Stereoselective 1,2-*cis* Glycosylation of 2-*O*-Allyl Protected Thioglycosides

Mahmoud Aloui,[a] David J. Chambers,[a] Ian Cumpstey,[a] Antony J. Fairbanks,*[a] Alison J. Redgrave,[b] and Christopher M. P. Seward[a]

Abstract: The technique of intramolecular aglycon delivery (IAD), whereby a glycosyl acceptor is temporarily appended to a hydroxyl group of a glycosyl donor is an attractive method that can allow the synthesis of 1,2-*cis* glycosides in an entirely stereoselective fashion. 2-*O*-Allyl protected thioglycoside donors are excellent substrates for IAD, and may be glycosylated stereoselectively through a three-step reaction sequence. This sequence consists of quantitative yielding allyl bond isomerisation, to produce vinyl ethers that can then undergo *N*-iodosuccinimide mediated tethering of the desired glycosyl acceptor, and subsequent intramolecular glycosylation, to yield either α-glucosides or β-mannosides accordingly. Although attempted one-pot tethering and glycosylation is hampered by competitive intermolecular reaction with excess glycosyl acceptor, this problem can be simply overcome by the use of excess glycosyl donor. Allyl mediated IAD is a widely applicable practical alternative to other IAD approaches for the synthesis of β-mannosides, that is equally applicable for α-*gluco* linkages. It is advantageous in terms of both simplicity of application and yield, and in addition has no requirement for cyclic 4,6-protection of the glycosyl donor.

Keywords: carbohydrates · glycosides · glycosylation · stereoselective synthesis

Introduction

One of the major complications inherent in the construction of an oligosaccharide is control of the stereochemistry of a newly formed anomeric linkage. Although judicious choice of solvent and protecting group pattern on the glycosyl donor can in many cases allow high levels of stereoselectivity, complete control of anomeric stereochemistry during the glycosylation process is still difficult. This difficulty is exacerbated when separation of mixtures of anomers becomes impossible. A logical partial solution to this problem is to take advantage of neighbouring group participation, whereby glycosyl donors possessing 2-*O*-ester protecting groups are almost universally used in order to stereoselectively synthesise 1,2-*trans* glycosidic linkages. The idea that the configuration of the 2-hydroxyl of the glycosyl donor can also be used to induce the formation of 1,2-*cis* linkages by the technique of intramolecular aglycon delivery (IAD), was originally introduced by Hindsgaul[1] and Stork[2] for the synthesis of β-mannosides.[3] Although several high yielding intermolecular approaches have been developed which allow the synthesis of β-mannosides,[4] most notably by Crich,[5] interest in the further development of IAD has continued.[6, 7] In particular a number of other methods have been developed for the temporary linking of donor and acceptor prior to glycosylation, the most successful of which involve modification of the donor 2-hydroxyl protecting group to provide a tethering site. The most notable of these is the Ogawa approach[8] which employs oxidation of a *p*-methoxybenzyl (PMB) protecting group allowing linking of donor and acceptor as a mixed acetal. There have also been some very successful attempts at more remote tethering and intramolecular glycosylation, whereby the glycosyl acceptor is either appended to the anomeric leaving group, or to more remote hydroxyl groups in particular as reported by the groups of Schmidt,[9] Ziegler,[10] Valverde[11] and others.[12] Following on from earlier studies[13] we report herein details on the use of the 2-*O*-allyl protecting group for IAD which allows entirely stereoselective access to both β-mannosides and α-glucosides.[14] The strategy employed uses a reaction sequence involving Wilkinson's catalyst mediated isomerisation of 2-*O*-allyl ethers of thioglycosides to produce 2-*O*-vinyl ethers, to which glycosyl acceptors may be tethered yielding mixed acetals. These mixed acetals can then finally undergo intramolecular glycosylation upon thioglycoside activation. In particular a discussion of the scope and limitations of the allyl mediated IAD is included.

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Results and Discussion

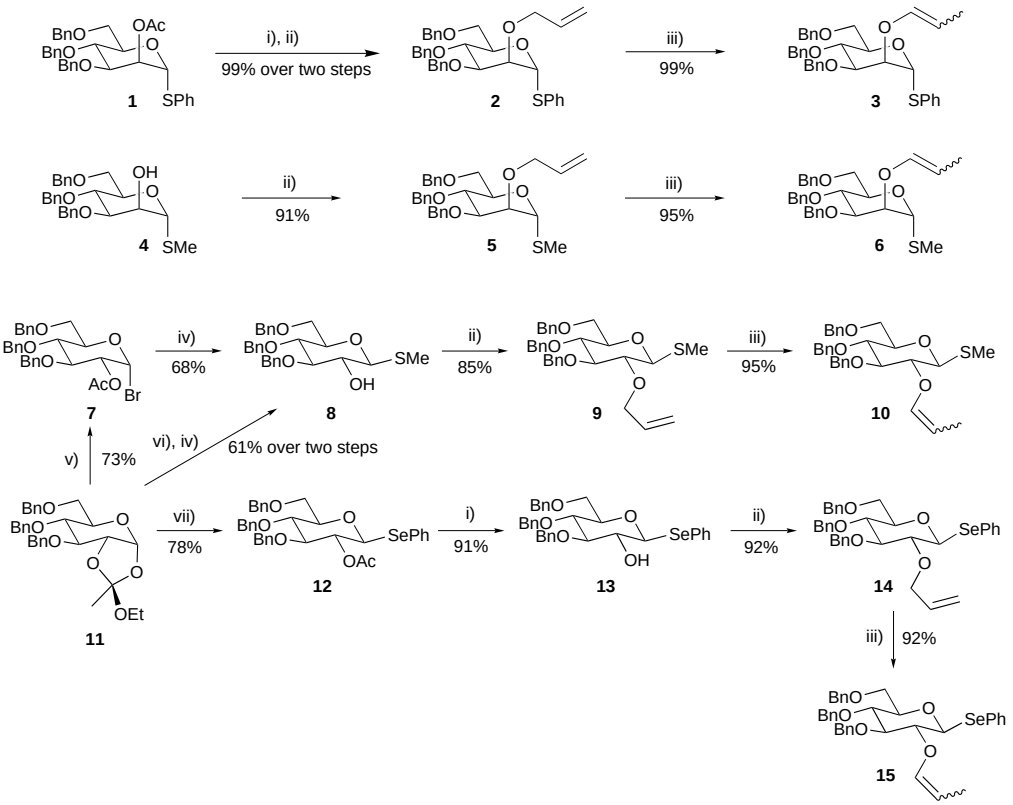
Synthesis of vinyl ethers

A selection of *manno* and *gluco* glycosyl donors with different anomeric leaving groups bearing 2-*O*-allyl protection were synthesised as substrates for isomerisation and subsequent tethering and glycosylation experiments (Scheme 1). The 2-*O*-allyl protected *manno* thiophenyl glycoside **2** was accessed from the known acetate **1**[15] by sodium methoxide mediated deacetylation and immediate allylation with sodium hydride and allyl bromide. The thiomethyl counterpart **5** was likewise synthesised by standard allylation of the known thiomethyl glycoside **4**.[16] The required *gluco* thiomethyl glycoside **9** was accessed by allylation of the alcohol **8**. Alcohol **8** was itself synthesised from the known orthoester **11**,[17] through a two-step sequence involving initial conversion of **11** to the glycosyl bromide **7**[15] by treatment with either HBr in acetic acid or acetyl bromide, and subsequent reaction of **7** with lithium methyl thiolate, generated in situ by reaction of dimethyl disulfide with *n*-butyllithium. The *gluco* 2-*O*-allyl selenoglycoside **14** was also synthesised from the *gluco* orthoester **11** by a reaction sequence involving mercury(II) promoted opening of **11** to yield the β-selenoglycoside **12**, subsequent sodium methoxide mediated deacetylation to yield alcohol **13**,[18] and finally allylation to yield **14**.[19]

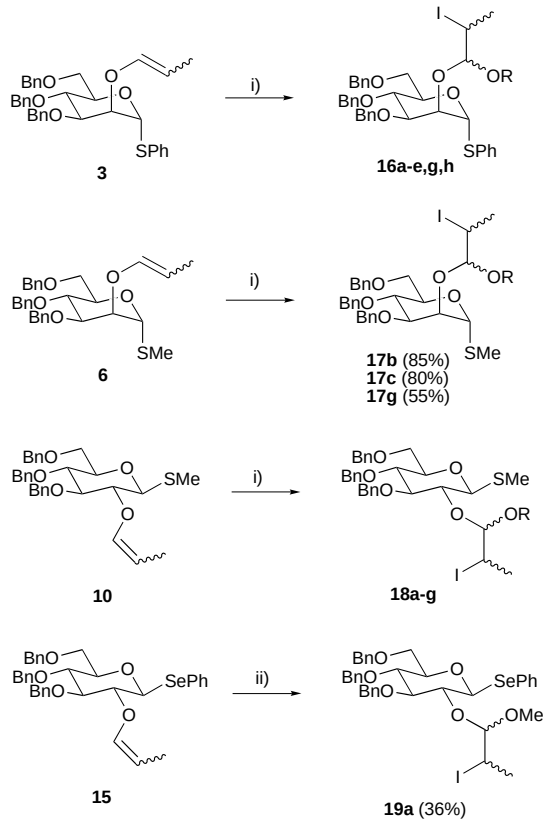
This selection of 2-*O*-allyl protected glycosyl donors **2**, **5**, **9** and **14** were then subjected to isomerisation using a combination of Wilkinson's catalyst and *n*-butyllithium according to the procedure recently reported by Boons.[20] This straightforward method proceeded extremely efficiently in all cases to yield the corresponding enol ethers **3**, **6**, **10** and **15** respectively, in excellent yields (Scheme 1).

Tethering reactions

Tethering with *N*-iodosuccinimide: *N*-Iodosuccinimide (NIS) mediated tethering was undertaken for the *manno* thiophenyl donor **3** with a series of primary and secondary alcohols (ROH, Table 1, Scheme 2) in the presence of 4 Å molecular sieves. Exclusion of water from these reactions was important in order to avoid competitive hydrolysis, and tethering yields rose appreciably after the addition of sieves. In the vast majority of cases tethering proceeded efficiently in either THF or 1,2-dichloroethane (DCE) as solvent, to yield mixed acetal intermediates **16a**–**e**. These mixed acetals are quite robust[21] and much more stable than the Hindsgaul-type acetals that we had previously worked with.[13] Pleasingly a secondary carbohydrate alcohol was also successfully tethered to yield mixed acetals **16g** in an excellent 85% yield. However, attempted tethering of the even more hindered 4-hydroxyl of a protected glucosamine derivative, required in order to complete the β-*manno* linkage found in the *N*-glycan core pentasaccharide, produced only an extremely disappointing 9% yield of the tethered product **16h**. The reason for this extremely low yield became apparent after the isolation of succinimide trapped material **22** in a total yield of 70% (as a 6:1 mixture of two diastereomers), together with approximately 10% of recovered starting material. Succinimide trapped material **22** was in fact also isolated in 10% yield



Scheme 1. i) Na, MeOH, RT; ii) NaH, allyl bromide, DMF, RT; iii) $(Ph_3P)_3RhCl$, *n*BuLi, THF, reflux; iv) BuLi, MeSSMe, THF, $-78\,^{\circ}C$; v) HBr, AcOH, CH_2Cl_2, $0\,^{\circ}C$; vi) AcBr, $0\,^{\circ}C$; vii) PhSeH, $HgBr_2$, MeCN, $50\,^{\circ}C$.



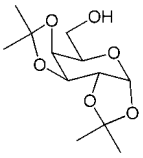
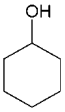
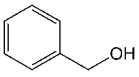
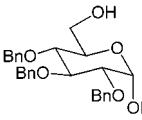
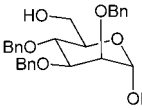
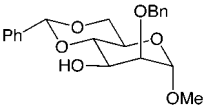
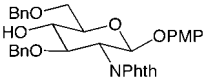
Scheme 2. i) ROH (see Table 1), *N*-iodosuccinimide, 4 Å molecular sieves, 1,2-dichloroethane, $-40\,^{\circ}C \rightarrow$ RT; ii) MeOH, *N*-iodosuccinimide, 4 Å molecular sieves, 1,2-dichloroethane, $-40\,^{\circ}C \rightarrow$ RT, 36 %.

during the formation of **16g**. Formation of **22** clearly occurs by competitive nucleophilic attack by succinimide, and therefore in the glucosamine case represents a limitation to the use of NIS for tethering in the construction of the *N*-glycan core pentasaccharide, an issue which was later addressed (see below).

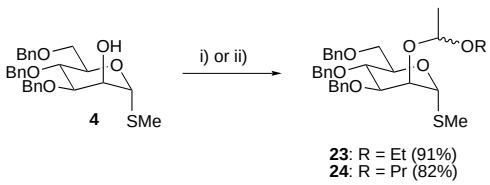
NIS-mediated tethering of the thiomethyl glycoside **6** with diacetone galactose and cyclohexanol again produced the corresponding mixed acetals **17b**, **c** in good yield. However, tethering of the secondary carbohydrate alcohol was less efficient, providing **17g** in 55 % yield, and in this case the use of protracted reaction times led to competitive activation of the anomeric leaving group.

A similar series of tethering experiments were undertaken in the *gluco* series with thiomethyl glycoside **10**. For the primary alcohols tethering was rapid and good yields of mixed acetals **18a–d** were obtained. However, for the more hindered alcohols yields of mixed acetals **18e–g** were much lower. This reduction in yield was again in part due to competitive activation of the anomeric thiomethyl group by NIS during tethering, and as such could not be overcome by the use of extended reaction times. A similar but more extreme situation was observed for the selenoglycoside **15**. In this case NIS activation of the more reactive anomeric leaving group was even competitive with tethering of methanol, and the desired acetals **19a** could only be isolated in 36 % yield. It can be concluded that fully armed selenoglycosides are unsuitable substrates for NIS mediated tethering reactions.

Table 1. Yields for tethering and glycosylation.

Entry	Alcohol ROH	Product/ yield of mixed acetals [%]	Product/ yield of glycosylation [%]
a)	MeOH	**16a**/93 **18a**/98	**20a**/77 **21a**/65
b)		**16b**/95 **18b**/85	**20b**/81 **21b**/70
c)		**16c**/76 **18c**/80	**20c**/68 **21c**/77
d)		**16d**/ > 99 **18d**/95	**20d**/76 **21d**/67
e)		**16e**/90 **18e**/36	**20e**/65 **21e**/74
f)		**18f**/63	**21f**/72
g)		**16g**/85 **18g**/22	**20g**/89
h)		**16h**/9	see text

Tethering with acid: The conclusion drawn from the above experiments was that efficient NIS mediated tethering could only be achieved for hindered alcohols with an unreactive anomeric leaving group, particularly thiophenyl. For this reason a series of acid-catalysed tethering reactions were also attempted. An initial investigation involving reaction of thiomethyl alcohol **4** with either ethyl or propyl vinyl ethers catalysed by pyridinium *p*-toluene sulfonate (PPTS) produced mixed acetals **23** and **24** in 91 and 82 % yield, respectively (Scheme 3), and therefore revealed PPTS as a potential acid catalyst. However, attempted PPTS-catalysed tethering of thiomethyl vinyl ether **10** with diacetone galactose did not result in the formation of any appreciable amount of mixed acetal products; nor was PPTS capable of tethering diacetone



Scheme 3. i) ethyl vinyl ether, PPTS, CH_2Cl_2, RT; ii) propyl vinyl ether, PPTS, CH_2Cl_2, RT.

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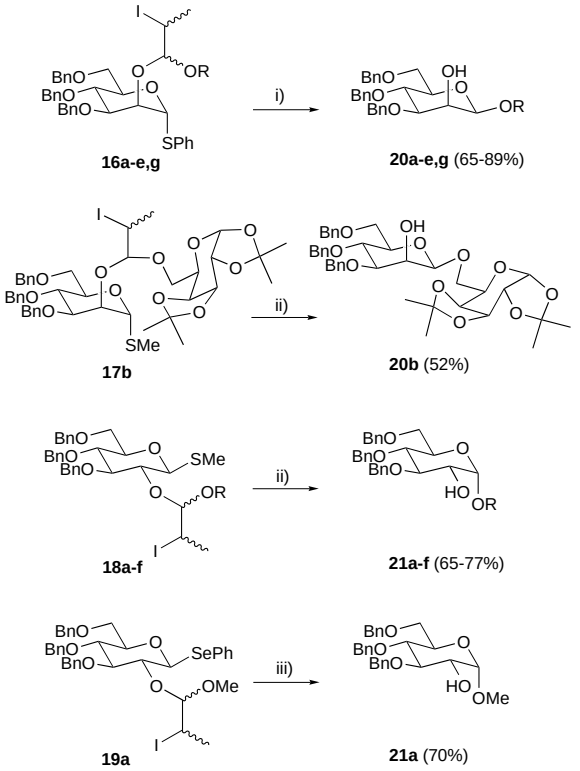
galactose and thiophenyl vinyl ether **3**, with complete recovery of starting material after reaction overnight at room temperature. The use of other acids such as camphor sulfonic acid and *p*-toluene sulfonic acid was similarly unsuccessful and the attempted use of triflic acid (TfOH) caused complete decomposition of the starting material.

Glycosylation reactions

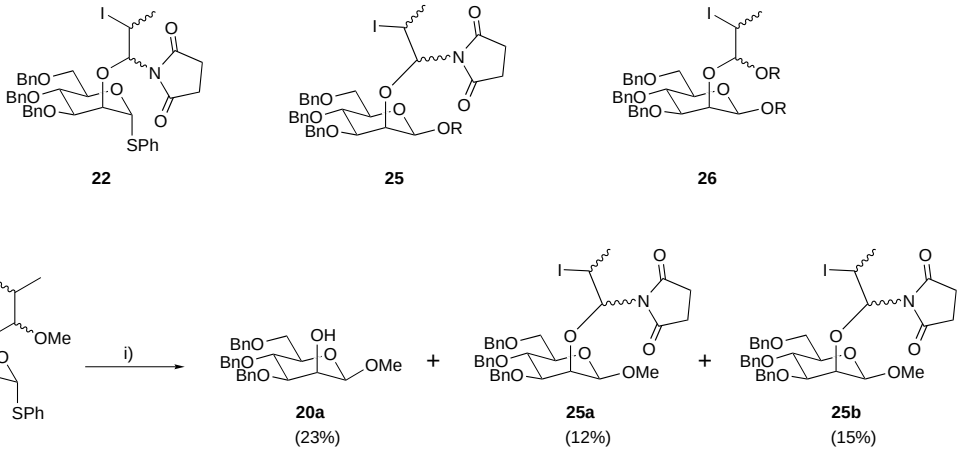
With a selection of mixed acetals in hand as a result of successful NIS-mediated tethering, intramolecular glycosylation was then undertaken (Scheme 4). In the case of the less reactive anomeric thiophenyl *manno* mixed acetals **16a–e,g**, a wide range of activation conditions were investigated using NIS either alone, or with co-activators which included triflic acid, silver triflate, tin(II) triflate, triethylsilyl triflate (TESOTf), and acetic acid. All reactions were performed in the presence of di-*tert*-butyl methyl pyridine (DTBMP) as an added base. Activation with NIS alone was much more sluggish than had been previously experienced.[13] In general, glycosylation was considerably slower than in the Hindsgaul-type system and little glycosylation was observed upon treatment with NIS alone at room temperature. Optimised reaction conditions required the addition of silver triflate, and more protracted reaction times at either room temperature or higher. In all cases intramolecular glycosylation occurred in a stereospecific fashion to furnish the corresponding β-mannosides **20a–e,g** in good yields.[22] However, the direct isolation of the desired reaction product was sometimes complicated by competitive trapping reactions whereby the oxonium ion produced subsequent to intramolecular glycosylation was trapped by a nucleophile. This nucleophile could either be succinimide, to yield compounds such as **25**, or any alcohol present[23] to produce glycosylated mixed acetals of general structure **26**.[24] A large scale glycosylation of mixed acetals **16a** without the addition of silver triflate in fact allowed the isolation and characterisation of two diastereomers of the succinimide trapped product **25a** and **b** (see Scheme 5).



Scheme 4. i) *N*-Iodosuccinimide, AgOTf, DTBMP, 4 Å molecular sieves, 1,2-dichloroethane, RT → 50 °C; ii) MeOTf, DTBMP, 1,2-dichloroethane, RT; iii) *N*-iodosuccinimide, CH_2Cl_2, −40 °C, 10 min.

A variety of hydrolytic work-up procedures were investigated in order to overcome this problem. The most efficient procedure involved treatment of the crude reaction mixture with trifluoroacetic acid (TFA), in a 1:1:1 mixture of MeOH/THF/water. In most cases this procedure efficiently converted all trapped materials to the desired 1,2-*cis* glycoside. Care had to be exercised for the cases involving glycosyl acceptors which contained acid labile protecting groups, most notably diacetone galactose (Table 1, entry b).

A brief investigation into the role of the added DTBMP was also undertaken for glycosylations of mixed acetals **16a**. Glycosylation was in fact much faster when DTBMP was omitted and the methyl acetals **16a** were glycosylated in 20 minutes, but the reactions were always less clean and resulted in the formation of unidentified, undesired side products, that were not trapped mixed acetals **25** or **26**. The use of alternative less hindered bases, such as collidine or

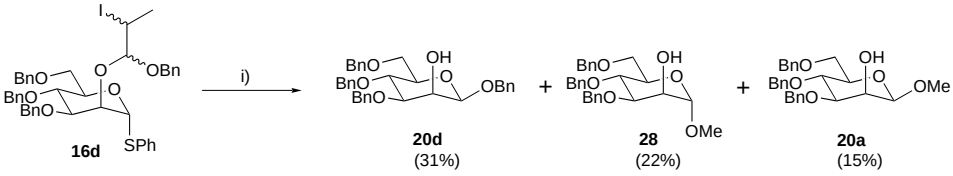


Scheme 5. i) *N*-Iodosuccinimide, 4 Å molecular sieves, DTBMP, 1,2-dichloroethane, RT, 17 h, then 50 °C, 7 h.

pyridine, slowed the rate of glycosylation so much that effective reaction could not be achieved.

Intramolecular glycosylation of the more reactive thiomethyl *manno* mixed acetals **17b** (derived from tethering **6** with diacetone galactose) was investigated under a number of different activation conditions. These included the use of dimethyl(methylthio)sulfonium triflate (DMTST), I_2, MeOTf, NIS/TESOTf, I_2/TESOTf and PhSeOTf, in all cases with DTBMP as an added base in DCE as solvent. Although the thiomethyl glycoside was activated in all cases, the reaction proceeded most cleanly when methyl triflate was used as an activator alone. The thiomethyl *gluco* mixed acetals **18a–f** were very efficiently activated by the addition of methyl triflate, yielding α-glucosides **21a–f**, again as single anomers following work-up. Again the formation of mixed acetals could complicate the glycosylation reaction (as observed by TLC) and the same general acid work-up procedure was adopted to maximise yields.

Mechanistic studies and one-pot reactions: With tethering and glycosylation methodology successfully in hand attention next turned to the potential one-pot reaction, whereby the two steps are achieved in a single reaction vessel. Unlike our previous results which were obtained with the Hindsgaul mixed ketal system, attempted one-pot glycosylation of either donors **3** or **6** with an excess of diacetone galactose or cyclohexanol (1.4 to 3 equivalents) produced anomeric mixtures of products. A subsequent competition experiment involving glycosylation of mixed acetals **16d** in the presence of methanol as an intermolecular nucleophile produced a mixture of products containing the desired β-benzyl mannoside **20d**, together with both the α- and β-methyl mannosides **28** and **20a** clearly indicating competitive intermolecular reaction by the alcohol present in solution (Scheme 7).



Scheme 7. i) MeOH (1 equiv), *N*-iodosuccinimide, AgOTf, DTBMP, 1,2-dichloroethane, 50 °C, 1.5 h.

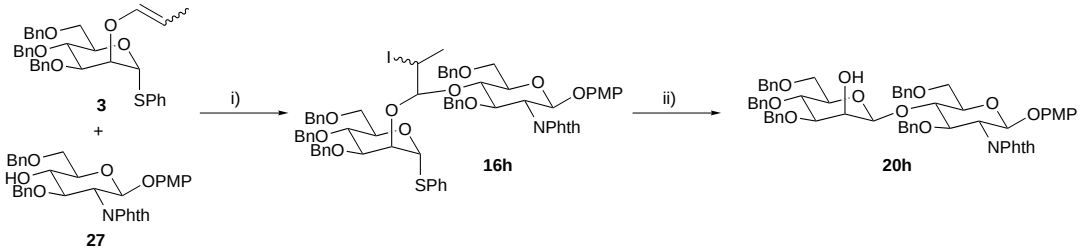
Synthesis of Man$\beta(1\rightarrow4)$-GlcNAc disaccharide

Due to the failure of NIS-mediated tethering with the most hindered glucosamine acceptor detailed above (Table 1, entry h), alternative reaction conditions were investigated which would hopefully allow the allyl mediated IAD approach to be applicable for even more hindered secondary alcohols. Clearly this was important in order to allow access to the core *N*-glycan Man$\beta(1\rightarrow4)$GlcNAc disaccharide. Since the major problem encountered with NIS tethering was competitive nucleophilic attack by succinimide, which appeared to be a better nucleophile than the 4-hydroxyl of the protected glucosamine derivative **27**,[25] it was thought that tethering may best be achieved by the use of a source of I^+ in the presence of a non-nucleophilic counterion. For this reason the use of iodonium dicollidine triflate (IDCT), prepared in situ from iodine, collidine and silver triflate, was investigated. Pleasingly IDCT mediated tethering of vinyl ether **3** with glucosamine acceptor **27** resulted in an 80% yield of mixed acetals **16h** (Scheme 6). Subsequent intramolecular glycosylation mediated by iodine and silver triflate, successfully yielded the key Man$\beta(1\rightarrow4)$GlcNAc disaccharide **20h** in 66% yield. The results imply that by judicious choice of tethering conditions that allyl mediated IAD may possibly be used for the most hindered of glycosyl acceptors.

These results lead to the conclusion that any one-pot reaction could only be successful with the use of an excess of glycosyl donor rather than glycosyl acceptor which contrary to the standard procedure up to this point. Gratifyingly the one-pot reaction of donor **6** (2.0 equivalents) with either diacetone galactose or cyclohexanol (in acetonitrile and DCE respectively) produced the corresponding β-mannosides **20b** and **20c** as single anomers in 72% and 67% yields, respectively (Scheme 8). Notably there was no product trapping in these reactions and therefore they did not require an acidic work up.

Conclusion

In summary we have demonstrated that 2-*O*-allyl protected glycosyl donors may be employed for the efficient synthesis of a variety of *cis*-1,2-glycosides by the technique of intramolecular aglycon delivery (IAD). Several points are worthy of note. Firstly installation and isomerisation of the allyl group is a very efficient process, and is superior to Tebbe approaches to similar vinyl ethers. Secondly NIS is able to successfully tether all but a very hindered glucosamine acceptor, whilst on the other hand a variety of acids were unsuccessful. Moreover



Scheme 6. i) I_2, AgOTf, collidine, CH_2Cl_2, -78 °C to RT, 80%; ii) I_2, AgOTf, DTBMP, 4 Å molecular sieves, 1,2-dichloroethane, RT, 66%.

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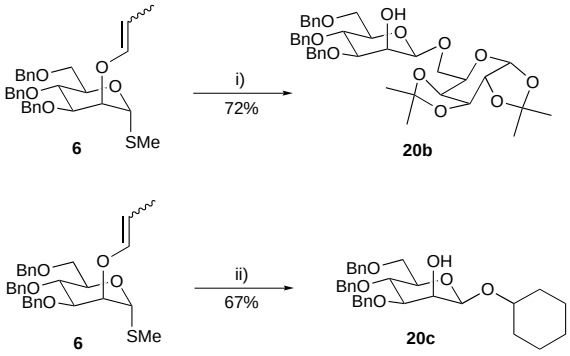

Scheme 8. i) Diacetone galactose, 4 Å molecular sieves, *N*-iodosuccinimide, DTBMP, 1,2-dichloroethane, $-40 \rightarrow 0\,^{\circ}C$, 1 h then MeOTf, $0\,^{\circ}C \rightarrow$ RT, 24 h; ii) cyclohexanol, 4 Å molecular sieves, *N*-iodosuccinimide, DTBMP, 1,2-dichloroethane, $-30 \rightarrow 0\,^{\circ}C$, 1 h then MeOTf, $0\,^{\circ}C$ to RT, 18 h.

even the hindered glucosamine acceptor may be tethered by the use of IDCT rather than NIS as coupling agent, ultimately allowing access to the crucial Man$\beta(1\rightarrow4)$GlcNAc disaccharide. A caveat to the tethering procedure is that yields for glycosyl donors with very reactive anomeric leaving groups (e.g. Se) may be lower due to competitive anomeric activation. Subsequent intramolecular glycosylation reactions are slower than in the related Hindsgaul system, and in fact intermolecular reaction can be competitive. However, the use of an excess of glycosyl donor allows both tethering and glycosylation to be performed in a single reaction vessel, obviating the need for handling of sensitive mixed acetal intermediates. By way of direct comparison with alternative methods, allyl IAD is amenable in terms of both simplicity of application, yield, and importantly is equally applicable for the formation of *β-manno* and *α-gluco* linkages. In addition there appears to be no requirement for cyclic 4,6-protection of the glycosyl donor in order to produce good yields for the glycosylation step. Further investigations into the use of allyl derived vinyl ethers for 1,2-*cis* glycosylation procedures are currently in progress, and the results will be reported in due course.

Experimental Section

General methods: Melting points were recorded on a Kofler hot block and are uncorrected. Proton NMR (δ_H) spectra were recorded on a Bruker DPX400 (400 MHz) or on a Bruker AMX500 (500 MHz) spectrometer. Carbon NMR (δ_C) spectra were recorded on a Bruker AC200 (50.3 MHz), or on a Bruker DPX400 (100.6 MHz), or on a Bruker AMX500 (125.7 MHz) spectrometer. Multiplicities were assigned using DEPT sequence. All chemical shifts are quoted on the δ scale in parts per million (ppm). IR spectra were recorded on a Perkin–Elmer 150 fourier transform spectrophotometer. Low resolution mass spectra were recorded on a Micromass Platform1 APCI using atmospheric pressure chemical ionisation (APCI). High resolution mass spectra (electrospray) were performed on a Waters 2790-Micromass LCT electrospray ionisation mass spectrometer, or by the EPSRC Mass Spectrometry Service Centre, Department of Chemistry, University of Wales, Swansea on a MAT900 XLT electrospray ionisation mass spectrometer. Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g per 100 mL. Microanalyses were performed by the microanalytical services of Elemental Microanalysis Ltd, Devon. Thin-layer chromatography (TLC) was carried out on Merck Kieselgel 0.22–0.25 mm thickness glass-backed sheets, pre-coated with $60F_{254}$ silica. Plates were developed using 5% *w*/*v* ammonium molybdate in 2 M sulfuric acid. Flash column chromatography was carried out using Sorbsil C60 40/60 silica or basic alumina. Solvents and reagents were dried and purified before use according to standard procedures; methanol was distilled from calcium hydride, dichloromethane was distilled from calcium hydride, and tetrahydrofuran was distilled from a solution of sodium/benzophenone immediately before use. Petrol refers to the fraction of light petroleum ether boiling in the range 40–60 °C. Ether refers to diethyl ether. All procedures requiring anhydrous conditions were performed under an atmosphere of argon in glassware which was flame-dried before use.

Phenyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (2): Acetate **1** (292 mg, 0.50 mmol) was dissolved in methanol (8 mL) under argon and sodium (18 mg, 0.78 mmol) was added with stirring. The reaction mixture was stirred at room temperature for 30 min, after which time TLC (petrol/ethyl acetate 3:1) showed no remaining starting material ($R_f = 0.5$) and formation of a single product ($R_f = 0.2$). The reaction mixture was co-evaporated with toluene and subsequently exposed to high vacuum for two hours. The resulting residue was taken up in DMF (3.5 mL) and NaH (60% dispersion in mineral oil, 80 mg, 1.67 mmol) was added portionwise, followed by allyl bromide (0.11 mL, 1.27 mmol). This solution was stirred for 1.5 h, after which time TLC (petrol/ethyl acetate 3:1) showed no remaining starting material ($R_f = 0.2$) and the formation of a major product ($R_f = 0.7$). Methanol (5 mL) was added slowly and the mixture was concentrated in vacuo. The residue was dissolved in ether (50 mL) and washed with brine (2×30 mL). The aqueous layers were re-extracted with ether (30 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash column chromatography (petrol/ether 3:1) gave the allylated thioglycoside **2** (289 mg, 99%) as a white solid. M.p. 60–62 °C (ether/petrol); $[\alpha]_D^{24} = +132$ ($c = 1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.52-7.49$ (m, 2H; $2\times$ Ar-H), 7.43–7.22 (m, 18H; $18\times$ Ar-H), 5.99–5.90 (m, 1H; C*H*=CH$_2$), 5.62 (s, 1H; H-1), 5.31 (dd, ^2J(H,H) = 1.3 Hz, ^3J(H,H) = 17.2 Hz, 1H; CH=CH_ECH$_Z$), 5.22 (dd, ^2J(H,H) = 1.3 Hz, ^3J(H,H) = 10.3 Hz, 1H; CH=H$_E$H$_Z$), 4.93, 4.54 (ABq, ^2J(H,H) = 10.8 Hz, 2H; PhCH_2), 4.74 (ABq, ^2J(H,H) = 12.6 Hz, 2H; PhCH_2), 4.67, 4.50 (ABq, ^2J(H,H) = 12.0 Hz, 2H; PhCH_2), 4.30 (dd, ^3J(H,H) = 9.7 Hz, 9.5 Hz, 1H; H-5), 4.21 (dd, ^2J(H,H) = 13.1 Hz, ^3J(H,H) = 5.5 Hz, 1H; CHH'CH=CH$_2$), 4.12 (dd, ^2J(H,H) = 13.1 Hz, ^3J(H,H) = 6.1 Hz, 1H; C*H*H′CH=CH$_2$), 4.04 (at, ^3J(H,H) = 9.5 Hz, 1H; H-4), 3.98 (dd, ^3J(H,H) = 1.6 Hz, 3.0 Hz, 1H; H-2), 3.89 (dd, ^3J(H,H) = 3.0 Hz, 9.4 Hz, 1H; H-3), 3.85 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 4.9 Hz, 1H; H-6′), 3.76 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 1.4 Hz, 1H; H-6); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 134.6$ (d, *C*H=CH$_2$), 138.4, 138.3, 138.1, 134.4 ($4\times$ s, Ar-C), 131.4, 129.0, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.4, 127.3 ($11\times$ d, Ar-CH), 117.9 (t, CH=*C*H$_2$), 85.8, 80.1, 76.1, 74.9, 72.6 ($5\times$ d, C-1, C-2, C-3, C-4, C-5), 75.2, 73.2, 72.2, 71.4, 69.1 ($5\times$ t, C-6, $3\times$ Ph*C*H$_2$, O*C*H$_2$CH=CH$_2$); IR (KBr): $\tilde{\nu} = 1643\ cm^{-1}$ (C=C); MS-APCI$^+$: *m*/*z* (%): 605 (21) $[M+Na]^+$; HRMS-ES: calcd for $C_{36}H_{42}NO_5S$ $[M+NH_4]^+$: 600.2784, found: 600.2776).

Phenyl 2-*O*-(prop-1-enyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (3): *n*-Butyllithium (1.3 M in hexanes, 250 μL) was added to a degassed solution of Wilkinson's catalyst (163 mg, 0.18 mmol) in THF (8 mL). This mixture was stirred for 10 min before being added to a solution of the allylated thioglycoside **2** (1.00 g, 1.72 mmol) in THF (5 mL) at reflux. After 10 min, TLC (petrol/ethyl acetate 5:1) showed no remaining starting material ($R_f = 0.65$) and the formation of a single product ($R_f = 0.75$). The solution was allowed to cool to room temperature before the addition of dichloromethane (20 mL) and concentration in vacuo. Purification by flash column chromatography (petrol/ether 7:1, with 1% added triethylamine) gave the vinyl ethers **3** (998 mg, >99%) as a clear, colourless oil, a partially separable mixture of *E* and *Z* isomers. *E* isomer: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.54-7.49$ (m, 2H; $2\times$ Ar-H), 7.44–7.23 (m, 18H; $18\times$ Ar-H), 6.11 (dd, ^3J(H,H) = 12.2 Hz, ^4J(H,H) = 1.1 Hz, 1H; OC*H*=CH), 5.64 (s, 1H; H-1), 4.97 (m, 1H; CH$_3$C*H*), 4.75 (s, 2H; PhCH_2), 4.93, 4.56 (ABq, ^2J(H,H) = 10.7 Hz, 2H; PhCH_2), 4.68, 4.50 (ABq, ^2J(H,H) = 11.9 Hz, 2H; PhCH_2), 4.34–4.30 (m, 1H; H-5), 4.23 (d, ^3J(H,H) = 2.9 Hz, 1H; H-2), 4.08 (at, ^3J(H,H) = 9.5 Hz, 9.3 Hz, 1H; H-4), 3.93 (dd, ^3J(H,H) = 2.9 Hz, 9.3 Hz, 1H; H-3), 3.87 (dd, ^2J(H,H) = 10.9 Hz, ^3J(H,H) = 4.9 Hz, 1H; H-6′), 3.76 (dd, ^2J(H,H) = 10.9 Hz, ^3J(H,H) = 1.3 Hz, 1H; H-6), 1.56 (dd, ^3J(H,H) = 6.4 Hz, ^4J(H,H) = 1.1 Hz, 3H; CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 144.8$ (d, O*C*H=CH), 138.4, 138.3, 137.9, 134.0 ($4\times$ s, Ar-C),

131.5, 129.0, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.7, 127.5, 127.5, 127.4 (15 × d, Ar-CH), 102.6, 85.1, 79.3, 77.0, 74.8, 72.6 (6 × d, C-1, C-2, C-3, C-4, C-5, *C*HCH$_3$), 75.1, 73.2, 72.2, 69.0 (4 × t, C-6, 3 × Ph*C*H$_2$), 12.4 (*C*H$_3$); IR (thin film): $\tilde{\nu}$ = 1675 cm^{-1} (C=C); MS-APCI$^+$: *m*/*z* (%): 606 (26) [*M*+Na]$^+$; *Z* isomer: ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 7.71 – 7.00 (m, 20H; 20 × Ar-H), 5.91 (dd, ^3J(H,H) = 6.0 Hz, ^4J(H,H) = 1.6 Hz, 1H; OC*H*=CH), 5.53 (d, ^3J(H,H) = 1.6 Hz, 1H; H-1), 4.92 (d, ^2J(H,H) = 10.8 Hz, 1H; PhCH*H′*), 4.75 (s, 2H; PhC*H*$_2$), 4.67, 4.50 (ABq, ^2J(H,H) = 12.0 Hz, 2H; PhC*H*$_2$), 4.61 – 4.53 (m, 2H; CH$_3$C*H*, PhC*H*H′), 4.31 (ddd, ^3J(H,H) = 9.7 Hz, 4.8 Hz, 1.7 Hz, 1H; H-5), 4.11 (at, ^3J(H,H) = 9.5 Hz, 8.9 Hz, 1H; H-4), 4.11 (d, ^3J(H,H) = 3.1 Hz, 1H; H-2), 3.92 (dd, ^3J(H,H) = 8.9 Hz, 3.1 Hz, 1H; H-3), 3.87 (dd, ^2J(H,H) = 10.9 Hz, ^3J(H,H) = 4.8 Hz, 1H; H-6′), 3.77 (dd, ^2J(H,H) = 10.9 Hz, ^3J(H,H) = 1.7 Hz, 1H; H-6), 1.64 (dd, ^4J(H,H) = 1.6 Hz, ^3J(H,H) = 6.4 Hz, 3H; C*H*$_3$); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 9.6 (q, *C*H$_3$), 75.3, 73.1, 72.3, 69.0 (4 × t, C-6, 3 × Ph*C*H$_2$), 105.0, 86.1, 79.5, 78.8, 74.8, 72.7 (6 × d, C-1, C-2, C-3, C-4, C-5, *C*HCH$_3$), 132.0, 131.7, 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.6, 127.5, 127.5, 127.4 (15 × d, Ar-CH), 138.4, 138.3, 138.0, 134.0 (4 × s, Ar-C), 143.9 (d, O*C*H=CH); IR (thin film) $\tilde{\nu}$ = 1670 cm^{-1} (C=C); MS-APCI$^+$: *m*/*z* (%): 605 (100) [*M*+Na]$^+$; elemental analysis calcd (%) for C$_{36}$H$_{38}$O$_5$S: C 74.20, H 6.57; found: C 74.44, H 6.58.

Methyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (5): Sodium hydride (60% dispersion in mineral oil, 0.068 g, 1.716 mmol) was added portionwise to a solution of alcohol **4**[8] (0.55 g, 1.144 mmol) in dry DMF (10 mL) at 0 °C. Allyl bromide (0.198 mL, 2.288 mmol) was then added and the resulting solution was stirred at 0 °C for 30 min, after which time TLC (ethyl acetate/petrol 1:4) indicated no remaining starting material (R_f = 0.1) and the formation of a major product (R_f = 0.4). Methanol (3 mL) was added carefully at 0 °C and the mixture was concentrated in vacuo. The residue was dissolved in dichloromethane (90 mL) and washed with brine (2 × 40 mL) and then water (30 mL). The aqueous layers were re-extracted with dichloromethane (40 mL) and the combined organic extracts were dried with anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (ethyl acetate/petrol 1:5) to give the allyl ether **5** (0.543 g, 91%) as a colourless oil. $[\alpha]_D^{21}$ = +18.0 (*c* = 1.5 in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 7.40 – 7.17 (m, 15H, Ar-H), 5.95 (ddt, ^3J(H,H) = 17.3 Hz, 10.3 Hz, 5.6, Hz, 1H; OCH$_2$C*H*=CH$_2$), 5.33 (dddd, ^2J(H,H) = 3.1 Hz, ^3J(H,H) = 17.3 Hz, ^4J(H,H) = 1.3 Hz, 1H; OCH$_2$CH=C*H*$_E$H$_Z$), 5.27 (d, ^3J(H,H) = 1.4 Hz, 1H; H-1), 5.23 (dddd, ^2J(H,H) = 3.1 Hz, ^3J(H,H) = 10.3 Hz, ^4J(H,H) = 1.3 Hz, 1H; OCH$_2$CH=CH$_E$*H*$_Z$), 4.89, 4.51 (ABq, ^2J(H,H) = 10.7 Hz, 2H; PhC*H*$_2$), 4.68 (s, 2H; PhC*H*$_2$), 4.67, 4.53 (ABq, ^2J(H,H) = 11.7 Hz, 2H; PhC*H*$_2$), 4.20 (ddat, ^2J(H,H) = 12.9 Hz, ^3J(H,H) = 5.4 Hz, ^4J(H,H) = 1.4 Hz, 1H; OCH*H′*), 4.13 (ddat, ^2J(H,H) = 12.9 Hz, ^3J(H,H) = 5.8 Hz, ^4J(H,H) = 1.3 Hz, 1H; OC*H*H′), 4.1 (ddd, ^3J(H,H) = 4.9 Hz, 2.1 Hz, 1H; H-5), 3.98 (at, ^3J(H,H) = 9.4 Hz, 1H; H-4), 3.87 (dd, ^3J(H,H) = 9.3 Hz, 3.3 Hz, 1H; H-3), 3.83 – 3.79 (m, 2H; H-6′, H-2), 3.73 (dd, ^2J(H,H) = 11.1 Hz, ^3J(H,H) = 2.1 Hz, 1H; H-6), 2.14 (s, 3H; SCH$_3$); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 138.4, 138.3, 138.1 (3 × s, Ar-C), 134.7 (d, OCH$_2$*C*H=CH$_2$), 128.4, 128.3, 128.2, 127.9, 127.9, 127.7, 127.7, 127.5, 127.4 (9 × d, Ar-CH), 117.8 (t, OCH$_2$CH=*C*H$_2$), 83.3, 80.1, 75.9, 75.0, 71.8 (5 × d, C-5, C-4, C-2, C-3, C-1), 75.1, 73.3, 72.2, 71.4, 69.1 (5 × t, C-6, 3 × Ph*C*H$_2$, O*C*H$_2$CH=CH$_2$), 13.7 (q, SCH$_3$); MS-CI: *m*/*z* (%): 473 (100) [*M* – SCH$_3$]$^+$; HRMS-ES: calcd for C$_{31}$H$_{40}$NO$_5$S [*M*+NH$_4$]$^+$: 538.2627, found: 538.2643.

Methyl 2-*O*-(prop-1-enyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (6): *n*-Butyllithium (1.2 M in hexanes, 0.076 mL) was added to a degassed solution of Wilkinson's catalyst (0.061 g, 0.062 mmol) in dry THF (90 mL). The resulting mixture was stirred for 10 min, before being added to a refluxing solution of the allyl ether **5** (0.345 g, 0.662 mmol) in THF (3 mL). After 15 min, TLC (ethyl acetate/petrol 1:4) indicated complete consumption of the starting material (R_f = 0.45) and the formation of a single product (R_f = 0.6). The solution was allowed to cool to room temperature then diluted with dichloromethane (20 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (ethyl acetate/petrol 1:8) to afford the desired vinyl ether **6** (0.326 g, 95%), as a clear colourless oil, as an inseparable mixture of *E* and *Z* isomers (*Z*:*E* ratio 1.25:1). *E* isomer: ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 7.40 – 7.18 (m, 15H; Ar-H), 6.1 (dd, ^3J(H,H) = 12.5 Hz, ^4J(H,H) = 1.4 Hz, 1H; OC*H*=CHCH$_3$), 5.29 (s, 1H; H-1), 4.96 (dd, ^3J(H,H) = 12.5 Hz, 6.8 Hz, 1H; OCH=C*H*CH$_3$), 4.91 – 4.56 (m, 6H; 3 × Ph*C*H$_2$), 4.14 – 3.69 (m, 6H; H-6′, H-6, H-5, H-4, H-3, H-2), 2.13 (s, 3H; SCH$_3$), 1.57 (dd, ^3J(H,H) = 6.8 Hz, 1.4 Hz, 3H; OCH=CHC*H*$_3$); *Z* isomer: ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 7.40 – 7.18 (m, 15H; Ar-H), 5.90 (dd, ^3J(H,H) = 6.1 Hz, ^4J(H,H) = 1.8 Hz, 1H; OC*H*=CHCH$_3$), 5.22 (d, ^3J(H,H) = 1.4 Hz, 1H; H-1), 4.91 – 4.50 (m, 6H; 3 × Ph*C*H$_2$), 4.60 (dd, ^3J(H,H) = 6.8 Hz, 6.1 Hz, 1H; OCH=C*H*CH$_3$), 4.14 – 3.69 (m, 6H; H-6′, H-6, H-5, H-4, H-3, H-2), 2.13 (s, 3H; SCH$_3$), 1.66 (dd, ^3J(H,H) = 6.8 Hz, ^4J(H,H) = 1.8 Hz, 3H; OCH=CHC*H*$_3$); MS-CI: *m*/*z* (%): 521 (100) [*M*+H]$^+$; HRMS-ES: calcd for C$_{31}$H$_{40}$NO$_5$S [*M*+NH$_4$]$^+$: 538.2627, found: 538.2635.

2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl bromide (7): Orthoester **11**[15] (400 mg, 0.77 mmol) was dissolved in dichloromethane (20 mL) and cooled to 0 °C under Ar. HBr (33% in acetic acid, 0.7 mL) was added. After 3 min, TLC (ethyl acetate/petrol 1:3) indicated complete consumption of starting material (R_f = 0.6) and formation of a product (R_f = 0.7). The reaction was quenched with ice water (30 mL) then extracted with dichloromethane (30 mL). The organic extracts were washed with satd aq sodium bicarbonate (2 × 20 mL), dried (MgSO$_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 4:1 with 1% added triethylamine) to afford the bromide **7** (312 mg, 73%) as a colourless oil. $[\alpha]_D^{22}$ = +150 (*c* = 0.45 in CHCl$_3$); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C): δ = 7.38 – 7.16 (m, 15H; Ar-H),6.67 (d, ^3J(H,H) = 4.0 Hz, 1H; H-1), 4.85, 4.80 (ABq, ^3J(H,H) = 11.3 Hz, 2H; PhC*H*$_2$), 4.78 (dd, ^3J(H,H) = 9.8 Hz, 4.0 Hz, 1H; H-2), 4.83, 4.56 (ABq, ^3J(H,H) = 10.1 Hz, 2H; PhC*H*$_2$), 4.62, 4.51 (ABq, ^3J(H,H) = 12.2 Hz, 2H; PhC*H*$_2$), 4.13 – 4.07 (m, 2H; H-3, H-5), 3.90 – 3.85 (m, 1H; H-4), 3.83 (dd, ^2J(H,H) = 11.1 Hz, ^3J(H,H) = 3.2 Hz, 1H; H-6′), 3.69 (dd, ^2J(H,H) = 11.1 Hz, ^3J(H,H) = 1.8 Hz, 1H; H-6), 2.06 (s, 3H; CH$_3$). The spectroscopic and analytical data were in agreement with those reported in the literature.[15]

Methyl 3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (8)

Method 1: *n*-Butyllithium (1.2 M in hexanes, 1.6 mL, 1.92 mmol) and dimethyl disulphide (0.17 mL, 1.92 mmol) were dissolved in THF (3 mL) at −78 °C under argon and stirred for 10 min. Bromide **7** (305 mg, mmol) was dissolved in THF (3 mL) and added to the reaction mixture by cannular. The mixture was stirred at at −78 °C and after 80 min, TLC (ethyl acetate/petrol 1:3) indicated formation of a product (R_f = 0.3) and very little remaining starting material (R_f = 0.6). An aq satd ammonium chloride solution (2 mL) was added and the mixture was partitioned between dichloromethane (30 mL) and water (30 mL). The organic layer was dried (MgSO$_4$), filtered and concentrated in vacuo. The residue was recrystallised from ether/petrol to afford methyl thioglycoside **8** (180 mg, 68%) as a white, crystalline solid. M.p. 76 – 78 °C (ether/petrol); $[\alpha]_D^{22}$ = +4.8 (*c* = 0.25 in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 7.39 – 7.16 (m, 15H; Ar-H), 4.93, 4.86 (ABq, ^2J(H,H) = 11.3 Hz, 2H; PhC*H*$_2$), 4.83, 4.56 (ABq, ^2J(H,H) = 10.5 Hz, 2H; PhC*H*$_2$), 4.60, 4.53 (ABq, ^2J(H,H) = 12.1 Hz, 2H; PhC*H*$_2$), 4.22 (d, ^3J(H,H) = 9.0 Hz, 1H; H-1), 3.75 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 2.0 Hz, 1H; H-6′), 3.71 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 4.3 Hz, 1H; H-6), 3.64 (at, ^3J(H,H) = 9.0 Hz, 1H; H-4), 3.60 – 3.55 (m, 2H; H-2, H-3), 3.53 – 3.50 (m, 1H; H-5), 2.20 (s, 3H; SCH$_3$); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 137.4, 137.0, 136.9 (3 × s, Ar-C), 128.5, 128.4, 128.4, 128.3, 127.6, 128.1, 128.0, 127.9, 127.8, 127.7 (10 × d, Ar-CH), 84.8, 84.5, 78.3, 76.2, 71.3 (5 × d, C-1, C-2, C-3, C-4, C-5), 74.1, 74.0, 72.3, 67.7 (4 × t, C-6, 3 × Ph*C*H$_2$), 10.4 (q, SCH$_3$); IR (thin film): $\tilde{\nu}$ = 3440 cm^{-1} (OH); MS-APCI$^+$: *m*/*z* (%): 504 (100) [*M*+Na]$^+$; elemental analysis calcd (%) for C$_{28}$H$_{32}$O$_5$S: C 69.97, H 6.71; found: C 70.00, H 6.79.

Method 2: Acetyl bromide (10 mL) was added to the orthoester **11** (1.0 g, 1.92 mmol) at 0 °C under argon. After 15 min, TLC (ethyl acetate/petrol 1:2) indicated formation of a product (R_f = 0.5) and complete consumption of starting material (R_f = 0.4). Toluene was added and the mixture concentrated in vacuo to give bromide **7** which was used without purification. *n*-Butyllithium (1.6 M in hexanes, 3.0 mL, 4.81 mmol) and dimethyl disulphide (0.43 mL, 4.81 mmol) were dissolved in THF (5 mL) at −78 °C under argon and stirred for 15 min. The crude residue was dissolved in THF (3 mL) and added to the reaction mixture by cannular under argon. The mixture was stirred at −78 °C and after 1 h, TLC (ethyl acetate/petrol 1:3) indicated formation of a product (R_f = 0.2) and very little remaining starting material (R_f = 0.5). Aq satd ammonium chloride (30 mL) was added and the mixture was partitioned between dichloromethane (2 × 50 mL) and water (100 mL). The organic layer was dried (MgSO$_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 4:1) to give a white solid which was

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recrystallised from ether/petrol to afford methyl thioglycoside **8** (561 mg, 61%) as a white, crystalline solid, identical to that previously described.

Methyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (9): Alcohol **8** (2.74 g, 5.71 mmol) was dissolved in anhydrous DMF (10 mL) and cooled to 0 °C. Allyl bromide (1.0 mL, 11.42 mmol) was added and then sodium hydride (60% dispersion in mineral oil, 457 mg, 11.42 mmol) was added portionwise. After 30 min, TLC (ethyl acetate/petrol 1:3) indicated formation of a single product ($R_f = 0.8$) and complete consumption of starting material ($R_f = 0.5$). The reaction was quenched with methanol (10 mL) the mixture adjusted to pH 7 with aqueous HCl (1M) and then concentrated in vacuo. The residue was partitioned between dichloromethane (3 × 100 mL) and water (200 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 6:1) to afford allylated thioglycoside **9** (2.52 g, 85%) as a pale yellow oil. $[\alpha]_D^{22} = -11$ ($c = 0.55$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.41-7.15$ (m, 15H; Ar-H); 6.01 (ddt, $^3J(H,H) = 17.1$ Hz, 10.4 Hz, 6.0 Hz, 1H; $OCH_2CH{=}CH_2$), 5.33 (dddd, $^2J(H,H) = 1.4$ Hz, $^3J(H,H) = 17.1$ Hz, $^4J(H,H) = 1.3$ Hz, 1.3 Hz, 1H; $OCH_2CH{=}CH_EH_Z$), 5.21 (dddd, $^2J(H,H) = 1.4$ Hz, $^3J(H,H) = 10.4$ Hz, $^4J(H,H) = 1.3$ Hz, 1.3 Hz, 1H; $OCH_2CH{=}CH_EH_Z$), 4.95, 4.86 (ABq, $^2J(H,H) = 10.9$ Hz, 2H; $PhCH_2$), 4.85, 4.58 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; $PhCH_2$), 4.63, 4.57 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 4.43 (ddat, $^2J(H,H) = 12.0$ Hz, $^3J(H,H) = 5.8$ Hz, $^4J(H,H) = 1.3$ Hz, 1H; $OCHH'$), 4.33 (d, $^3J(H,H) = 9.6$ Hz, 1H; H-1), 4.30 (ddat, $^2J(H,H) = 12.0$ Hz, $^3J(H,H) = 6.0$ Hz, $^4J(H,H) = 1.3$ Hz, 1H; $OCHH'$), 3.78 (dd, $^2J(H,H) = 10.9$ Hz, $^3J(H,H) = 1.9$ Hz, 1H; H-6′), 3.72 (dd, $^2J(H,H) = 10.9$ Hz, $J_{5,6}$ 4.4 Hz, $^3J(H,H) = 10.9$ Hz, 1H; H-6), 3.67 (at, $^3J(H,H) = 8.9$ Hz, 1H; H-3), 3.62 (at, $^3J(H,H) = 9.2$ Hz, 1H; H-4), 3.52–3.48 (m, 1H; H-5), 3.36 (dd, $^3J(H,H) = 9.6$ Hz, 8.6 Hz, 1H; H-2), 2.26 (s, 3H; SCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.4$, 138.2, 138.0 (3 × s, Ar-C), 134.6 (d, $OCH_2CH{=}CH_2$), 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6 (8 × d, Ar-CH), 117.5 (t, $OCH_2CH{=}CH_2$), 86.5 (d, C-3), 85.3 (d, C-1), 80.8 (d, C-2), 79.1 (d, C-5), 77.7 (d, C-4), 74.1 (t, $OCH_2CH{=}CH_2$), 75.8, 75.1, 73.4 (3 × t, 3 × $PhCH_2$), 68.9 (t, C-6), 13.0 (q, SCH_3); IR (thin film): $\tilde{\nu} = 1647$ cm^{-1} (C=C); MS-APCI$^+$: *m*/*z* (%): 559 (42) $[M+K]^+$, 543 (100) $[M+Na]^+$; elemental analysis calcd (%) for $C_{31}H_{36}O_5S$: C 71.51, H 6.97; found: C 71.49, H 6.89.

Methyl 2-*O*-(prop-1-enyl)-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (10): Wilkinson's catalyst (448 mg, 0.49 mmol) was dissolved in THF (10 mL) and degassed. *n*-Butyllithium (1.6M in hexanes, 0.45 mL, 0.73 mmol) was added and the mixture stirred for 10 min. Thioglycoside **9** (2.52 g, 0.485 mmol) was dissolved in THF (10 mL) and heated to reflux. The catalyst solution was added by cannular under argon. After 1 h, TLC (ethyl acetate/petrol 1:3) indicated formation of a single product ($R_f = 0.55$) and complete consumption of starting material ($R_f = 0.5$). The reaction was allowed to cool then diluted with dichloromethane (20 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 6:1 with 1% added triethylamine) to afford the vinyl ethers **10** (2.37 g, 94%) as a pale yellow oil, as a mixture of *E* and *Z* isomers, *E*:*Z* ratio 2.7:1; partial data: *E* isomer: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 6.23$ (dd, 1H; $OCH{=}CHCH_3$), 5.05 (dd, $^3J(H,H) = 12.2$ Hz, 1H; $OCH{=}CHCH_3$), 1.57 (dd, $^3J(H,H) = 6.9$ Hz, $^4J(H,H) = 1.5$ Hz, 3H; $OCH{=}CHCH_3$); *Z* isomer: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 6.16$ (dd, $^3J(H,H) = 6.2$ Hz, 1H; $OCH{=}CHCH_3$), 1.64 (dd, $^3J(H,H) = 6.9$ Hz, $^4J(H,H) = 1.6$ Hz, 3H; $OCH{=}CHCH_3$); MS-APCI$^+$: *m*/*z* (%): 543 (100) $[M+Na]^+$; HRMS-ES: calcd for $C_{31}H_{40}NO_5S$ $[M+NH_4]^+$: 538.2627, found: 538.2627.

Phenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-seleno-*β*-D-glucopyranoside (12): Orthoester **11**[17] (8.3 g, 16.0 mmol) was dissolved in acetonitrile (60 mL). Mercuric bromide (57.6 mg, 0.16 mmol) and then selenophenol (3.3 mL, 30.0 mmol) were added and the reaction mixture was stirred at 50 °C. After 90 min, TLC (dichloromethane/ether 30:1) indicated formation of a product ($R_f = 0.7$) and complete consumption of starting material ($R_f = 0.3$). The reaction was quenched with 5% aq sodium hydroxide (200 mL) then extracted with dichloromethane (2 × 200 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 6:1) and recrystallised from ethanol to afford the selenoglycoside **5** (7.85 g, 78%) as a white, crystalline solid. M.p. 122–125 °C (ethanol); $[\alpha]_D^{22} = +2.7$ ($c = 0.33$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.67-7.22$ (m, 20H; Ar-H), 5.11–5.06 (m, 1H; H-2), 4.84 (d, $^3J(H,H) = 10.1$ Hz, 1H; H-1), 4.82, 4.70 (ABq, $^2J(H,H) = 11.3$ Hz, 2H; $PhCH_2$), 4.81, 4.60 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; $PhCH_2$), 4.61, 4.55 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 3.81 (dd, $^2J(H,H) = 11.1$ Hz, $^3J(H,H) = 1.9$ Hz, 1H; H-6′), 3.75 (dd, $^2J(H,H) = 11.1$ Hz, $^3J(H,H) = 4.6$ Hz, 1H; H-6), 3.72–3.67 (m, 2H; H-3, H-4), 3.56–3.53 (m, 1H; H-5), 2.01 (s, 3H; CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 169.6$ (s, C=O),138.2, 138.0, 137.8 (3 × s, Ar-C), 134.7, 128.9, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6 (9 × d, Ar-CH), 84.3, 81.7, 80.4, 77.7, 72.6 (5 × d, C-1, C-2, C-3, C-4, C-5), 75.3, 75.1, 73.4, 68.8 (4 × t, C-6, 3 × $PhCH_2$), 21.1 (q, CH_3); IR (thin film):$\tilde{\nu} = 1737$ cm^{-1} (C=O); MS-APCI$^+$: *m*/*z* (%): 655 (100) $[M+Na]^+$; elemental analysis calcd for $C_{35}H_{36}O_6Se$: C 66.56, H 5.74; found: C 66.70, H 5.47.

Phenyl 3,4,6-tri-*O*-benzyl-1-seleno-*β*-D-glucopyranoside (13): The acetate **12** (7.34 g, 11.6 mmol) was suspended in methanol (900 mL). Sodium (870 mg, 37.8 mmol) was added to methanol (100 mL), and this solution was then added to the dissolved acetate. After 28 h, TLC (ethyl acetate/petrol 1:3) indicated formation of a product ($R_f = 0.45$) and complete consumption of starting material ($R_f = 0.5$). Aqueous HCl (1M) was added until pH 7 was reached and the mixture was concentrated to ca. 150 mL in vacuo. The solution was partitioned between ethyl acetate (400 mL) and water (200 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was recrystallised from ether/petrol to afford the alcohol **13** (6.24 g, 91%) as a white, crystalline solid. M.p. 61–63 °C (ether/petrol); $[\alpha]_D^{22} = -12$ ($c = 0.5$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.68-7.19$ (m, 20H; Ar-H),4.91, 4.84 (ABq, $^2J(H,H) = 11.2$ Hz, 2H; $PhCH_2$), 4.82, 4.57 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; $PhCH_2$), 4.73 (d, $^3J(H,H) = 9.6$ Hz, 1H; H-1), 4.61, 4.55 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 3.80 (dd, $^2J(H,H) = 11.1$ Hz, $^3J(H,H) = 2.0$ Hz, 1H; H-6′), 3.76 (dd, $^2J(H,H) = 11.1$ Hz, $^3J(H,H) = 4.0$ Hz, 1H; H-6), 3.64–3.56 (m, 2H; H-3, H-4), 3.54–3.47 (m, 2H; H-2, H-5). The spectroscopic and analytical data were in agreement with those reported in the literature.[18]

Phenyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-1-seleno-*β*-D-glucopyranoside (14): The alcohol **13** (3.0 g, 5.09 mmol) was dissolved in anhydrous DMF (10 mL) and cooled to 0 °C. Allyl bromide (0.88 mL, 10.18 mmol) was added then sodium hydride (60% dispersion in mineral oil, 407 mg, 10.18 mmol) was added portionwise. After 30 min, TLC (ethyl acetate/petrol 1:3) indicated formation of a single product ($R_f = 0.5$) and complete consumption of starting material ($R_f = 0.3$). The reaction was quenched with methanol (5 mL) then concentrated in vacuo. The residue was partitioned between dichloromethane (100 mL) and water (100 mL). The aqueous layer was extracted with dichloromethane (100 mL) and the combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was recrystallised from ethanol to afford allylated selenoglycoside **14** (2.97 g, 92%) as a white, crystalline solid. M.p. 61–62 °C (ethanol); $[\alpha]_D^{22} = -7.6$ ($c = 0.5$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.69-7.17$ (m, 20H; Ar-H), 5.97 (ddat, $^3J(H,H) = 17.2$ Hz, 10.7 Hz, 6.0 Hz, 1H; $OCH_2CH{=}CH_2$), 5.28 (dd, $^2J(H,H) = 1.6$ Hz, $^3J(H,H) = 17.2$ Hz, 1H; $OCH_2CH{=}CH_EH_Z$), 5.18 (dd, $^2J(H,H) = 1.6$ Hz, $^3J(H,H) = 10.4$ Hz, 1H; $OCH_2CH{=}CH_EH_Z$), 4.89, 4.83 (ABq, $^2J(H,H) = 10.7$ Hz, 2H; $PhCH_2$), 4.80 (d, $^3J(H,H) = 9.8$ Hz, 1H; H-1), 4.81, 4.58 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; $PhCH_2$), 4.59, 4.53 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 4.34 (dd, $^2J(H,H) = 11.8$ Hz, $^3J(H,H) = 5.6$ Hz, 1H; $OCHH'$), 4.24 (dd, $^2J(H,H) = 11.8$ Hz, $^3J(H,H) = 6.0$ Hz, 1H; $OCHH'$), 3.78 (dd, $^2J(H,H) = 10.9$ Hz, $^3J(H,H) = 2.0$ Hz, 1H; H-6′), 3.72 (dd, $^2J(H,H) = 10.9$ Hz, $^3J(H,H) = 4.3$ Hz, 1H; H-6), 3.64–3.62 (m, 2H; H-3, H-4), 3.49–3.45 (m, 1H; H-5), 3.42–3.37 (m, 1H; H-2); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.8$, 138.6 (2 × s, Ar-C), 135.1, 134.9 (2 × d, Ar-CH, $OCH_2CH{=}CH_2$), 129.5, 128.9, 128.8, 128.4, 128.4, 128.2, 128.1, 128.0 (8 × d, Ar-CH), 117.9 (t, $OCH_2CH{=}CH_2$),87.2, 83.5, 81.6, 80.6, 78.2 (5 × d, C-1, C-2, C-3, C-4, C-5), 76.3, 75.6, 74.5, 73.9, 69.4 (5 × t, C-6, 3 × $PhCH_2$, $OCH_2CH{=}CH_2$); MS-APCI$^+$: *m*/*z* (%): 653 (100) $[M+Na]^+$; elemental analysis calcd for $C_{36}H_{38}O_5Se$: C 68.67, H 6.08; found: C 68.77, H 6.09.

Phenyl 2-*O*-(prop-1-enyl)-3,4,6-tri-*O*-benzyl-1-seleno-*β*-D-glucopyranoside (15): Wilkinson's catalyst (31 mg, 0.033 mmol) was dissolved in THF (3 mL) and degassed. *n*-Butyllithium (1.2M in hexanes, 0.04 mL, 0.049 mmol) was added and the mixture stirred for 15 min. Selenoglycoside **14** (205 mg, 0.326 mmol) was dissolved in THF (3 mL) and heated to reflux. The catalyst solution was added by cannular under argon. After 140 min, the reaction was allowed to cool then diluted with dichloromethane (20 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 6:1) to give vinyl ethers **15** (190 mg, 92%) as a pale yellow oil. MS-APCI$^+$: *m*/*z* (%): 653 (45)

$[M+Na]^+$; HRMS: calcd for $C_{36}H_{42}NO_5Se$ $[M+NH_4]^+$: 648.2228, found: 648.2234.

General procedure A: ***manno*/*S*-phenyl NIS tethering**: Vinyl ether **3** (typically 0.15 mmol), the alcohol (1.5 equiv) and powdered 4 Å molecular sieves (ca. 500 mg) were stirred in dichloroethane (4 mL) under argon at −40 °C. NIS (2.5 equiv) was added and the mixture was allowed to warm slowly to room temperature overnight. After 16 h, dichloromethane was added, the mixture was filtered through Celite washed with 10 % aqueous sodium thiosulfate, dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash column chromatography to give the mixed acetals **16a–e**,**g**,**h**.

Phenyl 2-*O*-(2-iodo-1-methoxypropyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16a): Vinyl ether **3** (254 mg, 0.49 mmol) gave mixed acetals **16a** as a cloudy oil, an inseparable mixture of diastereomers (336 mg, 93 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.54–7.48 (m, 2H; 2 × Ar-H); 7.45–7.26 (m, 18H; 18 × Ar-H), 5.63, 5.59, 5.57 (3 × s, 1H; H-1), 4.93, 4.89 (ABq, ^2J(H,H) = 10.8 Hz, 1H; PhC*H*H), 4.83–4.51 (m, 6H; 5 × PhC*H*H, O_2CH), 4.36–4.17 (m, >2H; partial-H-2, H-5, C*H*I), 4.15 (ad, ^3J(H,H) = 2.5 Hz, <1H; partial-H-2), 4.10, 4.04 (2 × at, ^3J(H,H) = 9.4 Hz, 9.5 Hz, 1H; H-4), 3.96–3.91 (m, 1H; H-3), 3.90–3.84 (m, 1H; H-6′), 3.78 (d, ^2J(H,H) = 10.9 Hz, 1H; H-6), 3.43, 3.39, 3.33, 3.31 (4 × s [relative intensities: 1:1.4:1.7:2.3], 3H; OCH_3), 1.91–1.85 (m, 3H; $CHCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.4, 138.2, 137.9 (3 × s, Ar-C), 131.6, 129.1, 128.6, 128.5, 128.5, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.4 (14 × d, Ar-CH), 106.7, 106.5, 87.4, 87.2, 80.7, 80.7, 69.0, 77.4, 76.1, 75.9, 75.2, 75.1, 74.9, 74.8, 73.2, 73.2, 73.1, 73.0, 72.9, 72.9, 72.3 (21 × d/t, C-1, C-2, C-3, C-4, C-5, C-6, 3 × PhCH_2, O_2CH), 54.6, 54.1, 52.4, 51.8 (4 × q, OCH_3), 25.7, 25.5, 25.2, 23.7, 23.4, 21.5, 21.2 (7 × d/q, *C*H*I*CH_3); MS-APCI$^+$: *m*/*z* (%): 764 (100) $[M+Na]^+$; elemental analysis for $C_{37}H_{41}IO_6S$: C 60.00, H 5.58; found: C 59.94, H 5.57.

Phenyl 2-*O*-(1-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl)-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16b): Vinyl ether **3** (185 mg, 0.32 mmol) and diacetone galactose (133 mg, 0.51 mmol), gave mixed acetals **16b** as a clear, colourless oil, an inseparable mixture of diastereomers (293 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.53–7.19 (m, 20H; 20 × Ar-H), 5.75, 5.73, 5.64 (3 × d, ^3J(H,H) = 1.6 Hz, 1.4 Hz, 1.4 Hz, 1H; H-1_{man}), 5.58, 5.46, 5.39 (3 × d, $J_{1,2}$ = 5.0 Hz, 1H, H-1_{gal}), 4.93–4.48, 4.45–4.08, 4.02–3.68 (m, 20H; H-2_{man}, H-3_{man}, H-4_{man}, H-5_{man}, H-6_{man}, H-$6'_{man}$, H-2_{gal}, H-3_{gal}, H-4_{gal}, H-5_{gal}, H-6_{gal}, H-$6'_{gal}$, 3 × PhCH_2, C*H*CHI, CHC*H*I), 1.84, 1.87 (2 × d, ^3J(H,H) = 7.0 Hz, 6.9 Hz, 3H; $CHCH_3$), 1.56–1.30 (10 × s, 12H; 2 × $C(CH_3)_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.4, 138.3, 138.0, 137.7, 137.5, 134.8, 134.5, 134.0, 132.1, 131.0, 130.8, 129.0, 128.8, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.3, 126.9 (18 × d, Ar-CH; 9 × s, Ar-C), 109.3, 109.2, 109.1, 108.7, 108.6, 108.4 (6 × s, 2 × *C*$(CH_3)_2$), 105.1, 102.9, 96.2, 87.2, 87.1, 85.3, 81.0, 81.0, 74.9, 74.7, 74.1, 72.7, 72.6, 71.3, 70.7, 70.6, 70.6, 70.5, 70.3, 67.5, 66.6, 26.7, 26.6, 26.4, 26.3, 26.2, 26.1, 26.0, 25.9, 24.9, 24.4, 24.3, 23.2, 23.1 (34 × d+q, C-1_{gal}, C-2_{gal}, C-3_{gal}, C-4_{gal}, C-5_{gal}, C-1_{man}, C-2_{man}, C-3_{man}, C-4_{man}, C-5_{man}, $O_2CHCHICH_3$, 2 × $C(CH_3)_2$), 75.2, 73.2, 73.1, 72.5, 72.3, 71.8, 69.0, 65.4, 65.1, 63.8 (10 × t, C-6_{gal}, C-6_{man}, 3 × PhCH_2); MS-APCI$^+$: *m*/*z* (%): 991 (100) $[M+Na]^+$; elemental analysis calcd for $C_{48}H_{57}IO_{11}S$: C 59.23, H 5.83; found: C 59.50, H 5.93.

Phenyl 2-*O*-(1-cyclohexyloxy-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16c): Vinyl ether **3** (94 mg, 0.16 mmol) and cyclohexanol (0.33 mL, 0.33 mmol) gave mixed acetals **16c** as a clear oil, an inseparable mixture of diastereomers (99 mg, 76 %). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.67–7.25 (m, 20H; 20 × Ar-H), 5.65, 5.62, 5.60, 5.57 (4 × d, ^3J(H,H) = 2.0 Hz, 1.5 Hz, 1.5 Hz, 1.5 Hz, 1H; H-1), 4.92–4.48 (m, 7H [incorporating: 4.91, 4.63 (ABq, ^2J(H,H) = 11.0 Hz, <2H; PhCH_2), 4.88, 4.57 (ABq, ^2J(H,H) = 11.0 Hz, <2H; PhCH_2), 4.86, 4.75 (ABq, ^2J(H,H) = 12.0 Hz, <2H; PhCH_2), 4.75 (s, <2H; $PhCH_2$)], 4.69, 4.53 (ABq, ^2J(H,H) = 12.0 Hz, <2H; PhCH_2), 4.66, 4.50 (ABq, ^3J(H,H) = 12.0 Hz, <2H; 3 × PhCH_2, CHO_2), 4.10–4.23 (m, >2H; partial-H-2, partial-H-3, C*H*I), 4.37–4.27 (m, >1H; partial-H-2, H-5), 4.01–3.76 (m, >2H; partial-H-3, H-4, partial-H-6, H-6′), 3.72 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 2.0 Hz, <1H; partial-H-6), 3.67–3.48, 3.40–3.30 (2 × m, 1H; $OCH(CH_2)_2$), 1.95, 1.90, 1.89, 1.86 (4 × d, ^3J(H,H) = 7.0 Hz, 7.0 Hz, 7.0 Hz, 6.5 Hz, 3H; CH_3), 1.94–1.13 (m, 10H, $(CH_2)_5$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 138.9, 138.8, 138.6, 135.0, 134.5 (5 × s, Ar-C), 132.4, 132.0, 129.4, 129.0, 128.9, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9 (17 × d, Ar-CH), 104.7, 102.2, 102.0, 80.7, 81.4, 76.5, 75.7, 74.9, 73.6, 73.4, 73.0, 72.7, 70.7, 70.3, 29.8, 28.8, 28.5, 28.3, 22.6, 21.9, 21.7, 19.5 (22 × d/q, *CH*I*CH*$_3$, O*CH*$(CH_2)_2$, C-1, C-2, C-3, C-4, C-5, O_2CH), 75.6, 75.5, 73.8, 72.6, 69.6, 69.3, 36.0, 33.7, 33.5, 33.3, 33.2, 26.1, 26.0, 25.9, 25.8, 24.6, 24.4, 24.3 (18 × t, $(CH_2)_5$, C-6, 3 × PhCH_2); MS-APCI$^+$: *m*/*z* (%): 831 (27) $[M+Na]^+$; HRMS-CI: calcd for $C_{42}H_{53}INO_6S$ $[M+NH_4]^+$: 826.2638, found: 826.2635.

Phenyl 2-*O*-(1-benzyloxy-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16d): Vinyl ether **3** (250 mg, 0.43 mmol) and benzyl alcohol (0.11 mL, 1.06 mmol) gave mixed acetals **16d** as a cloudy oil, an inseparable mixture of diastereomers (341 mg, 97 %). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.75–7.14 (m, 25H; 25 × Ar-H), 5.61, 5.60, 5.55, 5.44 (4 × d, ^3J(H,H) = 2.0 Hz, 1H; H-1), 4.94–4.87, 4.78–4.50 (2 × m, >9H; 4 × PhCH_2, O_2CH, partial-C*H*I), 4.37–4.28 (m, <2H; partial-H-2, H-5, partial-C*H*I), 4.25 (at, ^3J(H,H) = 2.0 Hz, <1H; partial-H-2), 4.13–4.04 (m, >1H; partial-H-2, H-4), 3.95–3.82 (m, 2H; H-3, H-6′), 3.77 (dd, ^2J(H,H) = 11.0 Hz, ^3J(H,H) = 1.5 Hz, 1H; H-6), 1.92, 1.90 (2 × d, ^3J(H,H) = 7.0 Hz, 3H; CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 138.9, 138.7, 138.3, 134.0 (4 × s, Ar-C), 132.4, 132.1, 129.4, 129.0, 128.9, 128.9, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.8 (17 × d, Ar-CH), 105.6, 105.1, 87.8, 87.5, 86.3, 81.1, 81.0, 76.5, 74.4, 75.2, 74.4, 73.5, 73.4 (13 × d, C-1, C-2, C-3, C-4, C-5, O_2CH), 75.7, 75.4, 73.7, 73.5, 73.2, 73.0, 69.5, 69.4, 67.8, 67.4 (10 × t, C-6, 4 × PhCH_2), 26.7, 26.4, 23.9, 23.7, 21.6 (5 × d/q, *C*H*I*CH_3); MS-APCI$^+$: *m*/*z* (%): 839 (47) $[M+Na]^+$; HRMS-ES: calcd for $C_{43}H_{45}INaO_6S$ $[M+Na]^+$: 839.1879, found: 839.1868.

Phenyl 2-*O*-(2-iodo-1-(methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-*O*-yl)propyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16e): Vinyl ether **3** (100 mg, 0.17 mmol) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (213 mg, 0.46 mmol) gave mixed acetals **16e** as a clear oil, an inseparable mixture of diastereomers (181 mg, 90 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.56–7.18 (m, 35H; 35 × Ar-H), 5.83, 5.77, 5.73 (3 × d, ^3J(H,H) = 1.4 Hz, 1.0 Hz, 1.0 Hz, 1H; H-1_{man}), 5.04–4.44 (m, >14H; partial-H-1_{glc}, H-2_{man}, O_2CHCHI, 6 × PhCH_2), 4.43 (d, ^3J(H,H) = 3.5 Hz, <1H; partial-H-1_{glc}), 4.38–4.34 (m, 1H; H-5_{man}), 4.24–3.98 (m, 3H; H-3_{glc}, H-4_{man}, C*H*I), 3.96–3.56 (m, >6H; partial-H-2_{glc}, partial-H-4_{glc}, H-5_{glc}, H-6_{glc}, H-$6'_{glc}$, H-3_{man}, H-6_{man}, H-$6'_{man}$), 3.52 (dd, ^3J(H,H) = 9.6 Hz, 3.5 Hz, <1H; partial-H-2_{glc}), 3.44 (at, ^3J(H,H) = 9.4 Hz, <1H; partial-H-4_{glc}), 3.38, 3.37, 3.35 (3 × s [relative intensities: 2:1:9], 3H; OCH_3), 1.95, 1.92, 1.89 (3 × d, ^3J(H,H) = 7.0 Hz, 7.0 Hz, 6.9 Hz, 3H; $CHCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.8, 138.1, 138.0 (3 × s, Ar-C), 135.0, 132.5, 130.4, 129.0, 128.5, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 128.1, 128.0, 128.0, 127.8, 127.7, 127.7, 126.9 (18 × d, Ar-CH), 106.5, 106.4, 103.6, 98.0, 97.8, 97.5, 87.1, 85.9, 82.0, 81.1, 80.4, 77.8, 74.9, 74.1, 72.9, 72.7, 70.2 (17 × d, C-1_{glc}, C-2_{glc}, C-3_{glc}, C-4_{glc}, C-5_{glc}, C-1_{man}, C-2_{man}, C-3_{man}, C-4_{man}, C-5_{man}, O_2CH), 75.8, 75.3, 75.1, 75.0, 75.0, 73.4, 73.2, 73.1, 72.7, 72.6, 69.0, 66.0, 65.4, 64.3 (14 × t, C-6_{glc}, C-6_{man}, 6 × PhCH_2), 55.2, 55.2, 55.1 (3 × q, OCH_3), 26.7, 26.3, 25.8, 23.1, 23.1, 22.0 (6 × d/q, *CH*I*CH*$_3$); MS-APCI$^+$: *m*/*z* (%): 1195 (100) $[M+Na]^+$; HRMS-ES: calcd for $C_{64}H_{69}INaO_{11}S$ $[M+Na]^+$: 1195.3503, found: 1195.3494.

Phenyl 2-*O*-(2-iodo-1-(methyl 2-*O*-benzyl-(*R*)-4,6-*O*-benzylidene-α-D-mannopyranosid-6-*O*-yl)-propyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16g): Vinyl ether **3** (108 mg, 0.19 mmol) and methyl 2-*O*-benzyl-(*R*)-4,6-benzylidene-α-D-mannopyranoside (175 mg, 0.47 mmol) gave mixed acetals **16g** as a clear oil, a partially separable mixture of diastereomers (170 mg, 85 %). R_f = 0.55, 0.45 (petrol/ether 1:1). Data for partially separated diastereomer at R_f = 0.45: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.56 (d, ^3J(H,H) = 6.9 Hz, 2H; 2 × Ar-H), 7.43 (dd, ^3J(H,H) = 1.5 Hz, 8.0 Hz, 2H; 2 × Ar-H), 7.26–7.09 (m, 26H; 26 × Ar-H), 5.86 (d, ^3J(H,H) = 0.9 Hz, 1H; H-1_{SPh}), 5.62 (s, 1H; PhCHO_2), 4.87 (d, ^3J(H,H) = 3.6 Hz, 1H; O_2CHCHI), 4.70 (d, ^3J(H,H) = 12.0 Hz, 1H; PhCH*H*′), 4.69, 4.41 (ABq, ^2J(H,H) = 10.4 Hz, 2H; PhCH_2), 4.59–4.55 (m, 6H; H-1_{OMe}, H-2_{SPh}, PhCH_2, PhC*H*H′, PhC*H*H′), 4.39 (d, ^2J(H,H) = 11.9 Hz, 1H; PhC*H*H′), 4.16–4.08 (m, 2H; H-4_{OMe}, H-5_{SPh}), 3.99–3.93 (m, 2H; H-3_{OMe}, C*H*I), 3.88 (at, ^3J(H,H) = 9.7 Hz, 1H; H-4_{SPh}), 3.74–3.64 (m, 5H; H-2_{OMe}, H-5_{OMe}, H-$6'_{OMe}$, H-6_{SPh}, H-$6'_{SPh}$), 3.51 (d, ^2J(H,H) = 11.3 Hz, 1H; H-6_{OMe}), 3.45 (dd, ^3J(H,H) = 3.1 Hz, 9.4 Hz, 1H; H-3_{SPh}), 3.27 (s, 3H; OCH_3), 1.74 (3 × d, ^3J(H,H) = 7.0 Hz, 3H; $CHCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 139.0, 139.0, 138.8, 138.4, 137.8, 134.7 (6 × s, Ar-C),131.8, 130.0, 129.5, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5 (19 × d, Ar-CH), 107.7, 103.1, 101.0, 88.3, 81.0, 80.3, 78.6, 74.9, 74.9, 74.8, 72.9, 64.4 (12 × d, C-1_{OMe}, C-2_{OMe}, C-3_{OMe}, C-4_{OMe}, C-5_{OMe}, C-1_{SPh}, C-2_{SPh}, C-3_{SPh}, C-4_{SPh}, C-5_{SPh}, O_2CHCHI,

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PhCHO$_2$), 75.7, 74.7, 73.5, 71.1, 69.7, 69.4 (6 × t, C-6$_{OMe}$, C-6$_{SPh}$, 4 × PhCH$_2$), 55.3 (q, OCH$_3$), 26.4, 21.5 (2 × d/q, CHICH$_3$); MS-APCI$^+$: *m*/*z* (%): 1098 (3) $[M+NH_4]^+$; HRMS-ES: calcd for $C_{57}H_{65}INO_{11}S$ $[M+NH_4]^+$: 1098.3323, found: 1098.3308.

Selected data for mixture of diastereomers at $R_f = 0.55$ and minor component at $R_f = 0.45$: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 3.36$, 3.17 (2 × s, OCH$_3$), 1.82, 1.66 (2 × d, $^3J(H,H) = 6.9$ Hz, 7.0 Hz, CHCH$_3$). A side product was also isolated, a single diastereomer of succinimide trapped thioglycoside **22 (22b)**, a clear oil (16 mg, 10%). $R_f = 0.3$ (petrol/ether 1:1); $[\alpha]_D^{25.5} = +92.3$ ($c = 0.57$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta =$ 7.48–7.20 (m, 15H; 15 × Ar-H), 5.63 (d, 1H; NCH), 5.30 (d, $^3J(H,H) =$ 1.7 Hz, 1H; H-1), 5.13 (dq, $^3J(H,H) = 10.2$ Hz, 1H; CHI), 4.89, 4.68 (Abq, $^2J(H,H) = 10.9$ Hz, 2H; PhCH$_2$), 4.85, 4.54 (ABq, $^2J(H,H) = 10.9$ Hz, 2H; PhCH$_2$), 4.60, 4.47 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; PhCH$_2$), 4.20–4.16 (m, 1H; H-5), 4.10 (at, $^3J(H,H) = 2.0$ Hz, 1H; H-2), 3.96–3.83 (m, 2H; H-3, H-4), 3.75 (dd, $^2J(H,H) = 11.0$ Hz, $^3J(H,H) = 4.9$ Hz, 1H; H-6′), 3.69 (dd, $^2J(H,H) = 11.0$ Hz, $^3J(H,H) = 1.9$ Hz, 1H; H-6), 2.60–2.54 (m, 4H; (CH$_2$)$_2$), 2.00 (d, $^3J(H,H) = 6.9$ Hz, 3H; CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.3$, 138.0, 137.6, 133.8 (4 × s, Ar-C), 131.8, 129.1, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.5, 126.3, 125.5 (14 × d, Ar-CH), 86.6, 80.0, 76.2, 76.2, 74.6, 73.2 (6 × d, C-1, C-2, C-3, C-4, C-5, NCH), 75.1, 73.2, 72.8, 69.0 (4 × t, C-6, 3 × PhCH$_2$), 27.8 (t, (CH$_2$)$_2$), 25.0, 23.8 (2 × d/q, CHICH$_3$); IR (thin film): $\tilde{\nu} = 1715$ cm^{-1} (C=O); MS-APCI$^+$: *m*/*z* (%): 825 (8) $[M+NH_4]^+$; HRMS-ES: calcd for $C_{40}H_{46}IN_2O_7S$ $[M+NH_4]^+$: 825.2071, found: 825.2078.

Phenyl 2-*O*-(2-iodo-1-(*p*-methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosid-4-*O*-yl)-propyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16h): Vinyl ether **3** (94 mg, 0.16 mmol) and *p*-methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (128 mg, 0.21 mmol) gave mixed acetals **16h** as a clear oil, an inseparable mixture of diastereomers (19 mg, 9%). $R_f = 0.15$ (petrol/ethyl acetate 4:1). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.82-6.66$ (m, 38H; 38 × Ar-H), 6.43 (br s, 1H; H-1$_{Man}$), 5.61 (d, $^3J(H,H) = 8.2$ Hz, 1H; H-1$_{Glc}$), 5.11 (d, $^2J(H,H) = 13.0$ Hz, 1H; PhCHH′), 4.81–3.66 (m, 23H;), 3.72 (s, 3H; OCH$_3$), 1.60 (d, $^3J(H,H) = 7.1$ Hz, 3H; CHCH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 155.3$, 150.8 (2 × s, C=O), 138.9, 138.8, 138.3, 137.9, 137.7 (5 × s, Ar-C), 133.6, 133.2, 132.5, 129.3, 128.8, 128.7, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 126.9, 126.7, 123.2, 118.8, 114.3 (26 × d, Ar-CH), 104.5 (d, O$_2$CCHI), 97.8 (d, C-1$_{Glc}$), 86.1 (d, C-1$_{Man}$), 80.8, 80.0, 77.5, 76.0, 75.6, 75.4, 73.7, 56.0 (8 × d, C-2$_{Man}$, C-3$_{Man}$, C-4$_{Man}$, C-5$_{Man}$, C-2$_{Glc}$, C-3$_{Glc}$, C-4$_{Glc}$, C-5$_{Glc}$), 75.7, 75.1, 74.0, 73.0, 72.5, 69.3, 67.8 (7 × t, C-6$_{Man}$, C-6$_{Glc}$, 5 × PhCH$_2$), 55.6 (q, OCH$_3$), 29.7 (d, CHI), 23.7 (q, CHICH$_3$); IR (thin film): $\tilde{\nu} = 1716$ cm^{-1} (C=O); elemental analysis calcd for $C_{71}H_{70}INO_{13}S$: C 65.38, H 5.41, N 1.07; found: C 65.36, H 5.44, N 1.10.

Two side products were also isolated, being two diastereomers of succinimide trapped thioglycoside **22** as clear oils. Data for first diastereomer of **22** (**22a**) (13 mg, 10%). $R_f = 0.35$ (petrol/ethyl acetate 4:1); $[\alpha]_D^{24} = +22.4$ ($c = 0.62$ in $CHCl_3$); ^{1}H (500 MHz, $CDCl_3$, 25 °C): $\delta = 7.55-$ 7.21 (m, 15H; 15 × Ar-H), 5.54 (d, 1H; H-1), 5.30 (d, 1H; NCH), 5.18 (dq, $^3J(H,H) = 10.1$ Hz, 1H; CHI), 4.86, 4.59 (ABq, $^2J(H,H) = 10.9$ Hz, 2H; PhCH$_2$), 4.73, 4.57 (ABq, $^2J(H,H) = 11.6$ Hz, 2H; PhCH$_2$), 4.61, 4.51 (ABq, $^2J(H,H) = 11.9$ Hz, 2H; PhCH$_2$), 4.32 (ddd, $^3J(H,H) = 8.1$ Hz, 3.5 Hz, 1.8 Hz, 1H; H-5), 4.11 (dd, $^3J(H,H) = 2.5$ Hz, 2.1 Hz, 1H; H-2), 4.00 (at, $^3J(H,H) = 9.6$ Hz, 1H; H-4), 3.83–3.79 (m, 2H; H-3, H-6′), 3.75 (dd, $^2J(H,H) = 10.9$ Hz, $^3J(H,H) = 1.8$ Hz, 1H; H-6), 2.65–1.85 (br, 4H; (CH$_2$)$_2$), 1.99 (d, $^3J(H,H) = 6.8$ Hz, 3H; CH$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.2$, 138.0, 133.4 (3 × s, Ar-C), 132.5, 129.0, 128.4, 128.3, 128.2, 127.8, 127.8, 127.8, 127.6, 127.6, 127.4, 127.3 (12 × d, Ar-CH), 86.0, 85.9, 79.3, 78.2, 75.2, 72.9 (6 × d, C-1, C-2, C-3, C-4, C-5, NCH), 75.1, 73.1, 73.0, 68.8 (4 × t, C-6, 3 × PhCH$_2$), 27.6 (t, (CH$_2$)$_2$), 24.9, 22.8 (2 × d/q, CHICH$_3$); IR (thin film): $\tilde{\nu} = 1710$ cm^{-1} (C=O); MS-APCI$^+$: *m*/*z* (%): 825 (4) $[M+NH_4]^+$; HRMS-ES: calcd for $C_{40}H_{46}IN_2O_7S$ $[M+NH_4]^+$: 825.2071, found: 825.2078.

The second diastereomer of **22** (**22b**) (77 mg, 60%) was identical in all respects to the material described previously.

General procedure B: ***gluco*/*S*-methyl NIS tethering**: The alcohol (1.5 equiv), NIS (3 equiv) and powdered 4 Å molecular sieves (ca. 250 mg) were stirred in dichloroethane (4 mL) under argon at −40 °C. Vinyl ether **10** (typically ≈0.2 mmol) was added by cannula under argon and the mixture was allowed to warm slowly to room temperature. After 1 h, the mixture was partitioned between dichloromethane and 10% aqueous sodium thiosulfate. The organic phase was dried ($MgSO_4$), filtered, concentrated in vacuo and the resulting residue was purified by flash column chromatography to give the mixed acetals **18a–f** as clear oils. (Successful tethering to form **18f** required the addition of triethylamine before work-up, presumably to stabilise the mixed acetal.)

Methyl 2-*O*-(2-iodo-1-methoxypropyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18a): Vinyl ether **10** (100 mg, 0.19 mmol) and methanol (0.012 mL, 0.29 mmol) gave mixed acetals **18a** (128 mg, 98%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 701 (100) $[M+Na]^+$.

Methyl 2-*O*-(1-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl)-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18b): Vinyl ether **10** (100 mg, 0.19 mmol) and diacetone galactose (75 mg, 0.29 mmol) gave mixed acetals **18b** (147 mg, 84%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 929 (100) $[M+Na]^+$.

Methyl 2-*O*-(1-cyclohexyloxy-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18c): Vinyl ether **10** (100 mg, 0.19 mmol) and cyclohexanol (0.061 mL, 0.577 mmol) gave mixed acetals **18c** (115 mg, 80%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 769 (100) $[M+Na]^+$.

Methyl 2-*O*-(1-benzyloxy-2-iodopropyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18d): Vinyl ether **10** (80 mg, 0.15 mmol) and benzyl alcohol (0.03 mL, 0.31 mmol) gave mixed acetals **18d** (110 mg, 95%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 793 (72) $[M+K]^+$, 777 (100) $[M+Na]^+$, 772 (35) $[M+NH_4]^+$.

Methyl 2-*O*-(2-iodo-1-(methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-*O*-yl)propyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18e): Vinyl ether **10** (100 mg, 0.19 mmol) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (134 mg, 0.29 mmol) gave mixed acetals **18e** (76 mg, 36%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 1133 (100) $[M+Na]^+$.

Methyl 2-*O*-(2-iodo-1-(methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranosid-6-*O*-yl)propyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (18f): Vinyl ether **10** (40 mg, 0.077 mmol) and methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (71 mg, 0.15 mmol) gave mixed acetals **18f** (54 mg, 63%) as a colourless oil. MS-APCI$^+$: *m*/*z* (%): 1133 (100) $[M+Na]^+$.

General procedure C: **Intramolecular glycosylation with NIS/AgOTf**: The mixed acetals **16a–e**,**g** (typically ≈0.1 mmol), NIS (5 equiv), silver triflate (1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) (5 equiv) and powdered 4 Å molecular sieves (ca. 250 mg) were dissolved in dry dichloroethane under argon. The solution was then stirred at room temperature (or 50 °C) until TLC indicated disappearance of the starting material. Trifluoroacetic acid (10 mL), methanol (2 mL), THF (2 mL) and water (2 mL) were added and the solution was stirred for a further 1–4 h. Dichloromethane was added, the mixture filtered through Celite washed with saturated aqueous sodium bicarbonate, and the aqueous layers were re-extracted with dichloromethane. The combined organic extracts were washed with 10% sodium thiosulfate, dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash column chromatography to give the pure β-mannoside **20a–e**,**g**.

Methyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (20a): Mixed acetals **16a** (62 mg, 0.083 mmol) gave β-mannoside **20a** as a clear, colourless oil (30 mg, 77%). $[\alpha]_D^{22} = -16.6$ ($c = 0.95$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.40-7.20$ (m, 15H; 15 × Ar-H), 4.90, 4.55 (ABq, $^2J(H,H) =$ 10.8 Hz, 2H; PhCH$_2$), 4.78, 4.69 (ABq, $^2J(H,H) = 11.9$ Hz, 2H; PhCH$_2$), 4.65, 4.58 (ABq, $^2J(H,H) = 12.3$ Hz, 2H; PhCH$_2$), 4.35 (s, 1H; H-1), 4.11 (d, $^3J(H,H) = 3.0$ Hz, 1H; H-2), 3.88 (at, $^3J(H,H) = 9.4$ Hz, 1H; H-4), 3.80 (dd, $^2J(H,H) = 10.8$ Hz, $^3J(H,H) = 2.1$ Hz, 1H; H-6′), 3.74 (dd, $^2J(H,H) =$ 10.8 Hz, $^3J(H,H) = 5.1$ Hz, 1H; H-6), 3.57 (s, 3H; CH$_3$), 3.60–3.52 (m, 1H; H-3), 3.45 (ddd, $^3J(H,H) = 9.7$ Hz, 5.1 Hz, 2.1 Hz, 1H; H-5), 2.43 (br s, 1H; OH); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.2$, 138.1, 137.8 (3 × s, Ar-C), 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6 (9 × d, Ar-CH),100.7 (d, ^1J (C,H) = 158 Hz, C-1), 81.5, 75.2, 74.2, 68.2 (4 × d, C-2, C-3, C-4, C-5), 75.2, 73.5, 71.4, 69.1 (4 × t, C-6, 3 × PhCH$_2$), 57.0 (q, CH$_3$); MS-APCI$^+$: *m*/*z* (%): 487 (27) $[M+Na]^+$. The spectroscopic and analytical data were in agreement with those reported in the literature.[26]

3,4,6-Tri-*O*-benzyl-β-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (20b): Mixed acetals **16b** (62 mg, 0.064 mmol) gave β-*manno* disaccharide **20b** as a pale oil (28 mg, 63%). (Treatment of a mixture of isolated side products with lithium hydroxide in a solution of methanol/water (4:1), followed by treatment with Dowex 50WX8 (H$^+$

form) in a solution of methanol/water (4:1) led to the isolation of additional product (8 mg, 63→81%). $[\alpha]_D^{22} = -50$ ($c = 0.75$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.39-7.19$ (m, 15H; 15 × Ar-H), 5.55 (d, $^3J(H,H) = 5.0$ Hz, 1H; H-1$_a$), 4.66, 4.78 (ABq, $^2J(H,H) = 11.9$ Hz, 2H; PhCH_2), 4.60 (dd, $^3J(H,H) = 7.9$ Hz, 2.4 Hz, 1H; H-3$_a$), 4.64, 4.55 (ABq, $^2J(H,H) = 12.2$ Hz, 2H; PhCH_2), 4.91, 4.52 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; PhCH_2), 4.51 (s, 1H; H-1$_b$), 4.32 (dd, $^3J(H,H) = 5.0$ Hz, 2.4 Hz, 1H; H-2$_a$), 4.23–4.21 (m, 2H; H-4$_a$, H-2$_b$), 4.14 (dd, $^2J(H,H) = 11.2$ Hz, $^3J(H,H) = 2.9$ Hz, 1H; H-6′$_a$), 4.05–4.03 (m, 1H; H-5$_a$), 3.92 (at, $^3J(H,H) = 9.4$ Hz, 1H; H-4$_b$), 3.79–3.71 (m, 3H; H-6$_a$, H-6$_b$, H-6′$_b$), 3.56 (dd, $^3J(H,H) = 9.1$ Hz, 3.0 Hz, 1H; H-3$_b$), 3.42 (ddd, $^3J(H,H) = 9.7$ Hz, 4.6 Hz, 2.1 Hz, 1H; H-5$_b$), 2.50 (br s, 1H; O*H*), 1.54, 1.44, 1.34, 1.32 (4 × s, 12H; 4 × CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.3$, 138.2, 137.8 (3 × s, Ar-C), 128.4, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.6, 127.5 (9 × d, Ar-CH), 109.3, 108.7 (2 × s, 2 × $C(CH_3)_2$), 100.2 (d, ^1J (C,H) = 158 Hz, C-1$_b$), 96.3 (d, C-1$_a$), 81.2, 77.0, 75.2, 75.1, 74.1, 73.5, 71.4, 71.1, 70.7, 70.2, 69.1, 67.9, 67.8 (13 × d+t, C-2$_a$, C-3$_a$, C-4$_a$, C-5$_a$, C-6$_a$, C-2$_b$, C-3$_b$, C-4$_b$, C-5$_b$, C-6$_b$, 3 × PhCH_2), 26.1, 25.9, 24.9, 24.3 (4 × q, 4 × CH_3); MS-APCI$^+$: *m/z* (%): 715 (100) $[M+Na]^+$. The spectroscopic and analytical data were in agreement with those reported in the literature.[13b]

Cyclohexyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (20c): Mixed acetals **16c** (89 mg, 0.11 mmol) gave β-mannoside **20c** as a clear oil (40 mg, 68%). $[\alpha]_D^{22} = -23$ ($c = 0.93$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta =$ 7.41–7.23 (m, 15H; 15 × Ar-H), 4.91, 4.57 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; PhCH_2), 4.80, 4.68 (ABq, $^2J(H,H) = 11.9$ Hz, 2H; PhCH_2), 4.63, 4.58 (ABq, $^2J(H,H) = 12.5$ Hz, 2H; PhCH_2), 4.56 (s, 1H; H-1), 4.08 (d, $^3J(H,H) =$ 2.9 Hz, 1H; H-2), 3.86 (at, $^3J(H,H) = 9.4$ Hz, 1H; H-4), 3.80 (dd, $^2J(H,H) = 10.8$ Hz, $^3J(H,H) = 2.0$ Hz, 1H; H-6′), 3.77–3.68 (m, 2H; H-6, OC*H*(CH$_2$)$_2$), 3.58 (dd, $^3J(H,H) = 9.1$ Hz, 2.9 Hz, 1H; H-3), 3.43 (ddd, $^3J(H,H) = 9.7$ Hz, 5.6 Hz, 2.0 Hz, 1H; H-5), 2.49 (br s, 1H; O*H*), 2.06–1.16 (m, 10H; (CH_2)$_5$); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.3$, 138.2, 137.9 (3 × s, Ar-C), 128.4, 128.3, 128.3, 128.1, 127.9, 127.8, 127.7, 127.5 (8 × d, Ar-CH), 97.3 (d, ^1J (C,H) = 156 Hz, C-1), 81.7, 77.2, 75.2, 75.1, 74.3, 73.4, 71.3, 69.4, 68.9 (9 × d/t, C-2, C-3, C-4, C-5, C-6, OCH(CH$_2$)$_2$, 3 × PhCH_2), 33.5, 31.6, 25.5, 24.1, 24.0 (5 × t, (CH_2)$_5$); MS-APCI$^+$: *m/z* (%): 555 (53%) $[M+Na]^+$. The spectroscopic and analytical data were in agreement with those reported in the literature.[13b]

Benzyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (20d): Mixed acetals **16d** gave β-mannoside **20d** as a clear, transparent oil (45 mg, 76%). $[\alpha]_D^{22} = -50$ ($c = 1.3$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.39-7.13$ (m, 20H; 20 × Ar-H), 4.77, 4.68 (ABq, $^2J(H,H) = 11.9$ Hz, 2H; PhCH_2), 4.66, 4.60 (ABq, $^2J(H,H) = 10.8$ Hz, 2H; PhCH_2), 4.91, 4.56 (ABq, $^2J(H,H) =$ 10.8 Hz, 2H; PhCH_2), 4.48 (s, 1H; H-1), 4.13 (d, $^3J(H,H) = 3.1$ Hz, 1H; H-2), 3.90 (at, $^3J(H,H) = 9.3$ Hz, 1H; H-4), 3.82 (dd, $^2J(H,H) = 10.7$ Hz, $^3J(H,H) = 1.9$ Hz, 1H; H-6′), 3.76 (dd, $^2J(H,H) = 10.7$ Hz, $^3J(H,H) =$ 5.2 Hz, 1H; H-6), 3.56 (dd, $^3J(H,H) = 9.0$ Hz, 3.1 Hz, 1H; H-3), 3.44 (ddd, $^3J(H,H) = 9.4$ Hz, 5.2 Hz, 1.9 Hz, 1H; H-5), 2.50 (br s, 1H; O*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.2$, 138.2, 137.8, 136.8 (4 × s, Ar-C), 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (11 × d, Ar-CH), 98.1 (d, ^1J (C,H) = 157 Hz, C-1), 81.5, 75.3, 74.2, 68.3 (4 × d, C-2, C-3, C-4, C-5), 75.1, 73.5, 71.4, 70.5, 69.2 (5 × t, C-6, 4 × PhCH_2); MS-APCI$^+$: *m/z* (%): 558 (5) $[M+NH_4]^+$. The spectroscopic and analytical data were in agreement with those reported in the literature.[27]

Methyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (20e): Mixed acetals **16e** (94 mg, 0.08 mmol) gave the *β-manno* disaccharide **20e** as a white solid (47 mg, 65%). M.p. 105–108 °C (ether/petrol); $[\alpha]_D^{22} = +22$ ($c = 0.9$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.41-7.14$ (m, 30H; 30 × Ar-H), 5.02 (ABq, $^2J(H,H) = 13.6$ Hz, 1H; PhCH*H′*), 4.91–4.52 (m, 11H; 5 × PhCH_2, PhC*H*H′), 4.58 (d, $^3J(H,H) = 2.7$ Hz, 1H; H-1$_a$), 4.14 (s, 1H; H-1$_b$), 4.12 (d, ^2J (H,H) = 12.8 Hz, 1H; H-6′$_b$), 4.02 (at, $^3J(H,H) = 8.9$ Hz, 1H; H-4$_b$), 3.94 (s, 1H; H-2$_b$), 3.82 (at, $^3J(H,H) = 9.6$ Hz, 1H; H-4$_a$), 3.81–3.78 (m, 1H; H-5$_b$), 3.76–3.70 (m, 2H; H-6$_a$, H-6′$_a$), 3.60–3.45 (m, 4H; H-2$_a$, H-3$_a$, H-3$_b$, H-6$_b$), 3.36 (m, 1H; H-5$_a$), 3.36 (s, 3H; CH_3), 2.41 (br s, 1H; O*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.7$, 138.3, 138.2, 138.2, 138.0, 137.8 (6 × s, Ar-C), 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.9, 127.9, 127.7, 127.6, 127.5, 125.5 (13 × d, Ar-CH), 99.9 (d, ^1J (C,H) = 159 Hz, C-1$_b$), 97.8 (d, C-1$_a$), 82.1 (d, C-4$_b$), 81.2, 79.8, 77.4 (3 × d, C-2$_a$, C-3$_a$, C-3$_b$), 75.3 (d, C-5$_a$), 74.2 (d, C-4$_a$), 75.7, 75.2, 74.7, 73.4, 73.4, 71.3 (6 × t, 6 × PhCH_2), 69.7 (d, C-5$_b$), 69.2 (t, C-6$_a$), 68.2 (d, C-2$_b$), 68.0 (t, C-6$_b$), 55.2 (q, CH_3); MS-APCI$^+$: *m/z* (%): 919 (29) $[M+Na]^+$; HRMS-ES: calcd for $C_{55}H_{60}O_{11}Na$ $[M+Na]^+$: 919.4033; found: 919.4052. The spectroscopic and analytical data were in agreement with those reported in the literature.[2b]

Methyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→6)-2-*O*-benzyl-(*R*)-4,6-*O*-benzylidene-α-D-mannopyranoside (20g): Mixed acetals **16g** (86 mg, 0.08 mmol) gave the *β-manno* disaccharide **20g** as a clear oil (57 mg, 89%). $R_f = 0.25$ (petrol/ethyl acetate 5:2); $[\alpha]_D^{25} = +1.7$ ($c = 0.46$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.66-7.17$ (m, 25H; 25 × Ar-H), 5.60 (s, 1H; PhC*H*O$_2$), 4.86 (d, $^2J(H,H) = 10.8$ Hz, 1H; PhCH*H′*), 4.77 (d, $^3J(H,H) = 1.7$ Hz, 1H; H-1$_a$), 4.75 (d, $^2J(H,H) = 11.0$ Hz, 1H; PhCH*H′*), 4.72 (d, $^2J(H,H) = 12.3$ Hz, 1H; PhCH*H′*), 4.64–4.47 (m, 6H; H-3$_a$, 3 × PhC*H*H′, PhCH_2), 4.27 (dd, $^2J(H,H) = 9.7$ Hz, $^3J(H,H) = 4.1$ Hz, 1H; H-6$_a$′), 4.26 (d, $^3J(H,H) = 3.5$ Hz, 1H; H-1$_b$), 4.18 (at, $^3J(H,H) =$ 9.6 Hz, 1H; H-4$_a$), 3.94–3.80 (m, 4H; H-2$_a$, H-5$_a$, H-6$_a$, H-2$_b$), 3.88 (at, $^3J(H,H) = 9.8$ Hz, 1H; H-4$_b$), 3.38 (dd, $^3J(H,H) = 3.5$ Hz, 2H; H-6$_b$, H-6$_b$′), 3.32 (s, 3H; CH_3), 3.28–3.24 (d(at), $^3J(H,H) = 9.5$ Hz, 3.5 Hz, 3.5 Hz, 1H; H-5$_b$); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.5$, 138.3, 138.1, 137.7, 137.3 (5 × s, Ar-C), 129.2, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.7, 127.4, 126.1 (14 × d, Ar-CH), 101.8 (d, PhC*H*O$_2$), 99.7 (d, ^1J (C,H) = 169 Hz, C-1$_a$), 96.4 (d, ^1J (C,H) = 159 Hz, C-1$_b$), 80.9 (d, C-3$_b$), 77.3 (d, C-4$_a$), 75.9 (d, C-5$_b$), 75.1 (d, C-5$_a$), 74.0 (d, C-4$_b$), 73.5, 73.0, 71.1 (3 × t, 4 × PhCH_2), 71.9 (d, C-3$_a$), 69.0, 68.8 (2 × t, C-6$_a$, C-6$_b$), 68.4 (d, C-2$_a$), 64.0 (d, C-2$_b$), 54.9 (q, CH_3); IR (thin film): $\tilde{\nu} = 3480$ cm^{-1} (OH); MS-APCI$^+$: *m/z* (%): 827 (11) $[M+Na]^+$; HRMS-ES: calcd for $C_{48}H_{56}NO_{11}$ $[M+NH_4]^+$: 822.3853; found: 822.3845.

General procedure D: **Intramolecular glycosylation with MeOTf**: The mixed acetals **18a–f** (0.08–0.18 mmol) and DTBMP (3 equiv) were dissolved in dry dichloroethane under argon. Methyl triflate (5 equiv) was added and the solution was stirred at room temperature until TLC indicated disappearance of the starting material. Trifluoroacetic acid (2 mL) and water (1 mL) were added and the solution was stirred until a major product was detected (typically 1–4 h). The reaction mixture was partitioned between dichloromethane and 10% aqueous sodium bicarbonate. The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash column chromatography to give the pure α-glucosides **21a–f**.

Methyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (21a): Mixed acetals **18a** (125 mg, 0.184 mmol) gave α-glucoside **21a** (56 mg, 65%) as a white solid which was recrystallised from ether/petrol. M.p. 78–81 °C (ether/petrol); $[\alpha]_D^{22} = +71$ ($c = 1.2$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta =$ 7.36–7.11 (m, 15H; Ar-H), 4.88, 4.83 (ABq, $^2J(H,H) = 11.2$ Hz, 2H; PhCH_2), 4.79, 4.47 (ABq, $^2J(H,H) = 10.7$ Hz, 2H; PhCH_2), 4.78 (d, $^3J(H,H) = 3.2$ Hz, 1H; H-1), 4.62, 4.49 (ABq, $^2J(H,H) = 12.1$ Hz, 2H; PhCH_2), 3.76–3.60 (m, 6H; H-2, H-3, H-4, H-5, H-6, H-6′), 3.40 (s, 3H; OCH_3), 2.11 (d, $^3J(H,H) = 7.4$ Hz, 1H; OH-2). The spectroscopic and analytical data were in agreement with those reported in the literature.[26]

3,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (21b): Mixed acetals **18b** (64 mg, 0.075 mmol) gave *α-gluco* disaccharide **21b** (34 mg, 70%) as a colourless oil. $[\alpha]_D^{22} = +28$ ($c = 0.35$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.41-7.12$ (m, 15H; Ar-H),5.53 (d, $^3J(H,H) = 4.9$ Hz, 1H; H-1$_a$), 4.98, 4.82 (ABq, $^2J(H,H) = 10.7$ Hz, 2H; PhCH_2), 4.93 (d, $^3J(H,H) = 3.2$ Hz, 1H; H-1$_b$), 4.83, 4.49 (ABq, $^2J(H,H) = 10.3$ Hz, 2H; PhCH_2), 4.64, 4.50 (ABq, $^3J(H,H) = 11.7$ Hz, 2H; PhCH_2), 4.63 (dd, $^3J(H,H) = 7.8$ Hz, 2.2 Hz, 1H; H-3$_a$), 4.34 (dd, $^3J(H,H) = 4.9$ Hz, 2.2 Hz, 1H; H-2$_a$), 4.25 (dd, $^3J(H,H) =$ 7.8 Hz, 1.9 Hz, 1H; H-4$_a$), 4.00 (dat, $^3J(H,H) = 6.7$ Hz, 6.7 Hz, 1.9 Hz, 1H; H-5$_a$), 3.91 (dd, $^2J(H,H) = 10.2$ Hz, $^3J(H,H) = 6.7$ Hz, 1H; H-6′$_a$), 3.85 (ddd, $^3J(H,H) = 9.9$ Hz, 2.2 Hz, 3.0 Hz, 1H; H-5$_b$), 3.79–3.63 (m, 6H; H-2$_b$, H-3$_b$, H-4$_b$, H-6$_b$, H-6′$_b$, H-6$_a$), 1.54, 1.45, 1.35, 1.34 (4 × s, 12H; 4 × CH_3). The spectroscopic and analytical data were in agreement with those reported in the literature.[26]

Cyclohexyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (21c): Mixed acetals **18c** gave α-glucoside **21c** (44 mg, 77%) as a white solid which was recrystallised from ether/petrol. M.p. 92–94 °C (ether/petrol); $[\alpha]_D^{22} =$ +90.0 ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.42-$ 7.14 (m, 15H; Ar-H), 5.03 (d, $^3J(H,H) = 3.5$ Hz, 1H; H-1), 4.99, 4.84 (ABq, $^2J(H,H) = 11.0$ Hz, 2H; PhCH_2), 4.65, 4.51 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; PhCH_2), 4.83, 4.49 (ABq, $^2J(H,H) = 10.7$ Hz, 2H; PhCH_2), 3.90–3.87 (m, 1H; H-5), 3.77 (dd, $^2J(H,H) = 10.7$ Hz, $^3J(H,H) = 3.9$ Hz, 1H; H-6′), 3.75–3.61 (m, 5H; H-2, H-3, H-4, H-6, cyclohexyl OCH), 2.06 (d, $^3J(H,H) =$

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2.7 Hz, 1H; OH-2), 1.92–1.24 (m, 10H; cyclohexyl-H). The spectroscopic and analytical data were in agreement with those reported in the literature.[13b]

Benzyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (21d): Mixed acetals **18d** (110 mg, 0.146 mmol) gave α-glucoside **21d** (53 mg, 67%) as a colourless oil. $[\alpha]_D^{22} = +82$ ($c = 0.5$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta =$ 7.39–7.14 (m, 20H; Ar-H), 5.04 (d, ^3J(H,H) = 3.4 Hz, 1H; H-1), 4.95, 4.84 (ABq, ^2J(H,H) = 11.2 Hz, 2H; PhCH_2), 4.76, 4.56 (ABq, ^2J(H,H) = 11.7 Hz, 2H; PhCH_2), 4.65, 4.53 (ABq, ^2J(H,H) = 12.1 Hz, 2H; PhCH_2), 4.83, 4.50 (ABq, ^2J(H,H) = 10.6 Hz, 2H; PhCH_2), 3.85–3.81 (m, 1H; H-5), 3.80–3.64 (m, 4H; H-2, H-3, H-4, H-6′), 3.63 (dd, ^2J(H,H) = 10.5 Hz, ^3J(H,H) = 1.9 Hz, 1H; H-6). The spectroscopic and analytical data were in agreement with those reported in the literature.[13b]

Methyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (21e): Mixed acetals **18e** (153 mg, 0.14 mmol) gave *α-gluco* disaccharide **21e** (81 mg, 66%) as a colourless oil. $[\alpha]_D^{22} = +82$ (c = 0.85 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.39-7.13$ (m, 30H; Ar-H), 5.00, 4.81 (ABq, ^2J(H,H) = 10.9 Hz, 2H; PhCH_2), 4.93 (d, ^3J(H,H) = 3.4 Hz, 1H; H-1$_b$), 4.93, 4.82 (ABq, ^2J(H,H) = 11.1 Hz, 2H; PhCH_2), 4.92, 4.58 (ABq, ^2J(H,H) = 10.7 Hz, 2H; PhCH_2), 4.82, 4.47 (ABq, ^2J(H,H) = 10.9 Hz, 2H; PhCH_2), 4.79, 4.68 (ABq, ^2J(H,H) = 12.2 Hz, 2H; PhCH_2), 4.60 (d, ^3J(H,H) = 3.4 Hz, 1H; H-1$_a$), 4.58, 4.44 (ABq, ^2J(H,H) = 12.3 Hz, 2H; PhCH_2), 4.00 (at, ^3J(H,H) = 9.3 Hz, 1H; H-3$_a$), 3.93 (dd, ^2J(H,H) = 11.3 Hz, ^3J(H,H) = 4.5 Hz, 1H; H-6′$_a$), 3.79–3.76 (m, 1H; H-5$_a$), 3.75–3.61 (m, 6H; H-2$_b$, H-3$_b$, H-4$_b$, H-5$_b$, H-6′$_b$, H-6$_a$), 3.54 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 1.9 Hz, 1H; H-6$_b$), 3.51 (dd, ^3J(H,H) = 9.7 Hz, 3.4 Hz, 1H; H-2$_a$), 3.48 (at, ^3J(H,H) = 9.7 Hz, 1H; H-4$_a$), 3.36 (s, 3H; OCH_3). The spectroscopic and analytical data were in agreement with those reported in the literature.[28]

Methyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (21f): Mixed acetals **18f** (91 mg, 0.082 mmol) gave *α-gluco* disaccharide **21f** (53 mg, 72%) as a colourless oil. $[\alpha]_D^{22} = +66$ (c = 1.1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.39-7.14$ (m, 30H; Ar-H), 5.00 (d, ^3J(H,H) = 2.9 Hz, 1H; H-1$_b$), 4.98, 4.62 (ABq, ^2J(H,H) = 11.1 Hz, 2H; PhCH_2), 4.92, 4.71 (ABq, ^2J(H,H) = 11.1 Hz, 2H; PhCH_2), 4.84, 4.47 (ABq, ^2J(H,H) = 10.8 Hz, 2H; PhCH_2), 4.72 (s, 2H; PhCH_2), 4.70 (d, ^3J(H,H) = 2.0 Hz, 1H; H-1$_a$), 4.62 (s, 2H; PhCH_2), 4.61, 4.48 (ABq, ^2J(H,H) = 12.2 Hz, 2H; PhCH_2), 4.10–4.04 (m, 2H; H-4$_a$, H-6′$_a$), 3.91 (dd, ^3J(H,H) = 9.4 Hz, 1H; H-3$_a$), 3.80–3.59 (m, 8H; H-2$_b$, H-3$_b$, H-4$_b$, H-5$_b$, H-6$_b$, H-6′$_b$, H-5$_a$, H-6$_a$), 3.79 (dd, ^3J(H,H) = 3.0 Hz, 2.0 Hz, 1H; H-2$_a$), 3.30 (s, 3H; OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.9$, 138.4, 138.3, 138.2, 138.0 (5 × s, Ar-C), 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.4 (13 × d, Ar-CH), 100.6, 98.9 (2 × d, C-1$_b$, C-1$_a$), 83.3, 79.9, 77.0, 74.2, 73.8, 71.3, 70.7, 74.1 (8 × d, C-2$_b$, C-3$_b$, C-4$_b$, C-5$_b$, C-2$_a$, C-3$_a$, C-4$_a$, C-5$_a$), 75.2, 75.1, 75.0, 73.4, 72.8, 72.0, 68.4, 67.7 (8 × t, 6 × PhCH_2, C-6$_b$, C-6$_a$), 54.9 (q, CH_3); MS-APCI$^+$: *m/z* (%): 919 (55) $[M+Na]^+$; MS-APCI$^-$: *m/z* (%): 931 (10) $[M+Cl]^-$; HRMS-ES: calcd for $C_{55}H_{61}O_{11}$ $[M+H]^+$: 897.4214; found: 897.4229.

Synthesis of Manβ(1→4)GlcNAc disaccharide

Phenyl 2-*O*-(2-iodo-1-(*p*-methoxyphenyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosid-4-*O*-yl)-propyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16h): Iodine (76 mg, 0.30 mmol), silver trifluoromethane sulfonate (77 mg, 0.30 mmol) and 2,4,6-collidine (0.78 mL, 0.60 mmol) were dissolved in dichloromethane (1.5 mL) with molecular sieves (powdered, 4 Å, ca. 250 mg). After stirring for 15 min this mixture was cooled to −78 °C and a solution of vinyl ether **3** (86 mg, 0.15 mmol) and glucosamine acceptor **27** (178 mg, 0.30 mmol) in dichloromethane (1.5 mL) was added. The solution came to room temperature over 20 h, after which time, TLC (petrol/ethyl acetate 3:1) showed no remaining starting vinyl ether ($R_f = 0.9$) and the formation of a major product ($R_f = 0.3$). Dichloromethane (50 mL) was added and the solution was filtered through Celite, washed with 10% aq sodium thiosulfate (30 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash column chromatography (petrol/ether 1:1) gave mixed acetals **16h** as a white foam, an inseparable mixture of diastereomers (113 mg, 80% over recovered starting vinyl ether) identical to the material described previously.

***p*-Methoxyphenyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (20h)**: Mixed acetals **16h** (12.2 mg, 0.009 mmol), molecular sieves (powdered, 4 Å, ca. 250 mg) and DTBMP (9.7 mg, 0.047 mmol) were stirred at room temperature in dichloroethane (4 mL). Silver triflate (27.0 mg, 0.105 mmol), and iodine (7.0 mg, 0.028 mmol) were then added. The resulting mixture was stirred at room temperature for 20 min, after which time, TLC (petrol/ethyl acetate 2:1) showed no remaining starting material ($R_f = 0.80$) and the formation of a major product ($R_f = 0.25$). Dichloromethane (30 mL) was added and the mixture was filtered through Celite, washed with 10% aq sodium thiosulfate (20 mL) and the aqueous layers were re-extracted with dichloromethane (15 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate 2:1) to give disaccharide **20h** as a clear oil (6.4 mg, 66%). $[\alpha]_D^{25} = +52$ ($c = 0.59$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.78-7.73$ (br m, 4H; 4 × Ar-H), 7.34–7.20 (m, 21H; 21 × Ar-H), 7.02–7.00 (m, 2H; 2 × Ar-H), 6.85–6.77 (m, 4H; 4 × Ar-H), 6.72–6.68 (m, 2H; 2 × Ar-H), 5.62 (d, ^3J(H,H) = 8.0 Hz, 1H; H-1$_a$), 4.93 (d, ^2J(H,H) = 12.5 Hz, 1H; PhCHH'), 4.86 (d, ^2J(H,H) = 10.9 Hz, 1H; PhCHH'), 4.69 (s, 1H; H-1$_b$), 4.68 (d, ^2J(H,H) = 12.0 Hz, 1H; PhCHH'), 4.64 (d, ^2J(H,H) = 11.5 Hz, 1H; PhCHH'), 4.54 (br m, 1H; H-2$_a$), 4.57–4.43 (m, 6H; PhCH_2, 4 × PhCHH′), 4.17 (at, ^3J(H,H) = 8.9 Hz, 1H; H-3$_a$), 4.05 (br d, ^3J(H,H) = 3.0 Hz, 1H; H-2$_b$), 3.89–3.73 (m, 6H; H-4$_a$, H-5$_a$, H-6$_a$, H-6$_a$, H-4$_b$, H-6′$_b$), 3.71 (s, 3H; CH_3), 3.63 (dd, ^2J(H,H) = 10.8 Hz, ^3J(H,H) = 4.7 Hz, 1H; H-6$_b$), 3.43 (dd, ^3J(H,H) = 9.2 Hz, 3.0 Hz, 1H; H-3$_b$), 3.36 (ddd, ^3J(H,H) = 9.8 Hz, 4.7 Hz, 1.5 Hz, 1H; H-5$_b$), 2.56 (br s, 1H; OH); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 138.3, 138.2, 138.1, 137.7 (4 × s, Ar-C), 133.6, 128.4, 128.2, 128.2, 128.2, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.3, 126.9, 123.2, 118.7, 114.2 (18 × d, Ar-CH), 100.3 (d, ^1J (C,H) = 159 Hz, C-1$_b$), 97.6 (d, ^1J (C,H) = 169 Hz, C-1$_a$), 81.6 (d, C-3$_b$), 78.1 (d, C-3$_a$), 77.8 (d, C-5$_b$), 75.3, 74.6, 73.8 (3 × d, C-4$_a$, C-5$_a$, C-4$_b$), 75.0, 74.8, 73.4, 73.2, 71.2 (5 × t, 5 × PhCH_2), 68.8, 68.4 (2 × t, C-6$_a$, C-6$_b$), 67.9 (d, C-2$_b$), 55.6, 55.5 (2 × d/q, C-2$_a$, CH_3); IR (thin film): $\tilde{\nu} = 3500$ (OH), 1714, 1776 cm^{-1} (imide O=CNC=O); MS-ES$^+$: *m/z* (%): 1050.4 (100) $[M+Na]^+$, 1066.3 (45) $[M+K]^+$. MS-isotopic distribution $[M+Na]^+$: *m/z* (%): calcd for $C_{62}H_{61}NO_{13}Na$: 1st peak 1050.40 (100), 2nd peak 1051.41 (71), 3rd peak 1052.41 (27%); found: 1st peak 1050.38 (100), 2nd peak 1051.38 (74), 3rd peak 1052.37 (27%). The spectroscopic and analytical data were in agreement with those reported in the literature.[29]

General procedure E: **One-pot tethering and glycosylation with MeOTf**: A solution of vinyl ether **6** (0.092 g, 0.176 mmol), the aglycon alcohol (either cyclohexanol or diacetone galactose, 0.088 mmol) and powdered molecular sieves 4 Å (ca. 200 mg) was stirred for 1 h in dry acetonitrile (3 mL) at RT under argon. The mixture was cooled to at −30 °C and then DTBMP (0.036 g, 0.176 mmol) and NIS (0.0596 g, 0.265 mmol) were added. After stirring at −30 °C for 2 h, TLC (ethyl acetate/petrol 1:2) indicated complete consumption of the aglycon alcohol. Methyl triflate (0.05 mL, 0.441 mmol) was then added, and stirring continued for another 18 h at RT. The reaction was then quenched by the addition of triethylamine (2 mL), and stirred for a further 1 h, before being diluted with dichloromethane (50 mL) and filtered through Celite The organic extracts were washed with 10% aq sodium thiosulfate (20 mL), saturated aqueous sodium bicarbonate (20 mL), water (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The crude residue was purified by flash column chromatography (ethyl acetate/petrol 1:1), to afford solely either the desired β-mannoside **20b** (0.044 g, 72%) or β-mannoside **20c** (0.045 g, 67%), respectively.

Methyl 2-*O*-(1-ethoxyethyl)-1-thio-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (23): Alcohol **4** (182 mg, 0.38 mmol) and ethyl vinyl ether (0.10 mL, 0.95 mmol) were dissolved in dichloromethane (5 mL). Pyridinium *p*-toluenesulfonate (10 mg, 0.04 mmol) was added, and the mixture was stirred at room temperature under an atmosphere of argon. After 2 h 45 min, TLC (petrol/ethyl acetate 4:1) indicated the formation of a single product ($R_f = 0.4$) with no starting material remaining ($R_f = 0.1$). The reaction mixture was diluted with dichloromethane (20 mL) and washed with aq satd sodium bicarbonate (2 × 20 mL) and then aq satd brine (2 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by flash column chromatography (petrol/ethyl acetate 6:1) gave an inseparable diastereomeric mixture of mixed acetals **23** (190 mg, 91%) as a colourless oil (a:b 1.2:1). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.38-7.20$ (m, 15H; 15 × Ar-H), 5.28–5.27 (m, 1H; H-1), 4.94–4.53 (m, 7H; 3 × $PhCH_2$, O_2CH), 4.15–4.02 (m, 2H; H-2, H-4), 4.02–3.81 (m, 1H; H-5), 3.83–3.75 (m, 1H; H-3), 3.93–3.74 (m, 2H; H-6, H-6′), 3.87–3.61 (m, 1H; $OCH_aH_bCH_3$), 3.59–3.48 (m, 1H; $OCH_aH_bCH_3$), 2.16, 2.15 (2 × s, 3H; SCH_3), 1.43–1.39 (m, 3H; O_2CHCH_3), 1.21–1.16 (m, 3H;

OCH_2CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.6-138.1$ (5 × s, 5 × Ar-C), 128.4–127.4 (15 × d, Ar-CH), 101.0, 98.7 (2 × d, O_2CH), 85.2, 84.1 (2 × d, C-1), 80.4, 79.5 (2 × d, C-3), 75.0, 74.5 (2 × d, C-4, C-5), 73.3, 73.2, 72.3, 72.3 (4 × t, 2 × $PhCH_2$), 72.1, 72.0 (2 × d, C-2), 69.2 (t, C-6), 60.1, 60.0 (2 × t, OCH_2CH_3), 20.2, 20.1 (2 × q, O_2CHCH_3), 15.3, 15.2 (2 × q, OCH_2CH_3), 13.8, 13.8 (2 × q, SCH_3); HRMS-ES: calcd for $C_{32}H_{40}O_6SNa$ $[M+Na]^+$: 575.2443; found: 575.2441.

Methyl 2-*O*-(1-*n*-propoxyethyl)-1-thio-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (24): Alcohol **4** (156 mg, 0.33 mmol) and *n*-propyl vinyl ether (0.10 mL, 0.81 mmol) were dissolved in dichloromethane (5 mL). Pyridinium *p*-toluenesulfonate (8 mg, 0.03 mmol) was added, and the mixture stirred at room temperature under an atmosphere of argon. After 50 min, TLC (petrol/ethyl acetate 4:1) indicated the formation of two products ($R_f = 0.4$, 0.45) with no starting material remaining($R_f = 0.1$). The reaction mixture was diluted with dichloromethane (20 mL) and washed with aq satd sodium bicarbonate (2 × 20 mL) and then aq satd brine (2 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by flash column chromatography (petrol/ethyl acetate 6:1) gave a partially separable diastereomeric mixture of mixed acetals **24** (149 mg, 82 %) as a colourless oil (a:b 1.3:1). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.42-7.21$ (m, 15H; 15 × Ar-H), 5.30–5.29 (m, 1H; H-1), 4.92–4.53 (m, 7H; 3 × $PhCH_2$, O_2CH), 4.16–4.06 (m, 2H; H-2, H-4), 4.05–3.90 (m, 1H; H-5), 3.91–3.86 (m, 1H; H-3), 3.84–3.71 (m, 2H; H-6, H-6′), 3.69–3.47 (m, 1H; $OCH_aH_bCH_2$), 3.47–3.40 (m, 1H; $OCH_aH_bCH_2$), 2.15, 2.14 (2 × s, 3H; SCH_3), 1.61–1.55 (m, 2H; $OCH_2CH_2CH_3$), 1.41–1.38 (m, 3H; O_2CHCH_3), 0.96–0.91 (m, 3H; $OCH_2CH_2CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.5-137.6$ (6 × s, 3 × Ar-C), 128.6–127.4 (22 × d, 15 × Ar-CH), 101.2, 98.9 (2 × d, O_2CH), 85.3, 84.0 (2 × d, C-1), 80.5, 79.5 (2 × d, C-3), 75.1, 74.5 (2 × t, $PhCH_2$), 75.0, 73.4 (2 × d, C-5), 73.2, 72.4, 72.2, 72.2 (4 × t, 2 × $PhCH_2$), 72.0, 71.4, 69.6 (3 × d C-2, C-4), 69.2, 68.9 (2 × t, C-6), 67.3, 66.1 (2 × t, OCH_2CH_2), 23.1 (t, OCH_2CH_2), 23.0, 20.1 (2 × q, O_2CHCH_3), 13.8, 13.8 (2 × q, SCH_3), 10.7, 10.6 (2 × q, CH_2CH_3); HRMS-ES: calcd for $C_{33}H_{42}O_6SNa$ $[M+Na]^+$: 589.2599; found: 589.2570.

Methyl 2-*O*-(2-iodo-1-succinimidopropyl)-3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (25a and 25b): A solution of mixed acetals **16a** (439 mg, 0.59 mmol) in 1,2,-dichloroethane (10 mL) was added to a mixure of NIS (682 mg, 3.03 mmol), DTBMP (600 mg, 2.92 mmol) and molecular sieves (powdered, 4 Å, ca. 450 mg). This solution was stirred at room temperature for 70 h, and then subsequently at 50 °C for a further 7 h, after which time, TLC (petrol/ethyl acetate 3:1) showed no remaining starting material ($R_f = 0.7$) and the formation of several more polar products. After cooling to room temperature, dichloromethane (200 mL) was added and the mixture was filtered through Celite washed with 10 % aq sodium thiosulfate (2 × 50 mL) and brine (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash column chromatography (petrol/ethyl acetate 4:1 → 1:2, with 1 % added triethylamine) gave methyl β-mannoside **20a** as a clear, colourless oil (64 mg, 23 %). $R_f = 0.2$ (petrol/ethyl acetate 1:1), identical to the material described previously. Further purification allowed complete separation and isolation of two side products.

First diastereomer of succinimide trapped material, **25a**, a clear oil (52 mg, 12 %). $R_f = 0.3$ (petrol/ethyl acetate 3:1); $[\alpha]_D^{23} = +41$ ($c = 0.7$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 7.45-7.23$ (m, 15H; 15 × Ar-H), 5.58 (d, $^3J(H,H) = 10.2$ Hz, 1H; NC*H*), 5.31 (dq, $^3J(H,H) = 10.2$ Hz, 6.9 Hz, 1H; C*H*I), 4.88, 4.64 (ABq, $^2J(H,H) = 10.9$ Hz, 2H; $PhCH_2$), 4.76, 4.59 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 4.73, 4.65 (ABq, $^2J(H,H) = 12.3$ Hz, 2H; $PhCH_2$), 4.38 (s, 1H; H-1), 4.08 (d, $^3J(H,H) = 2.8$ Hz, 1H; H-2), 3.94 (at, $^3J(H,H) = 9.6$ Hz, 1H; H-4), 3.86–3.79 (m, 2H; H-6, H-6′), 3.58 (s, 3H; OCH_3), 3.48–3.44 (m, 2H; H-3, H-5), 2.81, 2.60–2.45, 2.40–2.03, 2.15–2.05 (4 × br, 4H; $(CH_2)_2$), 2.17 (d, $^3J(H,H) = 6.9$ Hz, 3H; $CHCH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 178.1$, 176.5 (2 × s, 2 × C=O), 138.9, 138.7, 138.5 (3 × s, Ar-C), 129.0, 128.8, 128.8, 128.7, 128.4, 128.3, 128.2, 128.2, 128.0, 127.4 (10 × d, Ar-CH), 101.9 (d, C-1), 88.2 (d, NCH), 81.8, 76.4 (2 × d, C-3, C-5), 77.2 (d, C-2), 76.4, 73.8, 73.3 (3 × t, 3 × $PhCH_2$), 75.7 (d, C-4), 69.5 (t, C-6), 57.0 (q, OCH_3), 28.1 (br t, $(CH_2)_2$), 25.9 (q, $CHCH_3$), 25.4 (d, CHI); IR (thin film): $\tilde{\nu} = 1710$ cm^{-1} (C=O); MS-APCI$^+$: *m*/*z* (%): 753 (100) $[M+Na]^+$; HRMS-ES: calcd for $C_{35}H_{44}IN_2O_8$ $[M+NH_4]^+$: 747.2142; found: 747.2130.

Second diastereomer **25b** (65 mg, 15 %) a white solid. $R_f = 0.4$ (petrol/ethyl acetate 1:1); m.p. 120–121 °C (ethyl acetate/petrol); $[\alpha]_D^{22.5} = +3.0$ ($c = 0.5$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 7.50-7.24$ (m, 15H; 15 × Ar-H), 5.52 (d, $^3J(H,H) = 10.2$ Hz, 1H; NC*H*), 5.34 (dq, $^3J(H,H) = 10.2$ Hz, 6.9 Hz, 1H; C*H*I), 4.89, 4.61 (ABq, $^2J(H,H) = 10.9$ Hz, 2H; $PhCH_2$), 4.88, 4.73 (ABq, $^2J(H,H) = 11.1$ Hz, 2H; $PhCH_2$), 4.67, 4.62 (ABq, $^2J(H,H) = 12.0$ Hz, 2H; $PhCH_2$), 4.22 (s, 1H; H-1), 4.03 (d, $^3J(H,H) = 2.8$ Hz, 1H; H-2), 3.82–3.73 (m, 3H; H-4, H-6, H-6′), 3.58 (dd, $^3J(H,H) = 9.3$ Hz, 2.8 Hz, 1H; H-3), 3.46 (s, 3H; OCH_3), 3.44 (ddd, $^3J(H,H) = 9.7$ Hz, 6.0 Hz, 1.8 Hz, 1H; H-5), 2.83–2.78, 2.75–2.69, 2.66–2.59 (3 × m, 4H; $(CH_2)_2$), 2.04 (d, $^3J(H,H) = 6.9$ Hz, 3H; $CHCH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 178.4$, 176.3 (2 × s, 2 × C=O), 138.9, 138.4, 138.0 (3 × s, Ar-C), 129.0, 128.8, 128.7, 128.6, 128.6, 128.4, 128.2, 127.9 (8 × d, Ar-CH), 100.9 (d, C-1), 88.1 (d, NCH), 82.4 (d, C-3), 76.5 (d, C-2), 76.1 (d, C-5), 75.5, 73.9, 72.8 (3 × t, 3 × $PhCH_2$), 74.9 (d, C-4), 69.8 (t, C-6), 57.4 (q, OCH_3), 28.4 (t, $(CH_2)_2$), 25.9 (q, $CHCH_3$), 24.1 (d, CHI); IR (thin film): $\tilde{\nu} = 1709$ cm^{-1} (C=O); MS-APCI$^+$: *m*/*z* (%): 752 (100) $[M+Na]^+$; elemental analysis calcd (%): for $C_{35}H_{40}INO_8$: C 57.62, H 5.53, N 1.92; found: C 57.42, H 5.76, N 1.91.

The remaining side products were not separated, although crude data (NMR/MS) suggested that further diastereomers of **25** were produced, along with material probably incorporating two units of the desired methyl β-mannoside linked through the 2-iodopropyl tether.

Competition reaction: Methanol (0.006 mL, 0.15 mmol), NIS (167 mg, 0.74 mmol), silver triflate (41 mg, 0.16 mmol), DTBMP (151 mg, 0.74 mmol) and molecular sieves (powdered, 4 Å, ca. 250 mg) were added to a solution of mixed acetals **16d** (119 mg, 0.14 mmol) in 1,2-dichloroethane (4 mL). This solution was heated to 50 °C and stirred for 1.5 h, after which time, TLC (petrol/ethyl acetate 3:1) showed no remaining starting material ($R_f = 0.7$) and the formation of several more polar products. After cooling to room temperature, dichloromethane (50 mL) was added and the mixture was filtered through Celite washed with 10 % aq sodium thiosulfate (50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Attempts to separate and analyse the product mixture using flash column chromatography and NMR, respectively, were inconclusive. Therefore, the combined products were treated with a mixture of TFA, THF, methanol and water (5:2:2:1, 20 mL). After stirring at room temperature overnight, the mixture was poured into saturated aqueous sodium bicarbonate (100 mL). Dichloromethane (50 mL) was added, the organic layers separated and washed with saturated aqueous sodium bicarbonate (100 mL). The aqueous layers were re-extracted with dichloromethane (50 mL) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash column chromatography (petrol/ethyl acetate 2:1 → 1:1) gave benzyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (**20d**) as a clear, transparent oil (24 mg, 31 %). $R_f = 0.6$ (petrol/ethyl acetate 1:1), data consistent with that reported above; methyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (**20a**) as a clear, transparent oil (10 mg, 15 %). $R_f = 0.25$ (petrol/ethyl acetate 1:1), data consistent with that reported above; and methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**28**) as a clear, transparent oil (15 mg, 22 %). $R_f = 0.4$ (petrol/ethyl acetate 1:1); $[\alpha]_D^{22} = +49$ ($c = 0.61$ in $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 7.22-6.99$ (m, 15H; 15 × Ar-H), 4.82 (d, $^3J(H,H) = 1.7$ Hz, 1H; H-1), 4.59 (*s*, 2H; $PhCH_2$), 4.68, 4.55 (ABq, $^2J(H,H) = 12.2$ Hz, 2H; $PhCH_2$), 4.84, 4.51 (ABq, $^2J(H,H) = 10.6$ Hz, 2H; $PhCH_2$), 4.05 (br s, 1H; H-2), 3.88–3.75 (m, 5H; H-3, H-4, H-5, H-6, H-6′), 3.38 (s, 3H; CH_3), 2.50 (br d, 1H; O*H*); MS-APCI$^+$: *m*/*z* (%): 487 (14) $[M+Na]^+$. The spectroscopic and analytical data were in agreement with those reported in the literature.[26]

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[1] a) F. Barresi, O. Hindsgaul, *Can. J. Chem.* **1994**, *72*, 1447–1465; b) F. Barresi, O. Hindsgaul, *Synlett* **1992**, 759–761; c) F. Barresi, O. Hindsgaul, *J. Am. Chem. Soc.* **1991**, *113*, 9376–9377.

[2] a) G. Stork, J. J. La Clair, *J. Am. Chem. Soc.* **1996**, *118*, 247–248; b) G. Stork, G. Kim, *J. Am. Chem. Soc.* **1992**, *114*, 1087–1088.

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[3] For a recent review on β-mannoside synthesis see: J. J. Gridley, H. M. I. Osborn, *J. Chem. Soc. Perkin Trans. 1* **2000**, 1471–1491.
[4] For some leading references to efficient intermolecular chemical and also enzymatic methods allowing the synthesis of β-mannosides see: a) O. Nashiru, D. L. Zechel, D. Stoll, T. Mohammadzadeh, R. A. J. Warren, S. G. Withers, *Angew. Chem.* **2001**, *113*, 431–434; *Angew. Chem. Int. Ed.* **2001**, *40*, 417–420; b) O. J. Plante, E. R. Palmacci, P. H. Seeberger, *Org. Lett.* **2000**, *2*, 3841–3843; c) F. W. Lichtenthaler, U. Kläres, Z. Szurmai, B. Werner, *Carbohydr. Res.* **1998**, *305*, 293–303; d) W. Guenther, H. Kunz, *Carbohydr. Res.* **1992**, *228*, 217–241; e) H. Kunz, W. Guenther, *Angew. Chem.* **1988**, *100*, 1118–1119; f) H. Paulsen, R. Lebuhn, O. Lockoff, *Carbohydr. Res.* **1982**, *103*, C7–C11.
[5] a) D. Crich, Z. M. Dai, *Tetrahedron* **1999**, *55*, 1569–1580; b) D. Crich, Z. M. Dai, *Tetrahedron Lett.* **1998**, *39*, 1681–1684; c) D. Crich, S. Sun, *J. Am. Chem. Soc.* **1998**, *120*, 435–436; d) D. Crich, S. Sun, *Tetrahedron* **1998**, *54*, 8321–8348; e) D. Crich, S. Sun, *J. Org. Chem.* **1997**, *62*, 1198–1199; f) D. Crich, S. Sun, *J. Org. Chem.* **1996**, *61*, 4506–4507.
[6] a) M. Bols, H. C. Hansen, *Chem. Lett.* **1994**, 1049–1052; b) M. Bols, *Tetrahedron* **1993**, *44*, 10049–10060; c) M. Bols, *J. Chem. Soc. Chem. Commun.* **1993**, 791–792; d) M. Bols, *J. Chem. Soc. Chem. Commun.* **1992**, 913–914.
[7] For a recent review on intramolecular glycosylation see: K.-H. Jung, M. Müller, R. R. Schmidt, *Chem. Rev.* **2000**, *100*, 4423–4442.
[8] a) M. Lergenmüller, T. Nukada, K. Kuramochi, A. Dan, T. Ogawa, Y. Ito, *Eur. J. Org. Chem.* **1999**, 1367–1376; b) Y. Ito, Y. Ohnishi, T. Ogawa, Y. Nakahara, *Synlett* **1998**, 1102–1104; c) Y. Ito, T. Ogawa, *J. Am. Chem. Soc.* **1997**, *119*, 5562–5566; d) Y. Ito, T. Ogawa, *Angew. Chem.* **1994**, *106*, 1843–1846; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1765–1767.
[9] For leading references to the work of Schmidt see: a) M. Müller, R. R. Schmidt, *Eur. J. Org. Chem.* **2001**, 2055–2066; b) M. Müller, U. Huchel, A. Geyer, R. R. Schmidt, *J. Org. Chem.* **1999**, *64*, 6190–6201; c) U. Huchel, R. R. Schmidt, *Tetrahedron Lett.* **1998**, *39*, 7693–7694; d) G. Scheffler, M. Behrendt, R. R. Schmidt, *Eur. J. Org. Chem.* **2000**, 3527–3539; e) G. Scheffler, R. R. Schmidt, *J. Org. Chem.* **1999**, *64*, 1319–1327; f) G. Scheffler, R. R. Schmidt, *Tetrahedron Lett.* **1997**, *38*, 2943–2946.
[10] For leading references to the work of Ziegler see: a) T. Ziegler, G. Lemanski, J. Hürttlen, *Tetrahedron Lett.* **2001**, *42*, 569–572; b) G. Lemanski, T. Ziegler, *Helv. Chim. Acta* **2000**, *83*, 2655–2675; c) T. Ziegler, R. Dettmann, M. Duszenko, *Carbohydr. Res.* **2000**, *327*, 367–375; d) G. Lemanski, T. Ziegler, *Tetrahedron* **2000**, *56*, 563–579; e) T. Ziegler, G. Lemanski, *Angew. Chem.* **1998**, *110*, 3367–3369; *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3129–3132; f) T. Ziegler, A. Ritter, J. Hurttlen, *Tetrahedron Lett.* **1997**, *38*, 3715–3718; g) T. Ziegler, R. Lau, *Tetrahedron Lett.* **1995**, *36*, 1417–1420.
[11] For leading references to the work of Valverde see: a) S. Valverde, M. Garcia, A. M. Gomez, J. C. López, *Chem. Commun.* **2000**, 813–814; b) S. Valverde, M. Garcia, A. M. Gomez, J. C. López, *Synlett* **2000**, 22–26; c) S. Valverde, A. M. Gomez, J. C. López, B. Herradón, *Tetrahedron Lett.* **1996**, *37*, 1105–1108; d) S. Valverde, A. M. Gomez, A. Hernandez, *J. Chem. Soc. Chem. Commun.* **1995**, 2005–2006.
[12] For some other leading references see: a) J. B. Laursen, L. Petersen, K. J. Jensen, *Org. Lett.* **2001**, *3*, 687–690; b) M. Wakao, K. Fukase, S. Kusumoto, *Synlett* **1999**, 1911–1914; c) R. J. Tennant-Eyles, B. G. Davis, A. J. Fairbanks, *Chem. Commun.* **1999**, 1037–1038; d) H. Yamada, K. Imamura, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 391–394.
[13] a) S. C. Ennis, A. J. Fairbanks, R. J. Tennant-Eyles, H. S. Yeates, *Synlett* **1999**, 1387–1390; b) S. C. Ennis, A. J. Fairbanks, C. A. Slinn, R. J. Tennant-Eyles, H. S. Yeates, *Tetrahedron* **2001**, *57*, 4221–4230.
[14] C. M. P. Seward, I. Cumpstey, M. Aloui, S. C. Ennis, A. J. Redgrave, A. J. Fairbanks, *Chem. Commun.* **2000**, 1409–1410.
[15] Y.-M. Zhang, J.-M. Mallet, P. Sinaÿ, *Carbohydr. Res.* **1992**, *236*, 73–88.
[16] Y. Ito, O. Kanie, T. Ogawa, *Angew. Chem.* **1996**, *106*, 2691–2693; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2510–2512.
[17] F. W. Lichtentaler, T. J. Schneider-Adams, *J. Org. Chem.* **1994**, *59*, 6728–6734.
[18] Y. C. Xin, J.-M. Mallett, P. Sinaÿ, *J. Chem. Soc. Chem. Commun.* **1993**, 864–865.
[19] A. De Mesmaeker, P. Hoffmann, B. Ernst, P. Hug, T. Winkler, *Tetrahedron Lett.* **1989**, *30*, 6307–6310. No data is supplied for compound **14** in this paper.
[20] G.-J. Boons, S. Isles, *J. Org. Chem.* **1996**, *61*, 4262–4271.
[21] Although light sensitive they can be left on the bench at room temperature in a foil coated flask for months with little degradation.
[22] The anomeric configurations of all β-mannosides were confirmed by measurement of the ^1J(C,H) coupling constants, which were in all cases less than 160 Hz. See K. Bock, C. Pedersen, *J. Chem. Soc. Perkin Trans. 2* **1974**, 293–297.
[23] This alcohol is the 2-OH free glycoside (or disaccharide) **20**, which is formed by hydrolysis of the oxonium ion produced subsequent to intramolecular glycosylation.
[24] Trapped species were identified by a combination of mass spectrometry and HMQC/HMBC NMR analysis.
[25] I. Robina, E. López-Barba, J. Fuentes, *Synth. Commun.* **1996**, *26*, 2847–2856.
[26] F. Nicotra, L. Panza, F. Ronchetti, G. Russo, L. Toma, *J. Chem. Soc. Perkin Trans. 1* **1987**, 1319–1324.
[27] B. Doboszewski, G. W. Hay, W. A. Szarek, *Can. J. Chem.* **1987**, *65*, 412–419.
[28] U. Schmid, H. Waldmann, *Chem. Eur. J.* **1998**, *4*, 494–501.
[29] Y. Ito, T. Ogawa, *Angew. Chem.* **1994**, *106*, 1843–1846; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1765–1767.

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