to investigate the potential scope of the propargyl IAD methodology by attempting the synthesis of core *N*-glycan oligosaccharides in a more convergent manner, using di- and tri-saccharides as the donor and acceptor components for the IAD reaction sequence. In this respect previous reports from Hindsgaul[7c] have highlighted the potential limitations of IAD reactions using donors and acceptors, which are larger than monosaccharides, whilst in contrast the PMB based approach of Ogawa has been reported[10] to be applicable to more convergent oligosaccharide syntheses, and our own previous studies[17] on allyl IAD had demonstrated the iterative use of IAD sequences for the construction of tri- and tetrasaccharides in which the acceptors were di- or tri-saccharides. Herein we report full details of investigations into the use of propargyl IAD for the synthesis of *N*-glycan oligosaccharides, including the core *N*-glycan pentasaccharide, both by linear and convergent approaches and highlights potential limitations of the use of IAD for such highly convergent syntheses.

2. Results and discussion

As reported previously, the propargyl IAD approach firstly requires the synthesis of glycosyl donors bearing a propargyl ether at the 2-position, which can then undergo base-mediated isomerisation to allow access to 2-*O*-allenyl protected carbohydrates.[18] Such allenes can then undergo a similar sequence as had previously been applied as the basis of the allyl IAD—namely, iodonium ion catalysed mixed acetal formation with an acceptor alcohol, and subsequent intramolecular glycosylation with complete control of stereochemistry. An envisaged advantage of the propargyl based approach over the allyl based methodology was that the oxonium ion produced subsequent to glycosylation would be stabilised by conjugation with the side chain alkene; a factor which may facilitate aglycon delivery, which had been the least efficient step in the allyl approach particularly when using disarmed glycosyl donors.

In order to demonstrate the applicability of this approach propargyl ether **3** was synthesised by the regioselective silylation of the known diol **1**[10b] to yield alcohol **2**, which then underwent subsequent etherification using propargyl bromide and sodium hydride in DMF to give propargyl ether **3**. Isomerisation by treatment with *tert*-butoxide[19] in ether then yielded the desired intermediate allene **4**. Iodonium ion mediated mixed acetal formation with the known glucosamine acceptor **5**[10d] gave mixed acetals **6** in an excellent 88% yield. Subsequent intramolecular glycosylation, using a Me_2S_2/Tf_2O mixture, as reported originally by Fügedi,[20] together with added di-*tert* butylmethylpyridine (DTBMP) which was found to further improve efficiency of glycosylation, proceeded smoothly to give the desired Manβ(1→4)GlcNAc disaccharide **7a**[10d] in an excellent 81% yield, with complete stereocontrol (Scheme 1). Deprotection of the silyl group of **7a** with TBAF gave diol **7b**, which was then glycosylated regioselectively at the 3-position with the known trichloroacetimidate donor **8**,[21] to give a trisaccharide, which was immediately acetylated to give **9a**. Removal of the 4,6-benzylidene protection to yield trisaccharide diol **9b** proved problematic. Simple treatment with aqueous acetic acid invariably resulted in formation of small quantities of the 6-*O*-acetate as a side product. An optimised procedure was therefore developed involving treatment with trifluoroacetic acid in aqueous acetonitrile. In this case although some of the corresponding 6-*O*-trifluoroacetate was formed initially; this material was readily hydrolysed upon work-up, yielding diol **9b** in 90% yield. A second regioselective glycosylation reaction with donor **8**[21] then smoothly gave tetrasaccharide **10a**. Removal of the acetates from **10a** with anhydrous potassium carbonate in methanol also unfortunately resulted in partial cleavage of the phthalamido protection, and necessitated a re-closure procedure involving treatment of the crude reaction product, firstly with acetic anhydride in methanol and, following concentration, with tosic acid in DMF to yield triol **10b**. Benzylation of **10b** was achieved with sodium hydride and benzyl bromide to produce fully protected tetrasaccharide **10c**. Removal of the anomeric PMP protecting group with ceric ammonium nitrate gave hemiacetals **10d**, which were then converted to the corresponding trichloroacetimidate **10e**, before final glycosylation with acceptor **5** to yield the desired pentasaccharide **11** (Scheme 1).

This sequence represents a completely linear approach to the core *N*-glycan pentasaccharide in which the IAD reaction is performed as the first glycosylation reaction. Clearly, a more convergent synthesis would be considerably more efficient, and such possibilities were investigated next. The most convergent reaction sequence would be a [3+2] approach in which the difficult β-*manno* linkage

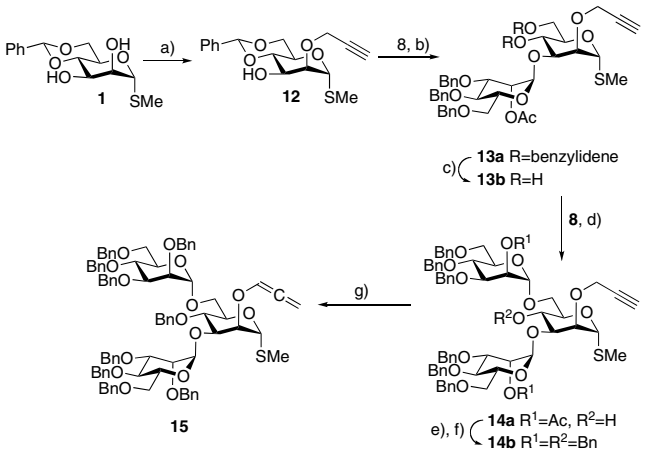


Scheme 1. Reagents and conditions: (a) $^{t}BuPh_2SiCl$, imidazole, CH_2Cl_2, rt, 84%; (b) propargyl bromide, NaH, DMF, rt, 72%; (c) $^{t}BuOK$, Et_2O, 66%; (d) **5**, I_2, AgOTf, DTBMP, CH_2Cl_2, −78 °C to rt, 88%; (e) Me_2S_2, Tf_2O, DTBMP, CH_2Cl_2, 0 °C to rt, 81%; (f) TBAF, THF, rt, 60%; (g) **8**, TMSOTf, CH_2Cl_2, −78 °C to rt; (h) Ac_2O, pyridine, rt, 86% over two steps; (i) 10% TFA in 10:1 MeCN–H_2O, 90%; (j) **8**, TMSOTf, CH_2Cl_2, −78 °C to rt, 76%; (k) K_2CO_3, MeOH, rt; (l) NaH, BnBr, DMF, rt, 77% over two steps; (m) $(NH_4)_2Ce(NO_3)_6$, toluene, MeCN, H_2O, rt, 77%; (n) Cl_3CCN, DBU, CH_2Cl_2, rt, 96%; (o) **5**, TMSOTf, CH_2Cl_2, −78 °C to rt, 85%.

was made as the final step by glycosylation of a tri-mannose donor with a chitobiose acceptor. The synthesis of the required tri-mannose donor was therefore undertaken as shown in Scheme 2. Regioselective propargylation of diol **1** was achieved using phase transfer conditions to give propargyl ether **12**, which was then glycosylated with trichloroacetimidate donor **8**[21] to yield disaccharide **13a**. Removal of the 4,6-benzylidene protection then yielded diol **13b**, which was regioselectively glycosylated[22] at the 6-position using the same donor **8**, to give trisaccharide **14a**. A protecting group exchange then allowed formation of the perbenzylated donor **14b**, which was finally isomerised to the required allene **15** by treatment with potassium *tert*-butoxide in DMSO (Scheme 2).

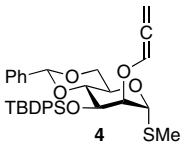
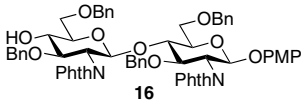
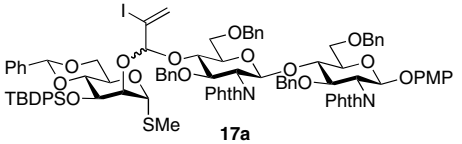
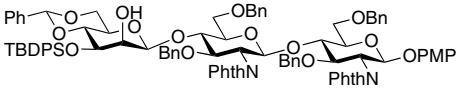
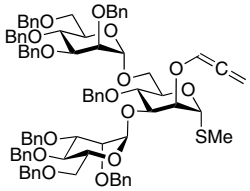
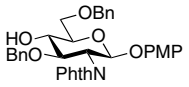
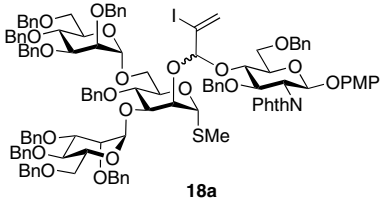
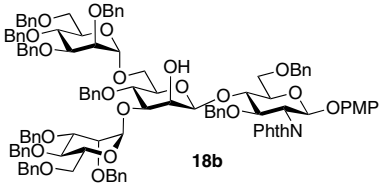
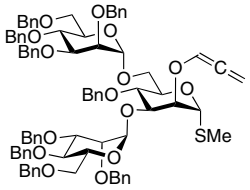
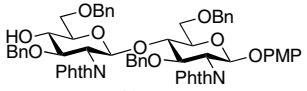
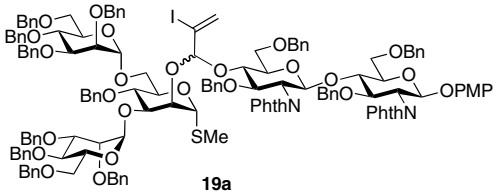
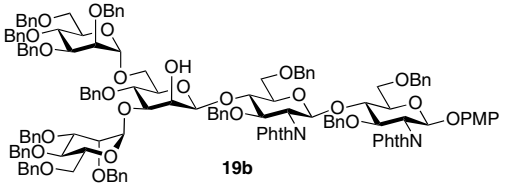
With trisaccharide allene **15** in hand, the efficiency of various possible convergent approaches was investigated (Table 1). Firstly a [1+2] IAD sequence was investigated using the monosaccharide allene **4** as donor, and the known chitobiose derivative **16** as acceptor. Iodonium ion mediated mixed acetal formation proceeded to give mixed acetals **17a** in good yield (Table 1, entry 1). However intramolecular glycosylation using the Fügedi conditions did not work as well as for the previous glycosylation of **6**, while trisaccharide **17b** was only produced in a modest 32% yield.

The next sequence investigated was a [3+1] IAD approach using trisaccharide allene **15** as the donor, and monosaccharide **5** as acceptor. Again mixed acetal formation proceeded in good yield to provide intermediates **18a** (Table 1, entry 2). However, the intramolecular glycosylation step did not work well at all and resulted in the formation of a complex mixture of products, from which the desired trisaccharide **18b** could only be isolated in pure form in a very poor yield (<10%). Finally, the most ambitious and most convergent [3+2] approach was attempted (Table 1, entry 3). Once



Scheme 2. Reagents and conditions: (a) Bu_4NHSO_4, propargyl bromide, CH_2Cl_2, 5% aqueous NaOH, rt, 60%; (b) **8**, TMSOTf, CH_2Cl_2, −78 °C to rt; (c) CF_3CO_2H, CH_3CN–H_2O, 10:1, 78% over two steps; (d) **8**, TMSOTf, CH_2Cl_2, −78 °C to rt, 77%; (e) K_2CO_3, MeOH, rt; (f) NaH, BnBr, DMF, rt, 91% over two steps; (g) $^{t}BuOK$, DMSO, 65 °C, 77%.

Table 1. Convergent approaches to *N*-glycan oligosaccharides using propargyl IAD

Entry	Allene donor	Acceptor	Mixed acetals/yield	Glycosylation product/yield
1	 **4**	 **16**	 **17a** 70%	 **17b** 32%
2	 **15**	 **5**	 **18a** 64%	 **18b** <5%
3	 **15**	 **16**	 **19a** 64%	 **19b** <5%

again mixed acetal formation proceeded as expected to produce **19a** (64% yield), but again the intramolecular glycosylation step failed to cleanly produce the desired pentasaccharide; indeed in this case it was not possible to isolate **19b** from the complex reaction mixture, although its presence was confirmed by mass spectrometric analysis.

These somewhat disappointing results are in line with the original findings of Hindsgaul,[7c] that is, that the intramolecular aglycon delivery approach only works well for the construction of the Manβ(1→4)GlcNAc linkage really with monosaccharide donors and acceptors. However these findings are in contrast with the reports of Ogawa,[23] and unfortunately it appears that, at least in our case, the use of IAD for the synthesis of *N*-glycan oligosaccharides is limited to a linear approach in which the β-mannose linkage is formed during the first glycosylation reaction.

3. Conclusions

In conclusion, the development of propargyl mediated IAD appears to represent a considerable improvement over the allyl IAD approach in terms of efficiency of the intramolecular glycosylation step for disarmed monosaccharide donors, and allows completion of the total synthesis of the core *N*-glycan pentasaccharide, which had not been achieved using the allyl approach. However, limitations of the use of this methodology become apparent when more convergent approaches to the *N*-glycan oligosaccharides are attempted and efficient sequences are only really achievable for the synthesis of *N*-glycan disaccharides.

4. Experimental

4.1. General

Melting points were recorded on a Kofler hot block. Proton and carbon nuclear magnetic resonance (δ_H, δ_C) spectra were recorded on Bruker DPX250 (250 MHz), Bruker DPX400 (400 MHz), Bruker AV400 (400 MHz), Bruker AV500 (500 MHz) or Bruker DRX500 (500 MHz) spectrometers. All chemical shifts are quoted on the δ-scale in parts per million using a residual solvent as an internal standard. ^{1}H and ^{13}C spectra were assigned using 2D NMR experiments including COSY, NOESY, ROESY, HSQC, HSQC 'non-decoupled', HSQC–TOCSY, TOCSY, HMBC, DEPT and APT. Identical proton coupling constants are averaged in each spectra and reported to the nearest 0.1 Hz. It should be noted that measured *J* values are limited by the digital resolution of 0.3 Hz per point. Carbohydrates and derivatives have been named in accordance with IUPAC recommendations and numbered according to the carbohydrate convention. The two protons on C-6 are labelled H-6 and H-6′. The individual components of oligosaccharides are distinguished by the assignment of a lowercase letter, given alphabetically starting from the reducing terminus. 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 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 Inorganic Chemistry Laboratory Elemental Analysis service. Thin-layer chromatography (TLC) was carried out on Merck Kieselgel $60F_{254}$ pre-coated 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. DCM was distilled from calcium hydride or dried via Alumina column (post January 2004). Anhydrous THF, DMF, pyridine, methanol 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.

4.2. General procedure for mixed acetal formation

Molecular sieves (4 Å) were suspended in freshly distilled DCM (1 ml) in a flame-dried flask under Ar. 2,6-Di-*tert*-butyl-4-methylpyridine (3 equiv), iodine (1.2 equiv) and silver triflate (1.2 equiv) were added. The mixture was stirred for 20 min at room temperature and then cooled to −78 °C. Allenyl donor (typically ∼100 mg, 1 equiv) and the acceptor alcohol (1.1 equiv) were dissolved in freshly distilled DCM (2 ml) and were then added to the reaction vessel by cannula under Ar. The reaction was stirred for 2 h at −78 °C and then allowed to warm to room temperature. After 17 h, TLC (typically petrol–ethyl acetate, 2:1) indicated complete consumption of starting allenyl ether and the formation of a major product. The reaction was quenched with sodium thiosulfate (typically 5 ml of a 10% aqueous solution) and then filtered. The aqueous layer was washed with DCM (2×10 ml) and the combined organic extracts dried over $MgSO_4$, filtered and concentrated in vacuo. The residue could be purified by flash column chromatography if desired (typically petrol–ethyl acetate, 4:1) to afford a pure sample of the mixed acetals, in which one diastereomer was predominant and could often be separately isolated.

4.3. General procedure for intramolecular glycosylation

Molecular sieves (4 Å) were suspended in freshly distilled DCM (typically 1 ml) in a flame-dried flask under Ar and 2,6-di-*tert*-butyl-4-methylpyridine (6 equiv), dimethyldisulfide (5 equiv) and triflic anhydride (5 equiv) were added. The mixture was stirred for 5 min at room temperature and then cooled at 0 °C. Mixed acetals (typically 30 mg, 1 equiv) were dissolved in freshly distilled DCM (typically 1 ml) and added to the reaction vessel by cannula under Ar. The stirred reaction was allowed to warm to room temperature. After 1 h, TLC (typically petrol–ethyl acetate, 2:1) indicated complete consumption of the starting material and formation of a major product (typically slightly more polar). The reaction was diluted with DCM (5 ml),

quenched with sodium bicarbonate (2 ml of a saturated aqueous solution) and then filtered. The aqueous layer was washed with DCM (2 × 10 ml) and the combined organic extracts dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was then purified by flash column chromatography (typically petrol–ethyl acetate, 2:1).

4.4. Methyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldiphenylsilyl-1-thio-α-D-mannopyranoside 2

Diol **1**[10b] (2.0 g, 6.70 mmol), imidazole (912 mg, 13.4 mmol) and *tert*-butyl (chloro)diphenylsilane (2.6 ml, 10.05 mmol) were dissolved in anhydrous DMF (30 ml). The reaction mixture was stirred under Ar at room temperature. After 14 h, TLC (petrol–ethyl acetate, 1:1) indicated the formation of a major product (R_f 0.92) and complete consumption of starting material (R_f 0.21). The reaction was concentrated in vacuo, and the residue was diluted with DCM and then washed with $NaHCO_3$ (150 ml of a saturated aqueous solution). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 85:15) to afford alcohol **2** (3.02 g, 84%) as a white amorphous foam. $[\alpha]_D^{17} = +115$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, $C(CH_3)_3$), 2.03 (3H, s, SCH_3), 2.97 (1H, br s, OH), 3.65 (1H, d, $J_{2,3}$ 2.6 Hz, H-2), 3.84 (1H, at, *J* 9.6 Hz, H-6), 4.01–4.10 (2H, m, H-4, H-5), 4.14–4.21 (2H, m, H-3, H-6′), 5.16 (1H, s, H-1), 5.47 (1H, s, PhCH), 7.21–7.44 (11H, m, 11 × Ar-H), 7.62–7.67 (4H, m, 4 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.4 (q, SCH_3), 19.2 (s, $C(CH_3)_3$), 27.0 (q, $C(CH_3)_3$), 63.7 (d, C-5), 68.6 (t, C-6), 70.9 (d, C-3), 72.6 (d, C-2), 79.0 (d, C-4), 85.2 (d, C-1), 101.9 (d, PhCH), 126.3, 127.5, 127.9, 128.0, 128.9, 129.7, 130.1, 135.8, 135.9 (9 × d, 15 × Ar-CH), 132.8, 132.9, 137.3 (3 × s, 3 × Ar-C); *m*/*z* (ES^+) 626 (100), 554 ($M+NH_4^+$, 92), 537 ($M+H^+$, 65). HRMS (ES^+) calcd for $C_{30}H_{37}O_5SSi$ ($M+H^+$) 537.2131. Found 537.2130.

4.5. Methyl 4,6-*O*-benzylidene-2-*O*-(prop-2-ynyl)-3-*O*-*tert*-butyldiphenylsilyl-1-thio-α-D-mannopyranoside 3

Alcohol **2** (2.04 g, 3.80 mmol) was dissolved in anhydrous DMF (5 ml) and cooled to 0 °C. Sodium hydride (60% in mineral oil) (167 mg, 4.18 mmol) and propargyl bromide (80% in toluene) (1.70 g, 11.4 mmol) were added and the reaction mixture stirred at 0 °C. After 10 min, TLC (petrol–ethyl acetate, 85:15) indicated formation of a major product (R_f 0.50) and complete consumption of starting material (R_f 0.23). The reaction was diluted with ether (100 ml) and quenched with NH_4Cl (50 ml of a saturated aqueous solution). The two phases were separated and the organic one washed with water (2 × 50 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 9:1) to afford propargyl ether **3** (1.58 g, 72%) as a white amorphous foam. $[\alpha]_D^{17} = +122$ (*c* 0.9, $CHCl_3$); 3278 (stretching C–H, C≡CH). δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, $C(CH_3)_3$), 2.05 (3H, s, SCH_3), 2.42 (1H, at, *J* 2.1 Hz, C≡CH), 3.59 (1H, d, $J_{2,3}$ 3.2 Hz, H-2), 3.83 (1H, at, *J* 10.0 Hz, H-6), 4.01 (1H, adt, *J* 4.8 Hz, *J* 9.7 Hz, H-5), 4.12 (1H, at, *J* 9.7 Hz, H-4), 4.16 (1H, dd, $J_{5,6'}$ 4.6 Hz, $J_{6,6'}$ 10.0 Hz, H-6′), 4.26–4.30 (2H, m, H-3, C*H*H′C≡CH), 4.38 (1H, dd, *J* 2.3 Hz, J_{gem} 15.8 Hz, CH*H*′C≡CH), 5.02 (1H, s, H-1), 5.41 (1H, s, PhCH), 7.23–7.46 (11H, m, 11 × Ar-H), 7.67–7.70 (4H, m, 4 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.8 (q, SCH_3), 19.4 (s, $C(CH_3)_3$), 26.9 (q, $C(CH_3)_3$), 59.0 (t, $CH_2C{\equiv}CH$), 64.5 (d, C-5), 68.6 (t, C-6), 71.0 (d, C-3), 74.9 (s, $CH_2C{\equiv}CH$), 79.0 (d, C-4), 79.5 (s, $CH_2C{\equiv}CH$), 79.9 (d, C-2), 84.9 (d, C-1), 101.8 (d, PhCH), 126.3, 127.4, 127.7, 128.0, 128.7, 129.5, 129.8, 136.0 (8 × d, 15 × Ar-CH), 133.5, 133.6, 137.4 (3 × s, 3 × Ar-C); *m*/*z* (ES^+) 664 (95), 649 (87), 575 ($M+H^+$, 100). HRMS (ES^+) calcd for $C_{33}H_{39}O_5SSi$ ($M+H^+$) 575.287. Found 575.286.

4.6. Methyl 4,6-*O*-benzylidene-2-*O*-(allenyl)-3-*O*-*tert*-butyldiphenylsilyl-1-thio-α-D-mannopyranoside 4

Propargyl ether **3** (878 mg, 1.53 mmol) was dissolved in anhydrous ether (15 ml). KO′Bu (515 mg, 4.59 mmol) was added and the reaction mixture stirred at room temperature. After 3.5 h, TLC (petrol–ethyl acetate, 9:1) indicated formation of a major product (R_f 0.40) and complete consumption of starting material (R_f 0.30). The reaction was diluted with ether (50 ml) and quenched with water (20 ml). The two phases were separated and the organic one washed with water (2 × 20 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 9:1, with 2% added triethylamine) to afford allene **4** (577 mg, 66%) as a colourless syrup. $[\alpha]_D^{20} = +67$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.05 (9H, s, $C(CH_3)_3$), 2.00 (3H, s, SCH_3), 3.69 (1H, d, $J_{2,3}$ 3.4 Hz, H-2), 3.82 (1H, at, *J* 10.1 Hz, H-6), 4.00 (1H, adt, *J* 4.7 Hz, *J* 9.7 Hz, H-5), 4.13 (1H, at, *J* 9.7 Hz, H-4), 4.16 (1H, dd, $J_{5,6'}$ 4.7 Hz, $J_{6,6'}$ 10.1 Hz, H-6′), 4.23 (1H, dd, $J_{3,4}$ 9.7 Hz, H-3), 5.08 (1H, s, H-1), 5.31 (1H, dd, *J* 5.9 Hz, J_{gem} 8.2 Hz, CH=C=C*H*H′), 5.42 (1H, dd, *J* 6.0 Hz, CH=C=CH*H*′), 5.50 (1H, s, PhCH), 6.77 (1H, at, *J* 5.9 Hz, C*H*=C=CHH′), 7.20–7.45 (11H, m, 11 × Ar-H), 7.67–7.70 (4H, m, 4 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.9 (q, SCH_3), 19.2 (s, $C(CH_3)_3$), 26.8 (q, $C(CH_3)_3$), 64.4 (d, C-5), 68.6 (t, C-6), 69.9 (d, C-3), 78.6 (d, C-2), 78.9 (d, C-4), 83.1 (d, C-1), 91.8 (t, CH=C=CH_2), 101.8 (d, PhCH), 120.9 (d, *C*H=C=CH), 126.3, 127.3, 127.7, 128.0, 128.8, 129.5, 129.7, 136.0 (8 × d, 15 × Ar-CH), 133.4, 133.7, 137.5 (3 × s, 3 × Ar-C), 200.4 (s, CH_2=*C*=CH); *m*/*z* (ES^+) 575 ($M+H^+$, 100). HRMS (ES^+) calcd for $C_{33}H_{38}O_5NaSSi$ ($M+H^+$) 597.2107. Found 597.2115.

4.7. Methyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldiphenylsilyl-2-*O*-(2-iodo-1-(*para*-methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosid-4-*O*-yl)prop-2-enyl)-1-thio-α-D-mannopyranoside 6

General procedure for mixed acetal formation using molecular sieves (4 Å), DCM (2 ml), 2,6-di-*tert*-butyl-4-methylpyridine (89 mg, 0.435 mmol), iodine (43 mg, 0.171 mmol), silver triflate (45 mg, 0.174 mmol), allenyl donor **4** (83 mg, 0.145 mmol) and *para*-methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside **5** (95 mg,

0.159), after purification by flash column chromatography (petrol–ethyl acetate, 8:2 to 1:1), afforded a pure sample of the major diastereomer of **6** (74 mg, 51%) and a mixture of both diastereomers of **6** (54 mg, 37%) as white amorphous foams. Data for major diastereomer: $[\alpha]_D^{20} = +79$ (*c* 0.8, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 0.98 (9H, s, $C(CH_3)_3$), 1.99 (3H, s, SCH_3), 3.63–3.78 (3H, m, H-5a, H-6a, H-2b), 3.73 (3H, s, OCH_3), 3.88–3.99 (3H, m, H-6′a, H-5b, H-6b), 4.17 (1H, dd, $J_{5b,6'b}$ 2.8 Hz, $J_{6b,6'b}$ 8.4 Hz, H-6′b), 4.22–4.28 (2H, m, H-4a, H-4b), 4.32 (1H, dd, $J_{2b,3b}$ 2.7 Hz, $J_{3b,4b}$ 9.9 Hz, H-3b), 4.42 (1H, at, *J* 9.4 Hz, H-3a), 4.48 (1H, dd, $J_{1a,2a}$ 8.1 Hz, $J_{2a,3a}$ 10.7 Hz, H-2a), 4.58, 5.40 (2H, ABq, *J* 12.2 Hz, $PhCH_2$), 4.62, 4.75 (2H, ABq, *J* 12.6 Hz, $PhCH_2$), 4.66 (1H, s, C*H*Cl=CH_2), 4.73 (1H, s, PhCH), 5.64 (1H, s, H-1b), 5.65 (1H, d, H-1a), 5.78 (1H, d, *J* 1.5 Hz, Cl=C*H*H′), 6.19 (1H, d, Cl=CH*H*′), 6.71–6.73 (2H, m, 2 × Ar-H), 6.84–6.88 (5H, m, 5 × Ar-H), 7.10–7.39 (18H, m, 18 × Ar-H), 7.58–7.62 (4H, m, 4 × Ar-H), 7.79–7.81 (4H, m, 4 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.6 (q, SCH_3), 19.3 (s, $C(CH_3)_3$), 27.2 (q, $C(CH_3)_3$), 55.6, 55.8 (OCH_3, C-2a), 65.3 (C-5b), 67.7, 68.5 (C-6a, C-6b), 70.6 (d, C-3b), 73.8, 75.8 (2 × t, 2 × $PhCH_2$), 74.9, 75.1 (2 × d, C-4a, C-5a), 78.0, 78.2, 78.3 (3 × d, C-3a, C-2b, C-4b), 82.6 (d, C-1b), 98.0 (d, C-1a), 101.5, 101.7 (2 × d, PhCH, CH(O)), 107.5 (s, *C*Cl=CH_2), 114.3, 118.8, 126.5, 127.2, 127.3, 127.4, 127.6, 127.9, 128.0, 128.3, 128.4, 128.6, 129.4, 129.5, 133.9, 136.1, 136.3 (33 × Ar-CH, Cl=*C*H_2), 133.4, 134.0, 137.6, 137.8, 138.9, 150.9, 155.4 (7 × s, 9 × Ar-C), 168.9 (2 × C=O). *m*/*z* (ES^+) 1354 (30), 1313 ($M+NH_4^+$, 100). HRMS (ES^+) calcd for $C_{68}H_{70}INO_{13}NaSSi$ ($M+Na^+$) 1318.3274. Found 1318.3267. Selected signals for the minor diastereomer: δ_H (400 MHz, $CDCl_3$) 0.98 (9H, s, $C(CH_3)_3$), 2.04 (3H, s, SCH_3), 3.71 (3H, s, OCH_3), 5.01 (1H, s, H-1b), 5.40 (1H, s, Cl=C*H*H′), 5.78 (1H, s, Cl=C*H*H′), 6.14 (1H, s, Cl=CH*H*′).

4.8. *p*-Methoxyphenyl-4,6-*O*-benzylidene-3-*O*-*tert*-butyldiphenylsilyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside 7a[10d]

General procedure for intramolecular glycosylation using molecular sieves (4 Å), DCM (2 ml), 2,6-di-*tert*-butyl-4-methylpyridine (19 mg, 0.092 mmol), dimethyldisulfide (7 μl, 0.077 mmol) and triflic anhydride (7 μl, 0.077 mmol), and mixed acetals **6** (20 mg, 0.0154 mmol) afforded a pure sample of disaccharide **7a** (13.5 mg, 81%) as white powder. $[\alpha]_D^{21} = +49$ (*c* 1.0, $CHCl_3$), lit.[10d] $[\alpha]_D^{21} = +51.1$ (*c* 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 1.06 (9H, s, $C(CH_3)_3$), 2.99 (1H, adt, *J* 4.9 Hz, *J* 9.7 Hz, H-5b), 3.53 (1H, dd, $J_{5a,6a}$ 3.5 Hz, $J_{6a,6'a}$ 11.3 Hz, H-6a), 3.58 (1H, at, *J* 10.2 Hz, H-6b), 3.64–3.69 (3H, m, H-5a, H-6′a, H-2b), 3.71 (3H, s, OCH_3), 3.78 (1H, dd, $J_{2b,3b}$ 3.2 Hz, $J_{3b,4b}$ 9.3 Hz, H-3b), 3.93 (1H, at, *J* 9.3 Hz, H-4b), 4.09 (1H, at, *J* 9.2 Hz, H-4a), 4.17 (1H, dd, $J_{5b,6'b}$ 4.9 Hz, $J_{6b,6'b}$ 10.4 Hz, H-6′b), 4.32, 4.61 (2H, ABq, *J* 11.9 Hz, $PhCH_2$), 4.39 (2H, m, H-2a, H-3a), 4.48 (1H, s, H-1b), 4.49, 4.85 (2H, ABq, *J* 12.3 Hz, $PhCH_2$), 5.38 (1H, s, PhCH), 5.58 (1H, d, $J_{1a,2a}$ 7.8 Hz, H-1a), 6.69 (2H, d, *J* 9.0 Hz, 2 × Ar-H), 6.80 (2H, d, *J* 9.0 Hz, 2 × Ar-H), 6.86–6.90 (3H, m, 3 × Ar-H), 7.03 (2H, d, *J* 6.8 Hz, 2 × Ar-H), 7.14–7.46 (10H, m, 10 × Ar-H), 7.67–7.71 (4H, m, 4 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 19.3 (s, $C(CH_3)_3$), 26.8 (q, $C(CH_3)_3$), 55.5 (OCH_3, C-2a), 66.5 (d, C-5b), 68.0 (t, C-6b), 68.5 (t, C-6a), 71.4 (d, C-2b), 72.6 (d, C-3b), 73.4 (2 × t, 2 × $PhCH_2$), 74.7 (C-5a, $PhCH_2$), 78.3 (d, C-4b), 78.7 (d, C-4a), 97.7 (d, C-1a), 100.3 (d, C-1b), 101.8 (d, PhCH), 114.3, 118.8, 123.3, 126.2, 127.1, 127.4, 127.7, 127.8, 127.9, 128.0, 128.4, 128.8, 129.7, 130.0, 132.8, 133.7, 135.6, 135.9 (33 × Ar-CH), 133.4, 134.0, 137.3, 137.7, 138.4, 150.8, 155.4 (7 × s, 9 × Ar-C), 168.9 (2 × C=O). *m*/*z* (ES^+) 1354 (30), 1313 ($M+NH_4^+$, 100). HRMS (ES^+) calcd for $C_{64}H_{65}NO_{13}NaSi$ ($M+Na^+$) 1106.4117. Found 1106.4118.

4.9. *p*-Methoxyphenyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside 7b

Disaccharide **7a** (400 mg, 0.37 mmol) was dissolved in dry DMF (5 ml) and treated with TBAF (0.74 ml of 1 M solution in THF). The reaction mixture was stirred overnight at room temperature under Ar. TLC (petrol–ethyl acetate, 1:1) indicated complete consumption of starting material (R_f 0.71) and formation of a major product (R_f 0.08). The reaction mixture was diluted with ethyl acetate (50 ml) and Et_2O (50 ml) and washed with water (20 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 4:6) to afford alcohol **7b** (190 mg, 60%) as white foam. $[\alpha]_D^{17} = +41$ (*c* 0.8, $CHCl_3$), ν_{max} (KBr disc) 1775, 1713 (s, C=O) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 2.58 (1H, d, $J_{3b,OH}$ 6.6 Hz, OH), 2.76 (1H, s, OH), 3.18 (1H, adt, *J* 5.0 Hz, *J* 9.7 Hz, H-5b), 3.59 (1H, at, *J* 10.2 Hz, H-6b), 3.63 (1H, ddd, $J_{2b,3b}$ 3.4 Hz, $J_{3b,4b}$ 9.5 Hz, H-3b), 3.72 (3H, s, OCH_3), 3.73 (1H, m, H-5a), 3.78 (1H, at, *J* 9.4 Hz, H-4b), 3.79 (1H, dd, $J_{5a,6a}$ 2.2 Hz, $J_{6a,6'a}$ 11.3 Hz, H-6a), 3.84 (1H, dd, $J_{5a,6'a}$ 3.4 Hz, H-6′a), 3.96 (1H, br s, H-2b), 4.18–4.21 (2H, m, H-4a, H-6b), 4.45 (2H, m, H-2a, H-3a), 4.47, 4.84 (2H, ABq, *J* 12.1 Hz, $PhCH_2$), 4.53, 4.76 (2H, ABq, *J* 11.9 Hz, $PhCH_2$), 4.77 (1H, s, H-1b), 5.48 (1H, s, PhCH), 5.63 (1H, m, H-1a), 6.70–6.73 (2H, m, 2 × Ar-H), 6.81–6.84 (2H, m, 2 × Ar-H), 6.89–6.97 (3H, m, 3 × Ar-H), 7.05 (2H, m, 2 × Ar-H), 7.34–7.41 (8H, m, 8 × Ar-H), 7.47–7.49 (2H, m, 2 × Ar-H) 7.64–7.86 (4H, m, 4 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 55.6 (OCH_3), 55.7 (d, C-2a), 66.6 (C-5b), 68.4 (C-6a), 68.5 (C-6b), 70.6 (d, C-3b), 70.7 (d, C-2b), 73.8, 74.8 (2 × t, 2 × $PhCH_2$), 74.6 (d, C-5a), 77.7 (d, C-3a), 78.4 (d, C-4b), 78.6 (d, C-4a), 97.8 (d, C-1a), 100.5 (d, C-1b), 102.1 (d, PhCH), 114.4, 118.8, 123.4, 126.2, 127.3, 128.0, 128.1, 128.3, 128.6, 129.2, 133.8 (33 × Ar-CH), 131.5, 137.1, 137.5, 138.1, 150.8, 155.4 (9 × Ar-C), 168.9 (2 × C=O). *m*/*z* (ES^+) 868 ($M+Na^+$, 10), 904 (M+59, 100), 1749 (2M+59, 100), HRMS (ES^+) calcd for $C_{48}H_{47}NO_{13}Na$ ($M+Na^+$) 868.2940. Found 868.2940.

4.10. *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-phthalamido-β-D-glucopyranoside 9a

Disaccharide **7b** (65 mg, 0.077 mmol) and trichloroacetimidate **8** (54 mg, 0.085 mmol) were dissolved in dry DCM

(8 ml) and transferred via cannula to a flame-dried flask containing powdered molecular sieves (4 Å, 100 mg). The solution was stirred for 30 min at room temperature, then cooled to −78 °C and stirred under an atmosphere of argon. TMSOTf (2.8 μl, 15.4 μmol) was added and the mixture was stirred at −78 °C for 1 h, after which the temperature was allowed to rise to room temperature overnight. TLC (petrol–ethyl acetate, 3:2) indicated the formation of a major product (R_f 0.32) and complete consumption of acceptor (R_f 0). Triethylamine (50 μl) was added and the solution stirred for a further 10 min. The reaction mixture was then filtered, diluted with DCM (50 ml), washed with sodium hydrogen carbonate (50 ml of a saturated solution), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was directly acetylated using standard conditions (Ac_2O, pyridine, DMAP) and after evaporation of solvent, the crude residue was purified by flash column chromatography (petrol–ethyl acetate, 7:3→6:4) to give trisaccharide **9a** (90 mg, 86%) as a white foam. R_f 0.43 (petrol–ethyl acetate, 3:2); $[\alpha]_D^{23} = +20$ (*c* 1.0, $CHCl_3$); ν_{max} (KBr disc) 1749, 1716 (s, C=O) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 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(O)), 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); δ_C (125.8 MHz, $CDCl_3$) 20.9, 21.1 (2 × q, 2 × OC(O)*C*H_3), 55.6 (d, C-2a), 55.6 (PhO*C*H_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, Ph*C*H_2), 72.1 (d, C-5c), 72.7 (d, C-4c), 73.5, 73.5 (2 × t, 2 × Ph*C*H_2), 74.1 (d, C-4b), 74.7 (t, Ph*C*H_2), 74.7 (d, C-5a), 74.8 (t, Ph*C*H_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.

4.11. *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-phthalamido-β-D-glucopyranoside 9b

Benzylidene acetal **9a** (90 mg, 0.066 mmol) was dissolved in DCM (8 ml) and trifluoroacetic acid (0.5 ml) was added. The reaction mixture was stirred for 2 h at room temperature and TLC (petrol–ethyl acetate, 1:2) indicated the formation of a major product (R_f 0.2) and full consumption of starting material (R_f 0.75). The reaction mixture was concentrated in vacuo after which the crude was dissolved in DCM (50 ml) and washed with sodium hydrogen carbonate (4 × 20 ml of a saturated solution). The organic phase was dried over $MgSO_4$, filtered and concentrated at reduced pressure and the residue was purified by flash column chromatography (petrol–ethyl acetate, 3:7) to give trisaccharide diol **9b** (76 mg, 91%) as a white foam. $[\alpha]_D^{23} = +40$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr disc) 3476 (br, OH), 1777, 1747, 1716 (s, C=O); δ_H (500 MHz, $CDCl_3$) 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); δ_C (125.8 MHz, $CDCl_3$) 21.1, 21.8 (2 × q, 2 × OC(O)*C*H_3), 55.6 (d, C-2a), 55.6 (O*C*H_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, 73.5, 73.6, 74.5, 74.9 (5 × t, 5 × PhCH_2), 74.3 (d, C-4c), 74.7 (d, C-5a), 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.

4.12. *p*-Methoxyphenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)-[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-phthalamido-β-D-glucopyranoside 10a

Trisaccharide diol **9b** (233 mg, 183 μmol) and trichloroacetimidate **8** (128 mg, 201 μmol) were dissolved in dry DCM (10 ml) and transferred via cannula to a flame-dried flask containing molecular sieves (4 Å, 200 mg). The solution was cooled to −78 °C and stirred under an atmosphere of argon. TMSOTf (3.31 μl, 18.3 μmol) was added and the temperature allowed to rise to 0 °C after 3 h. After 5 h, TLC (petrol–ethyl acetate, 1:1) indicated the formation of

a major product (R_f 0.3) and complete consumption of acceptor (R_f 0.05). Triethylamine (100 μl) was added and the solution stirred for a further 10 min. The reaction mixture was diluted with DCM (100 ml) washed with sodium hydrogen carbonate (50 ml of a saturated solution), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 1:1) to give tetrasaccharide **10a** (243 mg, 76%) as a white foam. $[\alpha]_D^{22} = +39$ (*c* 0.25, $CHCl_3$); ν_{max} (KBr disc) 3459 (br, OH), 1777, 1746, 1716 (s, C=O); δ_H (500 MHz, $CDCl_3$) 2.00, 2.06, 2.12 (9H, 3 × s, 3 × OC(O)CH_3), 3.07 (1H, dat, $J_{4b,5b}$ 9.6 Hz, *J* 2.7 Hz, H-5b), 3.50 (1H, br s, OH), 3.56 (1H, dd, $J_{2b,3b}$ 3.2 Hz, $J_{3b,4b}$ 9.7 Hz, H-3b), 3.58–3.60 (1H, m, H-5a), 3.65–3.78 (11H, m, H-5d, H-6a, H-6b, H-6c, H-6d, H-6′a, H-6′c, H-6′d, OCH_3), 3.82 (1H, at, *J* 9.5 Hz, H-4d), 3.82 (1H, dd, $J_{2d,3d}$ 2.3 Hz, $J_{3d,4d}$ 9.3 Hz, H-3d), 3.86–3.87 (2H, m, H-3c, H-5c), 3.91–3.98 (3H, m, H-4b, H-4c, H-6′b), 4.10 (1H, at, *J* 9.4 Hz, H-4a), 4.20, 4.41 (2H, ABq, *J* 11.1 Hz, $PhCH_2$), 4.25 (1H, dd, $J_{2a,3a}$ 10.6 Hz, $J_{3a,4a}$ 8.5 Hz, H-3a), 4.34 (1H, dd, $J_{1a,2a}$ 8.5 Hz, H-2a), 4.44, 4.77 (2H, ABq, *J* 10.6 Hz, $PhCH_2$), 4.45–4.53 (6H, m, 6 × PhCH), 4.64–4.69 (5H, m, H-1b, 4 × PhCH), 4.83 (1H, d, $J_{1d,2d}$ 1.7 Hz, H-1d), 4.85 (1H, d, *J* 11.2 Hz, PhCH), 4.86 (1H, d, *J* 12.8 Hz, PhCH), 5.20 (1H, d, $J_{1c,2c}$ 1.2 Hz, H-1c), 5.30 (1H, dd, H-2d), 5.35 (1H, br d, H-2b), 5.41 (1H, m, H-2c), 5.56 (1H, d, H-1a), 6.67–6.69 (2H, m, 2 × Ar-H), 6.74–6.79 (5H, m, 5 × Ar-H), 6.97–6.98 (2H, m, 2 × Ar-H), 7.10–7.11 (2H, m, 2 × Ar-H), 7.14–7.16 (2H, m, 2 × Ar-H), 7.19–7.36 (31H, m, 31 × Ar-H), 7.64–7.81 (4H, m, 4 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 20.9, 21.0, 21.1 (3 × q, 3 × OC(O)CH_3), 55.5 (q, OCH_3), 55.6 (d, C-2a), 66.1 (t, C-6b), 66.8 (d, C-4b), 68.1, 68.7, 68.9 (3 × t, C-6a, C-6c, C-6d), 68.4 (d, C-2d), 68.9 (d, C-2c), 71.0 (d, C-2b), 71.5, 71.8, 73.3, 73.3, 73.4, 74.5, 74.7, 75.3 (8 × t, $PhCH_2$), 71.8 (d, C-4d), 71.9 (d, C-4c), 74.1 (d, H-5c), 74.3 (d, H-5d), 74.6 (2 × d, C-5a, C-5b), 76.8 (d, C-3a), 77.7 (d, C-3c), 77.9 (d, C-3b), 78.2 (d, C-3d), 78.8 (d, C-4a), 97.5 (d, C-1a), 97.9 (d, C-1d), 99.1 (d, C-1b), 99.3 (d, C-1c), 114.3, 118.5, 123.2, 127.2, 127.4, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.0, 128.0, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 128.5 (21 × d, 46 × Ar-C), 131.6 (s, 2 × Ar-C), 133.6 (d, 2 × Ar-C), 137.8, 137.8, 137.9, 138.0, 138.0, 138.2, 138.5, 138.5, 150.8, 155.3 (10 × s, 10 × Ar-C), 170.0, 170.4, 170.5 (3 × s, 5 × C=O); $J_{C\text{-}1a/H\text{-}1a}$ 167 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ 160 Hz (β), $J_{C\text{-}1c/H\text{-}1c}$ 174 Hz (α), $J_{C\text{-}1d/H\text{-}1d}$ 173 Hz (α); *m*/*z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 1770.7 (84%), 1771.7 (100%), 1772.7 (51%), 1773.7 (16%), 1774.7 (5%), 1775.7 (1%), peaks calculated: 1770.7 (89%), 1771.7 (100%), 1772.7 (60%), 1773.7 (26%), 1774.7 (9%), 1775.7 (2%).

4.13. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalamido-β-D-glucopyranoside 10c

Tetrasaccharide **10a** (175 mg, 0.10 mmol) was dissolved in dry MeOH (5 ml) and anhydrous K_2CO_3 (28 mg, 0.20 mmol) was added at room temperature. The mixture was heated at 45 °C and stirred at room temperature overnight. The solution was concentrated and the residue was dissolved in dry MeOH (3 ml) and treated with Ac_2O (1 ml). The mixture was stirred for 3 h, then concentrated in vacuo and repeatedly co-evaporated with toluene. The residue was dissolved in DMF (3 ml), treated with TsOH (4 mg, 0.021 mmol) and stirred at room temperature for 5 h at reduced pressure (40 mbar). The reaction mixture was quenched by the addition of Et_3N (200 μl) and evaporated in vacuo. The crude residue containing **10b** was then dissolved in dry DMF (3 ml) and treated with BnBr (142 μl, 1.2 mmol) and sodium hydride (32 mg of a 60% mineral oil dispersion, 0.8 mmol). The mixture was stirred for 2 h at room temperature and a TLC (petrol–ethyl acetate, 3:2) revealed complete consumption of starting material (R_f 0) and formation of a major product (R_f 0.56). The reaction was quenched by adding MeOH and then diluted with ether (50 ml) and washed with water (50 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 7:3) to afford perbenzylated tetrasaccharide **10c** (153 mg, 77%) as a white amorphous foam; $[\alpha]_D^{17} = +42$ (*c* 0.50, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 3.21 (1H, dat, $J_{4b,5b}$ 9.2 Hz, *J* 2.7 Hz, H-5b), 3.40 (1H, dat, $J_{4a,5a}$ 9.8 Hz, *J* 2.5 Hz, H-5a), 3.49–3.64 (6H, H-3b, H-5d, H-6a, H-6d, H-6′a, H-6′d), 3.67–3.74 (4H, m, H-2d, H-6b, H-6c, H-6′c), 3.71 (3H, s, OCH_3), 3.75 (1H, at, *J* 2.2 Hz, H-2c), 3.82 (1H, dd, $J_{2d,3d}$ 3.0 Hz, $J_{3d,4d}$ 9.5 Hz, H-3d), 3.87 (1H, dd, $J_{5b,6'b}$ 3.9 Hz, $J_{6b,6'b}$ 12.1 Hz, H-6′b), 3.91–3.99 (6H, m, H-2b, H-3c, H-4b, H-4c, H-4d, H-5c), 4.06 (1H, dd, $J_{3a,4a}$ 8.5 Hz, H-4a), 4.22 (1H, dd, $J_{2a,3a}$ 10.6 Hz, H-3a), 4.30–4.37 (5H, m, H-2a, 4 × PhCH), 4.44–4.62 (14H, m, 14 × PhCH), 4.63 (1H, s, H-1b), 4.82 (1H, d, *J* 10.9 Hz, PhCH), 4.86 (2H, d, *J* 12.6 Hz, 2 × PhCH), 4.90 (1H, d, *J* 11.1 Hz, PhCH), 5.01 (1H, d, $J_{1d,2d}$ 1.5 Hz, H-1d), 5.04 (1H, d, *J* 12.0 Hz, PhCH), 5.19 (1H, d, $J_{1c,2c}$ 1.5 Hz, H-1c), 5.55 (1H, d, $J_{1a,2a}$ 8.5 Hz, H-1a), 6.60–6.71 (5H, m, 5 × Ar-H), 6.79–6.85 (4H, m, 4 × Ar-H), 7.07–7.35 (55H, m, 55 × Ar-H), 7.43–7.81 (4H, m, 4 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 55.5 (d, C-2a), 55.6 (q, OCH_3), 66.3 (t, C-6b), 68.1 (t, C-6a), 69.0 (t, C-6d), 70.0 (t, C-6c), 71.2 (t, $PhCH_2$), 72.2 (t, $PhCH_2$), 72.2 (d, C-5d), 72.4 (t, $PhCH_2$), 72.8 (d, C-5c), 73.2, 73.3, 73.4, 74.3, 74.3, 74.5 (6 × t, 7 × $PhCH_2$), 74.5, 74.6 (2 × d, C-4b, C-4c, C-4d, C-5b), 74.8 (t, $PhCH_2$), 74.8 (d, C-2d), 74.9 (d, C-5a), 75.0 (t, $PhCH_2$), 75.5 (d, C-2c), 76.8 (d, C-3a), 78.5 (d, C-2b), 79.5 (d, C-3d), 79.5 (d, C-4a), 80.0 (d, C-3c), 81.5 (d, C-3b), 97.6 (d, C-1a), 98.1 (d, C-1d), 100.3 (d, C-1c), 102.0 (d, C-1b), 114.3, 118.7, 123.2, 126.5, 127.0, 127.1, 127.2, 127.3, 127.3, 127.4, 127.5, 127.6, 127.7, 127.7, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 128.4 (25 × d, 66 × Ar-C), 131.7 (s, 2 × Ar-C), 133.5 (d, 2 × Ar-C), 138.0, 138.2, 138.3, 138.3, 138.4, 138.5, 138.6, 138.6, 138.7, 139.0, 150.9, 155.3 (12 × s, 14 × Ar-C), 167.4, 167.9 (2 × s, 2 × C=O); $J_{C\text{-}1a/H\text{-}1a}$ 166 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ 158 Hz (β), $J_{C\text{-}1c/H\text{-}1c}$ 172 Hz (α), $J_{C\text{-}1d/H\text{-}1d}$ 170 Hz (α); *m*/*z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 2004.8 (66%), 2005.8 (100%), 2006.8 (61%), 2007.8 (23%), 2008.8 (6%), 2009.8 (2%), peaks calculated: 2004.8 (74%), 2005.8 (100%), 2006.8 (71%), 2007.8 (35%), 2008.9 (13%), 2009.9 (4%).

4.14. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalamido-β-D-glucopyranose 10d

Tetrasaccharide **10c** (160 mg, 80 μmol) was dissolved in a mixture of toluene, acetonitrile and water 1:4:2 (3 ml). Ceric ammonium nitrate (222 mg, 0.40 mmol) was added and the solution stirred at room temperature overnight. TLC (petrol–ethyl acetate, 6:4) indicated the formation of a major product (R_f 0.20) and complete consumption of the starting material (R_f 0.56). The reaction mixture was diluted with DCM (20 ml) and washed with brine (10 ml), sodium hydrogen carbonate (2 × 10 ml of a saturated solution), water (10 ml) and finally dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 6:4) to give hemiacetals **10d** as a white amorphous foam (116 mg, 77%). *m/z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 1898.78 (73%), 1899.79 (100%), 1900.79 (57%), 1901.79 (17%), 1902.79 (4%), 1903.80 (1%), peaks calculated: 1898.79 (78%), 1899.80 (100%), 1900.80 (67%), 1901.81 (31%), 1902.81 (11%), 1903.81 (3%). δ_H (400 MHz, $CDCl_3$, significant peaks only) 5.00 (1H, br s, H-1d), 5.19 (1H, d, $J_{1c,2c}$ 1.3 Hz, H-1c), 5.56 (1H, d, $J_{1a,2a}$ 8.5 Hz, H-1a); δ_C (100.6 MHz, $CDCl_3$, significant peaks only) 93.2 (d, C-1a), 98.5 (d, C-1d), 100.0 (d, C-1c), 100.7 (d, C-1b).

4.15. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalamido-β-D-glucopyranosyl trichloroacetimidate 10e

Trichloroacetonitrile (53 μl, 0.53 mmol) was added to a solution of hemiacetals **10d** (100 mg, 53 μmol) in freshly distilled DCM (2 ml). DBU was added (2 μl,13 μmol) and the mixture stirred at room temperature overnight. TLC (petrol–ethyl acetate, 6:4) indicated the formation of a major product (R_f 0.38) and complete consumption of the starting material (R_f 0.20). The solution was concentrated at a reduced pressure and the residue purified on a plug of silica gel eluting with petrol–ethyl acetate 1:1 to afford pure trichloroacetimidate **10e** (103 mg, 96%), which was used directly in the next step. δ_H (400 MHz, $CDCl_3$, significant peaks only) 5.00 (1H, br s, H-1d), 5.19 (1H, br s, H-1c), 6.34 (1H, d, $J_{1a,2a}$ 8.9 Hz, H-1a), 8.53 (s, 1H, C=NH).

4.16. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalamido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalamido-β-D-glucopyranoside 11

Glycosyl acceptor **5** (59 mg, 99 μmol) and trichloroacetimidate **10e** (100 mg, 49 μmol) were dissolved in freshly distilled DCM (2 ml) and transferred via cannula to a flame-dried flask containing powdered molecular sieves (4 Å, 100 mg). The mixture was stirred for 30 min at room temperature, then cooled to −78 °C and stirred under an atmosphere of Ar. TMSOTf (2 μl, 11 μmol) was added after which the mixture was stirred at −78 °C for 1 h, then the temperature was allowed to rise to room temperature overnight. TLC (petrol–ethyl acetate, 1:1) revealed the formation of a major product (R_f 0.75) and complete consumption of trichloroacetimidate (R_f 0.90). Triethylamine (50 μl) was added and the solution stirred for a further 10 min. The reaction mixture was then diluted with DCM (20 ml), filtered, washed with sodium hydrogen carbonate (20 ml of a saturated solution), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 3:2) to give pentasaccharide **11** (103 mg, 85%). $[\alpha]_D^{17} = +30$ (*c* 0.9, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 3.17–3.21 (2H, m, H-5b, H-5c), 3.37–3.41 (2H, m, H-5a, H-6a), 3.44 (1H, dd, $J_{5b,6b}$ 2.7 Hz, $J_{6b,6'b}$ 11.5 Hz, H-6b), 3.47–3.51 (2H, m, H-6e, H-6′a), 3.57–3.60 (2H, m, H-5e, H-6′e), 3.62–3.74 (6H, H-2e, H-3c, H-6c, H-6d, H-6′b, H-6′d), 3.65 (3H, s, OCH_3), 3.76 (1H, m, H-2d), 3.81 (1H, dd, $J_{2e,3e}$ 3.1 Hz, $J_{3e,4e}$ 9.5 Hz, H-3e), 3.85–3.86 (1H, m, H-6′c), 3.90–3.97 (6H, m, H-2c, H-3d, H-4c, H-4d, H-4e, H-5d), 4.07 (1H, dd, $J_{3b,4b}$ 7.9 Hz, $J_{4b,5b}$ 9.8 Hz, H-4b), 4.15–4.20 (4H, m, H-2b, H-3a, H-3b, H-4a), 4.25–4.35 (5H, m, H-2a, 4 × PhCH), 4.39–4.62 (18H, m, 18 × PhCH), 4.65 (1H, d, *J* 11.9 Hz, PhCH), 4.65 (1H, s, H-1c), 4.81 (1H, d, *J* 10.3 Hz, PhCH), 4.85 (1H, d, *J* 11.1 Hz, PhCH), 4.85 (1H, d, *J* 12.9 Hz, PhCH), 4.87 (1H, d, *J* 12.2 Hz, PhCH), 4.90 (1H, d, *J* 11.1 Hz, PhCH), 4.97 (1H, d, $J_{1e,2e}$ 1.1 Hz, H-1e), 5.03 (1H, d, *J* 12.0 Hz, PhCH), 5.21 (1H, d, $J_{1d,2d}$ 1.3 Hz, H-1d), 5.23 (1H, d, $J_{1b,2b}$ 7.8 Hz, H-1b), 5.44 (1H, d, $J_{1a,2a}$ 8.5 Hz, H-1a), 6.58–6.6.84 (12H, m, 12 × Ar-H), 6.94–7.39 (54H, m, 54 × Ar-H), 7.43–7.90 (16H, m, 16 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 55.5 (d, C-2a), 55.6 (q, OCH_3), 56.5 (d, C-2b), 66.3 (t, C-6c), 67.6 (t, C-6b), 68.0 (t, C-6a), 69.0 (t, C-6e), 69.6 (t, C-6d), 71.2 (t, $PhCH_2$), 72.2 (2 × t, 2 × $PhCH_2$), 72.2 (d, C-5e), 72.4 (t, $PhCH_2$), 72.6 (t, $PhCH_2$), 72.9 (d, C-5d), 73.0, 73.2, 73.4, 74.3 (4 × t, 4 × $PhCH_2$), 74.3 (d, C-4d), 74.4 (t, $PhCH_2$), 74.5 (2 × d, C-4c, C-5c), 74.6, 74.6 (2 × t, 2 × $PhCH_2$), 74.6 (d, C-5a), 74.7 (d, C-5b), 74.8 (t, $PhCH_2$), 74.8 (2 × d, C-2e, C-4e), 75.0 (t, $PhCH_2$), 75.5 (d, C-2d), 76.0, 76.7, 76.9 (3 × d, C-3a, C-3b, C-4a), 78.6 (d, C-2c), 79.4 (d, C-3e), 79.7 (d, C-4b), 80.0 (d, C-3d), 81.4 (d, C-3c), 97.1 (d, C-1b), 97.4 (d, C-1a), 98.1 (d, C-1e), 100.2 (d, C-1d), 102.0 (d, C-1c), 114.2, 118.5, 123.0, 123.2, 126.5, 126.9, 127.0, 127.1, 127.2, 127.2, 127.3, 127.4, 127.5, 127.5, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 128.5, 128.5 (29 × d, 78 × Ar-C), 131.4, 131.8 (2 × s, 4 × Ar-C), 133.6, 133.9 (2 × d, 4 × Ar-C), 137.6, 138.0, 138.1, 138.2, 138.3, 138.3, 138.4, 138.4, 138.5, 138.6, 138.7, 138.8, 139.0, 150.8, 155.2 (15 × s, 16 × Ar-C), 167.4, 168.1 (2 × s, 4 × C=O); $J_{C\text{-}1a/H\text{-}1a}$ 167 Hz (β), $J_{C\text{-}1b/H\text{-}1b}$ 167 Hz (β), $J_{C\text{-}1c/H\text{-}1c}$ 158 Hz (β), $J_{C\text{-}1d/H\text{-}1d}$ 171 Hz (α), $J_{C\text{-}1e/H\text{-}1e}$ 171 Hz (α); *m/z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 2476.0 (49%), 2477.0 (100%), 2478.0 (79%), 2479.0 (36%), 2480.0 (10%), 2481.0 (3%), peaks calculated: 2476.0 (60%), 2477.0 (100%), 2478.0 (87%), 2479.0 (52%), 2480.0 (24%), 2481.0 (9%).

4.17. Methyl 4,6-*O*-benzylidene-2-*O*-(prop-2-ynyl)-1-thio-α-D-mannopyranoside 12

Diol **1** (5.0 g, 16.7 mmol) was dissolved in DCM (150 ml) and propargyl bromide (80% in toluene) (3.7 g, 25.05 mmol), Bu_4NHSO_4 (1.13 g, 3.34 mmol) and 5% aq NaOH (23 ml) were added. The mixture was stirred for 2 days at room temperature after which TLC (petrol–ethyl acetate, 7:3) revealed complete consumption of starting material (R_f 0.09) and formation of several products, the major one with R_f 0.39. The two phases were separated and the organic one was washed with water (100 ml) and brine (100 ml) and successively dried over $MgSO_4$, filtered and concentrated in vacuo. After recrystallisation (isopropanol), a pure sample of propargyl ether **12** was obtained (2.8 g, 50%); mp 175–177 °C (isopropanol); $[\alpha]_D^{20} = +122$ (*c* 0.8, $CHCl_3$); ν_{max} (KBr disc) 3274 (stretching C–H, C≡CH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.18 (3H, s, SCH_3), 2.41 (1H, at, *J* 2.4 Hz, C≡CH), 3.86 (1H, at, *J* 10.0 Hz, H-6), 3.92 (1H, at, *J* 9.4 Hz, H-4), 4.08–4.09 (2H, m, H-2, H-3), 4.18 (1H, adt, *J* 4.8 Hz, *J* 9.6 Hz, H-5), 4.25 (1H, dd, $J_{5,6'}$ 4.9 Hz, $J_{6,6'}$ 10.0 Hz, H-6′), 4.36 (1H, dd, *J* 2.4 Hz, J_{gem} 16.1 Hz, C*H*H′C≡CH), 4.43 (1H, dd, CH*H*′C≡CH), 5.35 (1H, s, H-1), 5.58 (1H, s, PhCH), 7.36–7.52 (5H, m, 5 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.9 (q, SCH_3), 58.5 (t, *C*H_2C≡CH), 63.9 (d, C-5), 68.6 (t, C-6), 68.9 (d, C-3), 75.6 (s, CH_2C≡*C*H), 79.0 (s, CH_2*C*≡CH), 79.1 (d, C-2), 79.6 (d, C-4), 84.1 (d, C-1), 102.2 (d, PhCH), 126.3, 128.3, 129.2 (3 × d, 5 × Ar-CH), 137.4 (s, Ar-C); *m*/*z* (ES^+) 395 (95), 337 ($M+H^+$, 90). HRMS (ES^+) calcd for $C_{17}H_{20}NaO_5S$ ($M+Na^+$) 359.0924. Found 359.0924.

4.18. Methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2-*O*-(prop-2-ynyl)-1-thio-α-D-mannopyranoside 13b

Alcohol **12** (1.10 g, 3.27 mmol) and trichloroacetimidate **8** (2.29 g, 3.60 mmol) were dissolved in dry DCM (120 ml) and transferred via cannula to a flame-dried flask containing powdered molecular sieves (4 Å, 5.0 g). The mixture was stirred for 30 min at room temperature, then cooled to −78 °C and stirred under an atmosphere of argon. TMSOTf (118 μl, 0.65 mmol) was added and the mixture stirred at −78 °C for 1 h, then the temperature was allowed to rise to room temperature overnight. TLC (petrol–ethyl acetate, 2:1) revealed the formation of a major product (R_f 0.50) and complete consumption of acceptor (R_f 0.43). Triethylamine (0.5 ml) was added and the solution stirred for a further 10 min. The reaction mixture was then filtered, diluted with DCM (150 ml), washed with sodium hydrogen carbonate (200 ml of a saturated solution), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was partially purified by flash column chromatography (petrol–ethyl acetate, 4:1) to give disaccharide **13a** which was then directly dissolved in a 10:1 CH_3CN–H_2O mixture (100 ml) and treated with trifluoroacetic acid (10 ml). The mixture was stirred at room temperature overnight and TLC (petrol–ethyl acetate, 2:1) revealed formation of a major product (R_f 0) and complete consumption of starting material (R_f 0.50). The mixture was concentrated under reduced pressure, repeatedly co-evaporated with toluene, and then dissolved in MeOH (10 ml), and treated at room temperature with Et_3N (1 ml). After 30 min the solution was concentrated in vacuo and the residue purified by flash column chromatography (petrol–ethyl acetate, 3:2) to give disaccharide **13b** (1.84 g, 78% over two steps). $[\alpha]_D^{19} = +35$ (*c* 0.8, $CHCl_3$); ν_{max} (KBr disc) 1777 (C=O) cm^{-1}. δ_H (400 MHz, $CDCl_3$) 2.12 (3H, s, SCH_3), 2.14 (3H, s, OC(O)CH_3), 2.41 (1H, at, *J* 2.3 Hz, C≡CH), 3.68 (1H, dd, $J_{5b,6b}$ 6.1 Hz, $J_{6b,6'b}$ 10.3 Hz, H-6b), 3.74–3.78 (2H, m, H-4b, H-6′b), 3.82–3.83 (2H, m, H-6a, H-6′a), 3.92 (1H, m, H-5a), 3.99 (1H, dd, $J_{2a,3a}$ 3.2 Hz, $J_{3a,4a}$ 9.8 Hz, H-3a), 4.04 (1H, dd, $J_{2b,3b}$ 3.3 Hz, $J_{3b,4b}$ 9.3 Hz, H-3b), 4.06–4.12 (3H, m, H-2a, H-4a, H-5b), 4.22 (1H, dd, *J* 2.3 Hz, J_{gem} 16.2 Hz, C*H*H′C≡CH), 4.28 (1H, dd, CH*H*′C≡CH), 4.49, 4.87 (2H, ABq, *J* 11.0 Hz, $PhCH_2$), 4.53, 4.64 (2H, ABq, *J* 12.0 Hz, $PhCH_2$), 4.56, 4.71 (2H, ABq, *J* 11.3 Hz, $PhCH_2$), 5.25 (1H, d, $J_{1a,2a}$ 0.7 Hz, H-1a), 5.40 (1H, d, $J_{1b,2b}$ 1.5 Hz, H-1b), 5.42 (1H, dd, H-2b), 7.16–7.19 (2H, m, 2 × Ar-H), 7.27–7.37 (13H, m, 13 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.9 (q, SCH_3), 21.1 (q, OC(O)*C*H_3), 57.5 (t, *C*H_2C≡CH), 62.6 (t, C-6a), 67.0 (d, C-4a), 69.1 (d, C-2b), 69.2 (t, C-6b), 71.7 (d, C-5b), 71.9, 73.5, 75.0 (3 × t, 3 × $PhCH_2$), 72.5 (d, C-5a), 74.6 (C-4b), 75.7 (s, CH_2C≡*C*H), 77.8, 77.9 (2 × d, C-3a, C-3b), 78.9 (d, C-2a), 79.4 (s, CH_2*C*≡CH), 83.2 (d, C-1a), 97.9 (d, C-1b), 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4 (7 × d, 15 × Ar-CH), 137.9, 138.4 (2 × s, 3 × Ar-C), 170.5 (s, C=O); *m*/*z* (ES^+) 745 ($M+Na^+$, 100), 781 (82). HRMS (ES^+) calcd for $C_{39}H_{46}NaO_{11}S$ ($M+Na^+$) 745.2653. Found 745.2646.

4.19. Methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2-*O*-(prop-2-ynyl)-1-thio-α-D-mannopyranoside 14a

Disaccharide diol **13b** (148 mg, 0.20 mmol) and trichloroacetimidate **8** (143 mg, 0.22 mmol) were dissolved in dry DCM (10 ml) and transferred via cannula to a flame-dried flask containing powdered molecular sieves (4 Å, 100 mg). The mixture was stirred for 30 min at room temperature, then cooled to −78 °C and stirred under an atmosphere of argon. TMSOTf (3.7 μl, 0.02 mmol) was added and the mixture was stirred at −78 °C for 4 h, then the temperature was allowed to rise to room temperature overnight. TLC (petrol–ethyl acetate, 1:1) revealed formation of a major product (R_f 0.57) and complete consumption of acceptor (R_f 0.1). Triethylamine (100 μl) was added and the solution stirred for a further 10 min. The reaction mixture was then filtered, diluted with DCM (40 ml) washed with sodium hydrogen carbonate (20 ml of a saturated solution), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 3:2) to give trisaccharide **14a** (185 mg, 77%). $[\alpha]_D^{17} = +58$ (*c* 1.0, $CHCl_3$); ν_{max} (KBr disc) 1743 (C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.07 (3H, s, SCH_3), 2.12, 2.15 (6H, 2 × s, OC(O)CH_3), 2.37 (1H, at, *J* 2.3 Hz, C≡CH), 3.70–3.75 (5H, m, H-6a, H-6b, H-6′b, H-6c, H-6′c), 3.80, 3.82 (2H, 2 × at, *J* 9.0 Hz, *J* 9.6 Hz, H-4b, H-4c), 3.88–4.13 (9H, m, H-2a, H-3a, H-3b, H-3c, H-4a, H-5a, H-5b, H-5c, H-6′a), 4.18 (1H, dd, J_{gem} 16.2 Hz, C*H*H′C≡CH), 4.30 (1H, dd, CH*H*′C≡CH),

4.47, 4.85 (2H, ABq, J 10.7 Hz, $PhCH_2$), 4.48, 4.86 (2H, ABq, J 11.0 Hz, $PhCH_2$), 4.51–4.56 (4H, m, $PhCH_2$), 4.65–4.73 (4H, m, $PhCH_2$), 4.89 (1H, d, $J_{1c,2c}$ 1.8 Hz, H-1c), 5.25 (1H, d, $J_{1a,2a}$ 0.9 Hz, H-1a), 5.35 (1H, d, $J_{1b,2b}$ 1.6 Hz, H-1b), 5.48 (1H, dd, $J_{2b,3b}$ 3.2 Hz, H-2b), 5.49 (1H, dd, $J_{2c,3c}$ 3.3 Hz, H-2c), 7.14–7.17 (4H, m, 4 × Ar-H), 7.26–7.38 (26H, m, 26 × Ar-H); δ_C (100.6 MHz, $CDCl_3$) 13.7 (q, SCH_3), 21.1 (2 × q, 2 × OC(O)CH_3), 57.1 (t, $CH_2C{\equiv}CH$), 66.4 (t, C-6a), 66.5 (d, C-4a), 68.7, 68.9 (2 × d, C-2b, C-2c), 68.7, 69.1 (2 × t, C-6b, C-6c), 71.6, 71.8, 71.9 (3 × d, C-5a, C-5b, C-5c), 71.7, 71.9, 73.4, 73.5, 74.9, 75.3 (6 × t, 6 × $PhCH_2$), 74.4, 74.5 (C-4b, C-4c), 75.7 (s, $CH_2C{\equiv}CH$), 77.7, 77.9, 78.1, 78.4 (4 × d, C-2a, C-3a, C-3b, C-3c), 79.5 (s, $CH_2C{\equiv}CH$), 82.8 (d, C-1a), 98.0 (d, C-1c), 98.6 (d, C-1b), 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4 (10 × d, 30 × Ar-CH), 137.9, 138.1, 138.2, 138.5 (4 × s, 6 × Ar-C), 170.3 (s, 2 × C=O); m/z (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 1219.47 (100%), 1220.47 (74%), 1221.47 (27%), 1222.48 (4%), 1223.48 (0.3%), peaks calculated: 1219.47 (100%), 1220.47 (76%), 1221.47 (36%), 1222.48 (13%), 1223.48 (4%).

4.20. Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-4-*O*-benzyl-2-*O*-(prop-2-ynyl)-1-thio-α-D-mannopyranoside 14b

Diacetate **14a** (300 mg, 0.25 mmol) was dissolved in dry MeOH (5 ml) and anhydrous K_2CO_3 (7.0 mg, 0.050 mmol) was added. The mixture was stirred at room temperature overnight. TLC (petrol–ethyl acetate, 1:1) revealed complete consumption of starting material (R_f 0.57) and formation of a major product (R_f 0). The solution was evaporated in vacuo and the residue dissolved in dry DMF (10 ml) and treated with sodium hydride (45 mg of a 60% mineral oil dispersion, 1.125 mmol). The mixture was stirred for 30 min, then BnBr was added (178 μl, 1.5 mmol) and, after 1 h stirring, TLC (petrol–ethyl acetate, 4:1) revealed complete consumption of the starting material (R_f 0) and formation of a major product (R_f 0.13). The reaction was quenched by adding MeOH and then diluted with ether (50 ml) and washed with water (50 ml). The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol–ethyl acetate, 4:1→3:1) to afford fully protected trisaccharide **14b** (316 mg, 91%) as a white amorphous foam. $[\alpha]_D^{17} = +50$ (c 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 2.03 (3H, s, SCH_3), 2.36 (1H, at, J 2.3 Hz, C≡CH), 3.60–3.63 (2H, m, H-6a, H-6c), 3.67–3.73 (2H, m, H-5b, H-6′c), 3.76–3.86 (5H, m, H-5a, H-6′a, H-2b, H-6b, H-6′b), 3.87–3.92 (3H, m, H-2c, H-3c, H-5c), 3.98–4.06 (6H, m, H-2a, H-3a, H-3b, H-4b, H-5b, H-4c), 4.11–4.17 (2H, m, H-4a, CHH′C≡CH), 4.22 (1H, dd, J_{gem} 16.1 Hz, CHH′C≡CH), 4.39, 4.70 (14H, m, $PhCH_2$), 4.75 (2H, s, $PhCH_2$), 4.87 (1H, d, J_{AB} 10.9 Hz, $PhCH_2$), 4.90 (1H, d, J_{AB} 10.7 Hz, $PhCH_2$), 5.07 (1H, d, $J_{1c,2c}$ 1.5 Hz, H-1c), 5.17 (1H, s, H-1a), 5.27 (1H, d, $J_{1b,2b}$ 1.1 Hz, H-1b), 7.13–7.41 (45H, m, 45 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 13.8 (q, SCH_3), 57.3 (t, $CH_2C{\equiv}CH$), 65.5 (t, C-6a), 69.1, 69.2 (2 × t, C-6b, C-6c), 71.6, 72.2, 72.4, 73.3, 73.5, 74.4, 75.1, 75.2 (8 × t, 9 × $PhCH_2$), 71.8, 71.9 (2 × d, C-4b, C-5b), 72.6 (C-4c), 74.7, 74.8, 75.0 (3 × d, C-5a, C-2b, C-3b, C-5b, C-2c), 75.2 (s, $CH_2C{\equiv}CH$), 76.0, 77.3 (2 × d, C-4a, C-3c), 78.6 (d, C-2a), 79.4 (d, C-5c), 79.7 (d, C-3a), 79.9 (s, $CH_2C{\equiv}CH$), 82.6 (d, C-1a), 98.2 (d, C-1c), 99.7 (d, C-1b), 126.7, 127.1, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 129.0, 129.8 (18 × d, 45 × Ar-CH), 138.2, 138.3, 138.4, 138.6, 138.7, 140.9 (6 × s, 9 × Ar-C); m/z (ESI^+) species observed ($M+Na^+$); ($M+Na^+$) peaks observed: 1405.59 (100%), 1406.60 (91%), 1407.59 (44%), 1408.59 (8%), 1409.59 (1%), peaks calculated: 1405.59 (100%), 1406.59 (94%), 1407.59 (52%), 1408.60 (21%), 1409.60 (7%), 1410.60 (2%).

4.21. Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-4-*O*-benzyl-2-*O*-(allenyl)-1-thio-α-D-mannopyranoside 15

Propargylated trisaccharide **14b** (165 mg, 0.119 mmol) was dissolved in dry DMSO (1 ml). ^{t}BuOK (7 mg, 62 μmol) was added and the reaction mixture stirred at 65 °C overnight. TLC (petrol–ethyl acetate, 7:3) indicated the formation of a major product (R_f 0.45) and complete consumption of a starting material (R_f 0.39). The reaction was diluted with ether (10 ml) and quenched with water (5 ml). The two phases were separated and the organic one washed with water (2 × 5 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (petrol–ethyl acetate, 7:3, with 2% added triethylamine) to afford allene **15** (128 mg, 77%) as a colourless syrup. $[\alpha]_D^{17} = +52$ (c 0.6, $CHCl_3$); δ_H (400 MHz, $CDCl_3$, significant peaks only) 2.00 (3H, s, SCH_3), 5.08 (1H, s, H-1), 5.07 (1H, d, $J_{1c,2c}$ 1.2 Hz, H-1c), 5.17 (2H, br s, H-1a, H-1b), 5.34 (1H, dd, J 6.0 Hz, J_{gem} 8.6 Hz, CH=C=CHH′), 5.43 (1H, dd, J 6.0 Hz, CH=C=CHH′), 6.77 (1H, at, J 6.0 Hz, CH=C=CHH′).

4.22. *p*-Methoxyphenyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldiphenylsilyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside 17b[10d]

General procedure for mixed acetal formation using molecular sieves (4 Å), DCM (3 ml), 2,6-di-*tert*-butyl-4-methylpyridine (38 mg, 0.186 mmol), iodine (25 mg, 0.10 mmol), silver triflate (26 mg, 0.101 mmol), allene donor **4** (49 mg, 84 μmol) and chitobiose acceptor**16** (70 mg, 65 μmol) afforded mixed acetals **17a** as a mixture of diastereoisomers (81 mg, 70%) as a white amorphous foam. δ_H (400 MHz, $CDCl_3$) major diastereoisomer 0.98 (9H, s, $C(CH_3)_3$), 1.99 (3H, s, SCH_3), 3.67 (3H, s, OCH_3), 5.35 (1H, d, $J_{1b,2b}$ 8.2 Hz, H-1b), 5.49 (1H, d, $J_{1a,2a}$ 8.5 Hz, H-1a), 5.65 (1H, s, H-1c), 5.79 (1H, s, CI=CHH′), 6.27 (1H, s, CI=CHH′). m/z (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 1789.48 (78%), 1790.48 (100%), 1791.48 (60%), 1792.49 (19%), 1793.48 (6%), 1794.51 (2%), peaks calculated: 1789.50 (89%), 1790.50 (100%), 1791.50 (67%), 1792.50 (32%), 1793.50 (13%), 1794.51 (5%). The general procedure for intramolecular glycosylation using molecular sieves (4 Å),

DCM (3 ml), 2,6-di-*tert*-butyl-4-methylpyridine (12.5 mg, 61 μmol), dimethyldisulfide (4.6 μl, 51 μmol), triflic anhydride (8.6 μl, 51 μmol) and mixed acetals **17a** (18 mg, 10 μmol) then afforded trisaccharide **17b**[10d] (5 mg, 32%); $[\alpha]_D^{22} = +44$ (*c* 1.0, $CHCl_3$), lit.[10d] $[\alpha]_D = +45.1$ (*c* 1.0, $CHCl_3$); ν_{max} (KBr disc) 3474 (br, OH), 1777, 1716 (s, C=O); δ_H (500 MHz, $CDCl_3$) 1.06 (9H, s, $C(CH_3)_3$), 2.72 (1H, br s, OH), 2.96 (1H, adt, *J* 4.9 Hz, *J* 9.6 Hz, H-5c), 3.29 (1H, dd, $J_{5b,6b}$ 2.6 Hz, $J_{6b,6'b}$ 11.3 Hz, H-6b), 3.33 (1H, m, H-5b), 3.38–3.44 (2H, m, H-5a, H-6a), 3.51–3.56 (2H, m, H-6′a, H-6c), 3.59 (1H, d, $J_{2c,3c}$ 3.4 Hz, H-2c), 3.64 (1H, m, H-6′b), 3.66 (3H, s, OCH_3), 3.77 (1H, dd, $J_{3c,4c}$ 9.4 Hz, H-3c), 3.92 (1H, at, *J* 9.4 Hz, H-4c), 4.08–4.30 (6H, m, H-3a, H-4a, H-2b, H-4b, H-6′c, $PhCH_2$), 4.36 (1H, dd, $J_{1a,2a}$ 8.6 Hz, $J_{2a,3a}$ 10.7 Hz, H-2a), 4.37 (1H, dd, $J_{2b,3b}$ 10.7 Hz, $J_{3b,4b}$ 8.6 Hz, H-3b), 4.43–4.56 (6H, m, $PhCH_2$), 4.47 (1H, s, H-1c), 4.85 (1H, d, *J* 12.6 Hz, $PhCH_2$), 5.25 (1H, d, $J_{1b,2b}$ 8.4 Hz, H-1b), 5.39 (1H, s, PhCH), 5.44 (1H, d, $J_{1a,2a}$ 8.6 Hz, H-1a), 6.59–6.61 (2H, m, 2 × Ar-H), 6.70–6.77 (5H, m, 5 × Ar-H), 6.85–7.03 (9H, m, 9 × Ar-H), 7.14–7.39 (13H, m, 13 × Ar-H), 7.41–7.93 (18H, m, 18 × Ar-H); δ_C (125.8 MHz, $CDCl_3$) 19.3 (s, $C(CH_3)_3$), 26.9 (q, $C(CH_3)_3$), 55.5 (OCH_3, C-2a), 56.5 (d, C-2b), 66.4 (d, C-5c), 67.3 (t, C-6b), 67.9 (t, C-6a), 68.5 (C-6c), 71.5 (d, C-2c), 72.5, 73.0, 74.4, 74.7 (4 × t, 4 × $PhCH_2$), 72.6 (d, C-3c), 74.5, 74.6 (2 × d, C-5a, C-5b), 75.5 (d, C-4a), 76.4, 76.7 (2 × d, C-3a, C-3b), 78.3 (d, C-4c), 78.9 (d, C-4b), 96.9 (d, C-1b), 97.4 (d, C-1a), 100.1 (d, C-1c), 101.7 (d, PhCH), 114.2, 118.5, 123.2, 123.3, 123.6, 126.1, 126.3, 126.9, 127.1, 127.2 127.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.8, 129.8, 130.1, 132.7, 133.3, 133.7, 133.8, 134.0, 135.8, 136.0 (47 × Ar-CH), 131.4, 131.7, 134.0, 137.3, 137.7, 138.4, 150.8, 155.1 (13 × Ar-C), 167.6, 168.2 (4 × C=O). $J_{C\text{-}1c/H\text{-}1c}$ 161 Hz (β).

4.23. Attempted [3+1] IAD sequence

The general procedure for mixed acetal formation, using molecular sieves (4 Å), DCM (5 ml), 2,6-di-*tert*-butyl-4-methylpyridine (197 mg, 0.96 mmol), iodine (96 mg, 0.378 mmol), silver triflate (99 mg, 0.384 mmol), allenyl trisaccharide **15** (443 mg, 0.32 mmol) and monosaccharide acceptor **5** (286 mg, 0.48 mmol), afforded mixed acetals **18a** (430 mg, 63%) as white amorphous foams. *m*/*z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 2126.71 (67%), 2127.71 (100%), 2128.72 (62%), 2129.72 (26%), 2130.72 (8%), 2131.72 (2%), peaks calculated: 2126.71 (75%), 2127.71 (100%), 2128.71 (73%), 2129.71 (39%), 2130.72 (17%), 2131.72 (6%), 2132.72 (2%). The general procedure for intramolecular glycosylation afforded only small amounts of tetrasaccharide **18b** (10 mg, 3%), as a white amorphous foam.

4.24. Attempted [3+2] IAD sequence

The general procedure for mixed acetal formation, using molecular sieves (4 Å), DCM (2 ml), 2,6-di-*tert*-butyl-4-methylpyridine (38 mg, 0.185 mmol), iodine (27.7 mg, 0.109 mmol), silver triflate (28.5 mg, 0.111 mmol), allenyl trisaccharide **15** (128 mg, 92.5 μmol) and the chitobiose acceptor **16** (66 mg, 61.7 μmol), afforded mixed acetals **19a** (100 mg, 63%) as white amorphous foams. *m*/*z* (ESI^+) species observed ($M+NH_4^+$), ($M+Na^+$) (major); ($M+Na^+$) peaks observed: 2597.51 (55%), 2598.51 (100%), 2599.51 (86%), 2600.51 (47%), 2601.52 (19%), 2602.51 (5%), peaks calculated: 2597.87 (61%), 2598.88 (100%), 2599.88 (89%), 2600.88 (55%), 2601.89 (28%), 2602.89 (11%). The general procedure for intramolecular glycosylation afforded an inseparable complex mixture of products. Mass spectrometry revealed the presence of the desired pentasaccharide **19b** as a minor component of this mixture of products. *m*/*z* (ESI^+) species observed: ($M+NH_4^+$) 2381.94 ($M+Na^+$) 2386.89.

Acknowledgement

The authors gratefully acknowledge the European Union (Marie Curie Intra-EU Fellowship to E.A.) for financial support.

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