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Allyl protecting group mediated intramolecular aglycon delivery (IAD): synthesis of α-glucofuranosides and β-rhamnopyranosides

Ian Cumpstey,[a] Antony J. Fairbanks[a,*] and Alison J. Redgrave[b]

[a]*Chemistry Research Laboratory, Oxford University, Mansfield Road, Oxford OX1 3TA, UK*
[b]*GlaxoSmithKline, Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, UK*

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Abstract—The use of allyl protecting group mediated intramolecular aglycon delivery (IAD) as a strategy for intramolecular glycosylation has been extended to allow the stereoselective synthesis of α-glucofuranosides and β-rhamnopyranosides, in a totally stereoselective fashion. The efficiency of intramolecular glycosylation is dependent on the protecting group pattern of the glycosyl donor, and on the steric bulk of the glycosyl acceptor.

1. Introduction

The formal sub-division of glycosidic linkages into two categories depending on whether the 2-hydroxyl group is formally *cis* or *trans* to the anomeric substituent is strategically useful when planning the synthesis of a particular oligosaccharide. The use of participating protecting groups on the 2-hydroxyl of a glycosyl donor readily allows the stereoselective formation of 1,2-*trans* glycosidic linkages,[1] and therefore the construction of glycosides and oligosaccharides containing 1,2-*trans* linkages may be readily achieved by employing monosaccharide building blocks which posses 2-*O*-acyl protection. However, the stereoselective synthesis of glycosides and oligosaccharides containing 1,2-*cis* linkages is considerably more difficult. At the very least, the presence of such 1,2-*cis* linkages necessitates the use of glycosyl donors with non-participating protecting groups at the 2-position. However, in general, intermolecular glycosylation reactions of such donors are very rarely completely stereoselective,[2] and the undesired anomer must be separated, if possible, and discarded.

One of the most ingenious approaches to overcome this problem of stereoselectivity is to temporarily attach, or 'tether', the glycosyl acceptor to the C-2 hydroxyl of the glycosyl donor. This process can then be followed by a stereospecific intramolecular glycosylation, or Intramolecular Aglycon Delivery (IAD), wherein the aglycon is delivered to the same face of the glycosyl donor as the C-2 hydroxyl, hence forming a 1,2-*cis* linkage. The most notable applications of IAD to the synthesis of β-mannosides have arisen from the laboratories of Hindsgaul,[3] Stork,[4] and Ogawa,[5] whilst Bols extended the Stork 'silicon tether' approach to the synthesis of α-glucosides.[6] Following on from methodological developments[7] of the original Hindsgaul IAD approach,[3] we recently reported the development of an IAD strategy based on the use of glycosyl donors possessing allyl protection of the 2-hydroxyl group.[8] Herein the 2-*O*-allyl protecting group is isomerised to yield an enol ether, which can then undergo iodonium ion mediated tethering of a range of aglycon alcohols. Subsequent intramolecular glycosylation then yields the 1,2-*cis* glycoside product, with complete control of

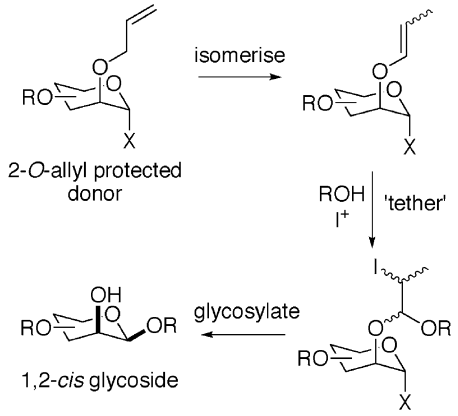

Figure 1.

Keywords: Carbohydrates; Glycosylation; Stereocontrol; Thioglycosides; Intramolecular aglycon delivery (IAD).
* Corresponding author. Tel.: +44-1865-275-647; fax: +44-1865-275-674; e-mail: antony.fairbanks@chem.ox.ac.uk

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anomeric stereochemistry (Fig. 1). This strategy has been applied to allow the synthesis of a variety of β-mannnopyranosides and α-glucopyranosides, using either thioglycosides[9] or glycosyl fluorides[10] as donors, and in addition, both steps have also been achieved in a one-pot reaction.[9]

Despite considerable methodological investigation into the development of IAD, this type of intramolecular glycosylation approach has not yet become a widely and generally used approach for glycoside and oligosaccharide synthesis. This is perhaps in part due to the limited number of examples of the different types of 1,2-*cis* glycosidic linkages that have so far been prepared by this strategy.[11] In particular, the vast majority of work published to date[12] has focused on the synthesis of the notorious β-*manno* linkage, which, although it forms part of the core *N*-glycan pentasaccharide, does not otherwise have particularly widespread occurrence in nature. In order to begin to address this problem, and hopefully expand the utility of IAD as a method for stereoselective glycosylation in a more general context, we detail herein extensions of the allyl IAD approach to other 1,2-*cis* glycosides, namely α-glucofuranosides and β-rhamnopyranosides.

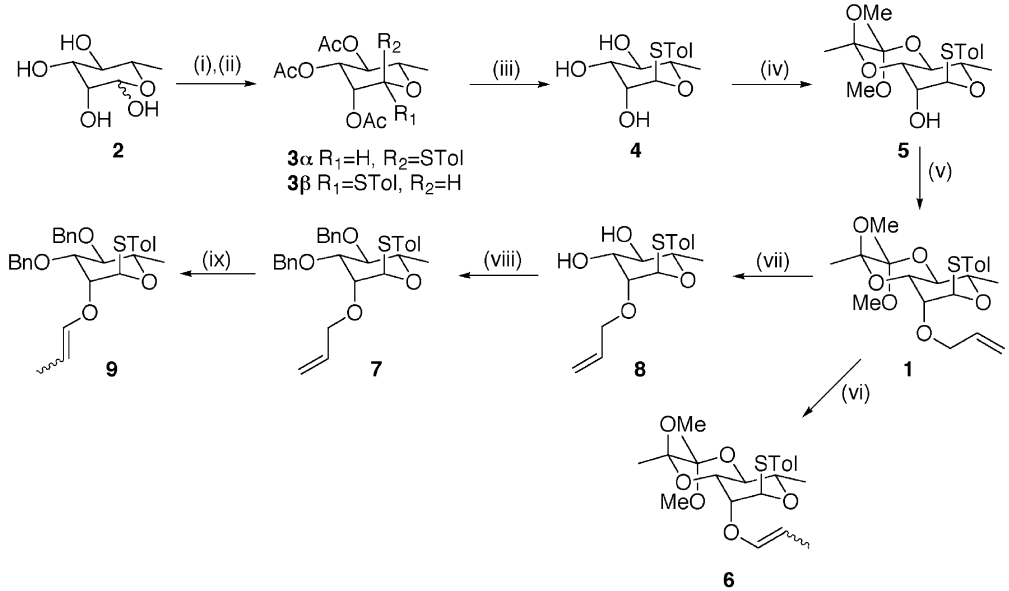
2. Results and discussion

2.1. Synthesis of β-rhamnopyranosides

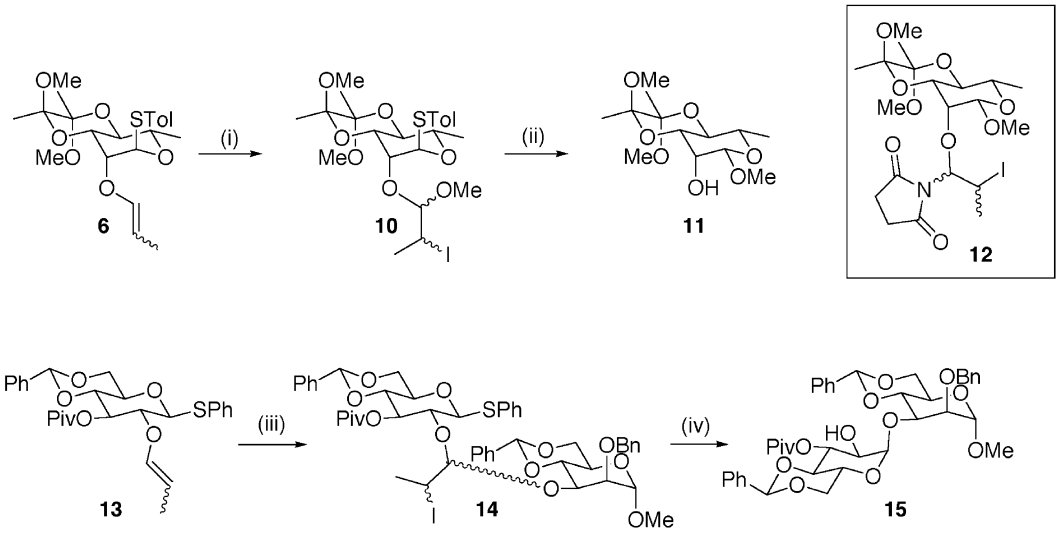
2.1.1. Synthesis of glycosyl donors. The allyl IAD approach requires selective access to the 2-hydroxyl of the glycosyl donor. As rhamnose is a 6-deoxy sugar, any protecting group strategy therefore only requires differentiation of the axial 2-hydroxyl from the equatorial 3- and 4-hydroxyl groups, and this may be most readily achieved by the use of a butane diacetal (BDA) protecting group.[13] The BDA protected rhamnose thioglycoside **1** was therefore chosen as an initial donor for study. L-Rhamnose **2** was peracetylated using acetic anhydride in combination with iodine[14] to give a tetraacetate which was then directly treated with *para*-thiocresol and $BF_3 \cdot OEt_2$ to give thioglycosides **3α/3β** as a separable 3.6:1 α/β mixture (76% yield over two steps, Scheme 1). Zemplen deacetylation of the pure α-anomer **3α** gave the triol **4** (97% yield). Treatment of triol **4** with butanedione and trimethyl orthoformate in methanol, in the presence of an acid catalyst as described by Ley,[13b] afforded the selectively 3,4-protected derivative **5** (74% yield). Allylation with sodium hydride and allyl bromide gave the fully protected sugar **1** (83% yield). Finally, isomerisation of the allyl group by treatment with Wilkinson's catalyst[15] yielded the enol ethers **6** as substrates for tethering and glycosylation of aglycon alcohols (95% yield).

Protection by 1,2-diacetal groups, such as BDA, is known to reduce the reactivity of a glycosyl donor, and indeed such torsional deactivation has been successfully applied in a reactivity tuning approach to one-pot oligosaccharide synthesis.[16] In order to investigate any potential effect of BDA protection on the efficiency of the intramolecular glycosylation reaction inherent in the IAD approach, glycosyl donor **1** was also elaborated into the dibenzylated donor **7**. Thus, BDA protected donor **1** was treated with aqueous trifluroacetic acid to afford the diol **8** (95% yield), which was then benzylated by treatment with sodium hydride and benzyl bromide to give the benzyl-protected donor **7** (88% yield). Finally, **7** was isomerised by treatment with Wilkinson's catalyst, as before, to give the required enol ethers **9** as substrates for subsequent tethering and glycosylation (80% yield, Scheme 1).

2.1.2. Tethering and intramolecular glycosylation reactions. Investigations initially focused on the use of the more readily available BDA protected donors. Enol ethers **6** were treated with *N*-iodosuccinimide (NIS) and methanol, and the desired mixed acetals **10** were obtained in good yield



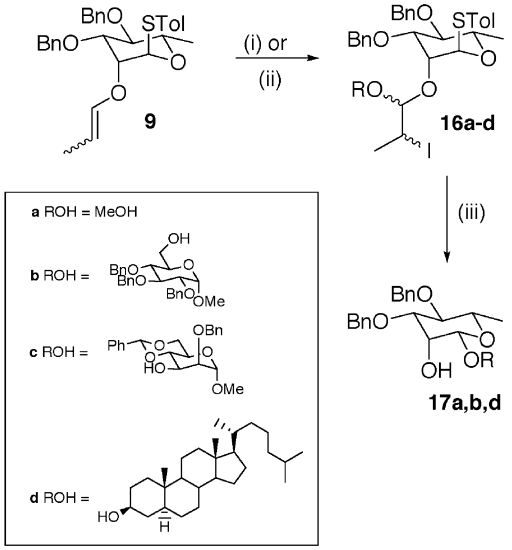
Scheme 1. (i) I_2, Ac_2O, rt; (ii) TolSH, $BF_3 \cdot OEt_2$, DCM, rt, 76% over 2 steps (**3α**:**3β**, 3.6:1); (iii) Na, MeOH, rt, 97%; (iv) $CH_3C(O)C(O)CH_3$, $CH(OMe)_3$, CSA, MeOH, 75 °C, 74%; (v) allyl bromide, DMF, NaH, 0 °C, 83%; (vi) Wilkinson's catalyst, BuLi, THF, 70 °C, 95%; (vii) TFA/H_2O (9:1), 95%; (viii) BnBr, DMF, NaH, 0 °C, 88%; (ix) Wilkinson's catalyst, BuLi, THF, 70 °C, 80%.



Scheme 2. (i) NIS, MeOH, DCE, −40 °C→rt, 96%; (ii) NIS, DTBMP, AgOTf, DCE, 50 °C, 29%; (iii) NIS, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside, DTBMP, CH_2Cl_2, −40 °C→rt, 60%; (iv) NIS, DTBMP, AgOTf, DCE, rt, 70%.

(Scheme 2). However, when tethered material **10** was treated under a range of reaction conditions commonly used for the activation of thioglycosides, the desired methyl β-rhamnoside **11** was only obtained in poor yield: the best yield (30%) was obtained by the use of NIS and silver triflate in the presence of di-*tert*-butylmethyl pyridine (DTBMP) in dichloroethane (DCE) as solvent, at 50 °C; all reactions required heating to proceed at an appreciable rate indicating torsional deactivation of the glycosyl donor. In all reactions in which NIS was used as activator, succinimide-trapped products, such as **12**, were observed to a varying degree, which was found to be concentration dependent. Despite the disappointing efficiency of this intramolecular glycosylation process, it was noted that no α-rhamnoside products were observed in any reaction, and the low yields were perplexing as no other major products were isolated. This observation that allyl-mediated IAD does not work efficiently for BDA-protected donors in the *rhamno* series, is particularly interesting in light of results obtained by Ogawa which indicated that *para*-methoxybenzyl (PMB) mediated IAD worked more efficiently for glycosyl donors that possessed cyclic 4,6-protection,[5c] and which could therefore also be considered as torisionally deactivated. It was therefore thought prudent at this juncture to investigate if allyl-mediated IAD was actually compatible with cyclic 4,6-protection of the glycosyl donor. To this end, the enol ethers **13**[17] were tethered to a secondary carbohydrate alcohol to give mixed acetals **14**. Intramolecular glycosylation of **14**, mediated by NIS and silver triflate, proceeded smoothly to give the α-*gluco* disaccharide **15** in good yield as the sole product (Scheme 2). This result therefore indicates that whilst allyl mediated IAD is apparently not compatible with 3,4-BDA protection of the donor, it is indeed compatible with 4,6-benzylidene protection.

In light of the failure of the BDA protected donor to undergo efficient intramolecular glycosylation, the enol ethers **9**, derived from the benzylated donor **7**, were investigated. Iodonium-mediated tethering of a range of aglycon alcohols with the enol ethers **9** was undertaken either using NIS or alternatively by using iodine, silver triflate and DTBMP, and good yields of the mixed acetals **16a**−**d** were obtained in all cases (Scheme 3). Intramolecular glycosylation of the methanol (**16a**) and the primary carbohydrate (**16b**) tethered materials, mediated by NIS and silver triflate, cleanly furnished the desired β-rhamnosides[18] **17a** and **17b** in good yield in a totally stereoselective fashion. Attempted alternative activation of **16b** with MeOTf resulted in no appreciable glycosylation, indicating that in this system NIS/AgOTf is a more potent activator. In contrast to the BDA-protected glycosylations outlined above, which required heating in order for efficient reaction to be seen, these reactions did proceed at an appreciable rate at room temperature, in line with the expected higher reactivity of these 'armed' benzylated donors over the torsionally deactivated BDA-protected counterparts. However, when the steroid-tethered material **16d** was treated under the same conditions, only a relatively poor 29% yield of the

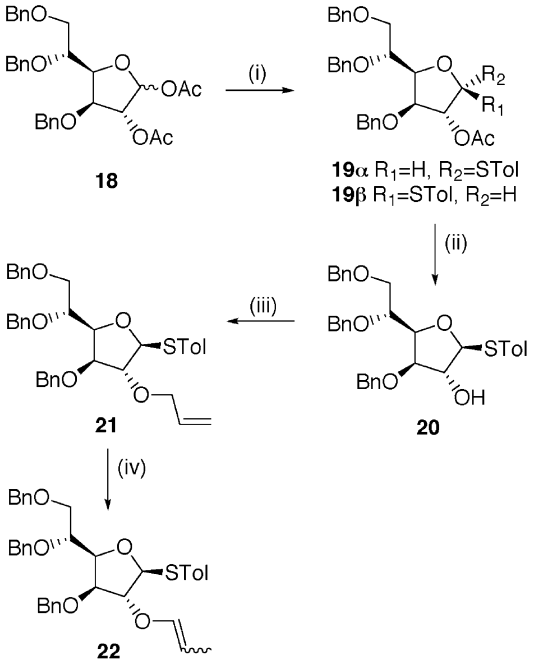


Scheme 3. (i) ROH, NIS, DCE, −40 °C→rt; **16a**, 88%; **16b**, 75%; (ii) ROH, I_2, AgOTf, DTBMP, CH_2Cl_2, −78 °C→rt; **16c**, 82%; **16d**, 69%; (iii) NIS, DTBMP, AgOTf, DCE, 50 °C; **17a**, 54%; **17b**, 62%; **17c**, –; **17d**, 29%.

β-rhamnoside **17d** was obtained. Moreover for the case of the tethered material derived from the secondary carbohydrate alcohol **16c**, only decomposition and no appreciable glycosylation was observed.

2.2. Synthesis of α-glucofuranosides

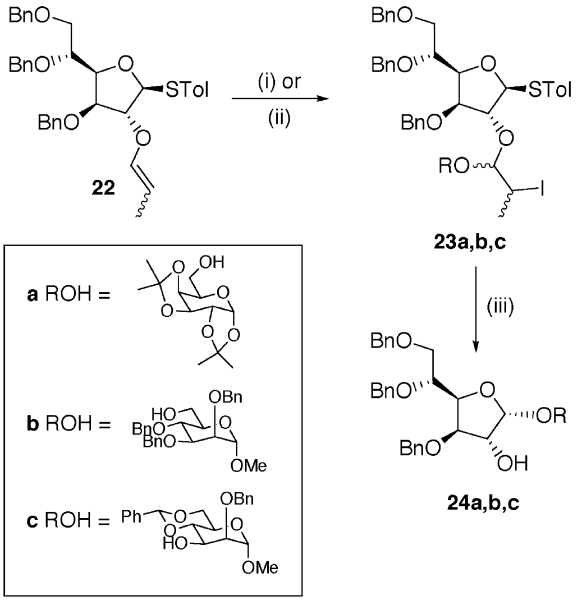
2.2.1. Synthesis of the glycosyl donor. Investigations required access to a glucofuranosyl donor bearing 2-*O*-allyl protection, which was readily available from diacetone glucose via the known diacetate **18**.[19] Treatment of diacetate **18** with *para*-thiocresol at room temperature in the presence of $BF_3 \cdot OEt_2$ gave the desired thioglycoside **19α/β** as a disappointing anomeric mixture (1.3:1, **19β**:**19α**,[20] in a poor overall yield (31%). However, conducting the reaction at lower temperature (−30 °C) increased both the yield and selectivity (58%, 50:1 **19β**:**19α**, Scheme 4). Subsequent studies focused on the major β-product as a donor for IAD.[21] Amine-mediated deacetylation of **19β** gave the alcohol **20** (91% yield). Subsequent allylation with sodium hydride and allyl bromide gave the glycosyl donor **21** (94% yield) and finally Wikinson's catalyst mediated isomerisation gave the required enol ethers **22** (96% yield, Scheme 4).



Scheme 4. (i) HSTol, $BF_3 \cdot OEt_2$, CH_2Cl_2, −30 °C, 58%, **19β**:**α**, 50:1; (ii) $^nPrNH_2$, MeOH, THF, rt, 91%; (vi) allyl bromide, DMF, NaH, 0 °C, 94%; (vii) Wilkinson's catalyst, BuLi, THF, 70 °C, 96%.

2.2.2. Tethering and intramolecular glycosylation reactions. Iodonium ion-mediated tethering reactions of a selection of carbohydrate aglycon alcohols to the β-glucofuranose enol ethers **22** were undertaken, both using NIS as a source of I^+, and also by the use of iodine, silver triflate and di-*tert*-butylmethylpyridine, to form mixed acetals **23a–c** in good yield in all cases (Scheme 5).

Treatment of the mixed acetals derived from diacetone galactose **23a** with NIS and silver triflate in the presence of



Scheme 5. (i) ROH, NIS, DCE, −40 °C→rt; **23a**, 75%; **23b**, 53%; (ii) ROH, I_2, AgOTf, DTBMP, CH_2Cl_2, −78 °C→rt; **23b**, 64%; **23c**, 88%; (iii) NIS, DTBMP, AgOTf, DCE, rt; **24a**, 70%; **24b**, 39%; (iv) MeOTf, Me_2S_2, DTBMP, CH_2Cl_2, rt; **24c**, 32%.

DTBMP resulted in the formation of the desired α-glucofuranoside **24a**, as a single anomer,[22] in a good 75% yield. When mixed acetals **23b**, derived from the more hindered primary *manno* alcohol, were treated under the same conditions again only a single α anomer of the desired glycosylated product **24b** was formed, but in a rather poor 35% yield. Moreover, treatment of mixed acetals **23c**, derived from the hindered secondary *manno* alcohol with NIS, siver triflate and DTBMP resulted in a complex mixture of products.[23] However, the use of dimethyl(thiomethyl)sulfonium triflate (DMTST) as an alternative activator[11c] gave a much cleaner glycosylation reaction, and the 1,2-*cis* disaccharide **24c** was isolated without any formation of the aglycon alcohol, albeit in a very modest overall yield (32%, Scheme 5).

3. Summary and conclusion

The potential of allyl-mediated IAD as a tool for the synthesis of α-glucofuranosyl and β-rhamnosyl bonds has been investigated with a range of substrates. In all cases, tethering reactions of aglycon alcohols to enol ethers derived from 2-*O*-allyl protected glycosyl donors by Wilkinson's catalyst mediated isomerisation has been efficiently achieved. However the efficacy of the subsequent intramolecular glycosylation reaction has been demonstrated to depend markedly both on the protecting group pattern of the glycosyl donor, and on the steric bulk of the glycosyl acceptor. Importantly, intramolecular glycosylation was completely stereoselective in all cases, and only the 1,2-*cis* isomer of glycosylated product was isolated from all glycosylation reactions. However, in the rhamnopyranose series, butane diacetal protection (BDA) of the 3- and 4-hydroxyls of the donor is seen to be currently incompatible with high yielding intramolecular glycosylation. Since efficient intramolecular glycosylation of a 4,6-*O*-benzylidene

protected *gluco* donor was observed using identical reaction conditions, this implies that the effect may not be simply due to torsional deactivation of the glycosyl donor. In the glucofuranose series, intramolecular glycosylation of mixed acetals derived from a simple unhindered primary alcohol aglycon is efficient. However, the yield of intramolecular glycosylation is seen to decrease with increasing bulk of the aglycon alcohol, and only low yields were achieved for a hindered secondary carbohydrate alcohol. It is clear that in order for allyl IAD to become a useful and widely applicable technique for the stereoselective synthesis of di- and higher oligosaccharides, the efficiency of the intramolecular glycosylation step requires substantial improvement. Investigations into the improvement and optimisation of allyl mediated IAD in the cases of hindered secondary carbohydrate alcohols are currently in progress, and the results will be reported in due course.

4. Experimental

4.1. General

Melting points were recorded on a Kofler hot block and are uncorrected. Proton nuclear magnetic resonance spectra were recorded on Bruker DPX 400 or AV 400 (400 MHz), Bruker AMX 500 or DRX 500 (500 MHz) or Bruker DPX 200, AC 200 or Varian Gemini 200 (200 MHz) spectrometers. Spectra were assigned using COSY, edited HSQC, HMQC and/or HMBC experiments. Carbon nuclear magnetic resonance spectra were recorded on Bruker DPX 400 or AV 400 (100.6 MHz), Bruker AMX 500 or DRX 500 (125.7 MHz) or Bruker DPX 200, AC 200 or Varian Gemini 200 (50.3 MHz) spectrometers. Multiplicities were assigned using APT or DEPT sequence. Proton-carbon coupling constants were measured either from proton-coupled carbon spectra (125.7 MHz) or from carbon-coupled HSQC spectra (400 MHz). Fluorine nuclear magnetic resonance spectra were recorded on a Bruker DPX 250 (235 MHz) spectrometer. All chemical shifts are quoted on the δ scale in ppm and coupling constants are quoted once. Residual signals from the solvents were used as an internal reference. Infrared spectra were recorded on a Perkin–Elmer 150 Fourier transform spectrophotometer. Low resolution mass spectra were obtained by atmospheric pressure chemical ionisation (APCI) on a Micromass Platform 1 APCI spectrometer; or by electrospray ionisation (ES) on a Micromass Platform 1 APCI spectrometer, or on a Micromass LCT spectrometer, or on a VG BioQ spectrometer, or by on a Micromass ZMD spectrometer, or by the EPSRC Mass Spectrometry Service Centre, Department of Chemistry, University of Wales, Swansea, on a Micromass Quattro II spectrometer; or using chemical ionisation (CI) on a Micromass AutoSpec-oa Tof spectrometer, or by the EPSRC Mass Spectrometry Service Centre on a Micromass Quattro II spectrometer; or using solid probe temperature programmed field ionisation (TOF FI) on a Micromass GCT Tof spectrometer by the Inorganic Chemistry Laboratory, Oxford University, UK. High-resolution mass spectra were performed on a Waters 2790-Micromass LCT electrospray ionisation mass spectrometer, or by the EPSRC Mass Spectrometry Service Centre on a MAT900 XLT electrospray ionisation mass spectrometer, or by the Inorganic Chemistry Laboratory using solid probe temperature programmed field ionisation (TOF FI) on a Micromass GCT Tof spectrometer. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g/100 ml. Microanalyses were performed by the 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. Solvents and reagents were dried and purified before use according to standard procedures; dichloromethane was distilled from CaH_2 immediately before use; methanol was distilled from NaH or anhydrous methanol was purchased from Acros; THF and ether were distilled from solutions of sodium benzophenone ketal immediately before use; anhydrous DMF and anhydrous dichloroethane were purchased from Aldrich or Acros. Petrol refers to the fraction of light petroleum ether boiling in the range 40–60 °C. Reactions performed under an atmosphere of argon or hydrogen gas were maintained by an inflated balloon.

4.1.1. *para*-Tolyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside 3α and *para*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside 3β. L-Rhamnose **2** (10.0 g, 61 mmol) was suspended in acetic anhydride (40 ml). Iodine (250 mg, 0.98 mmol) was dissolved in acetic anhydride (10 ml). The mixture was warmed until an exothermic reaction was initiated, then added to the sugar suspension. The reaction mixture was kept cool in a water bath. After 10 min, TLC (petrol/ethyl acetate, 1:1) indicated formation of major (R_f 0.5) and minor (R_f 0.45) products and the absence of starting material (R_f 0). The reaction was diluted with CH_2Cl_2 (200 ml), washed with $Na_2S_2O_3$ (200 ml of a 10% aqueous solution) and $NaHCO_3$ (200 ml of a saturated aqueous solution), dried ($MgSO_4$), filtered and concentrated in vacuo to afford the crude tetraacetate (20.1 g, 99%) as a pale yellow oil which was used without further purification. Crude tetraacetate (18.7 g, 56 mmol) and *para*-thiocresol (10.7 g, 86.2 mmol) were dissolved in CH_2Cl_2 (50 ml). $BF_3{\cdot}OEt_2$ (9.1 ml, 74.7 mmol) was added and the reaction mixture stirred at rt under Ar. After 3 h, TLC (petrol/ethyl acetate, 3:2) indicated formation of two products (R_f 0.5 and 0.45) complete consumption of starting materials (R_f 0.35 and 0.3). The reaction mixture was diluted with CH_2Cl_2 (300 ml) and washed with $NaHCO_3$ (300 ml of a saturated aqueous solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 4:1) and recrystallised from ether/petrol to afford thioglycoside **3** (α/β ratio 3.6:1 determined by ^{1}H NMR spectroscopy) (17.0 g, 76%). Separation of the anomers by flash column chromatography gave pure α-thioglycoside **3α** as white crystals, mp 112–114 °C (ether/petrol); $[\alpha]_D^{25} = -87.2$ (*c*, 3.4 in $CHCl_3$); ν_{max} 1749 (s, C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.23 (3H, d, $J_{5,6}=6.1$ Hz, CH_3-6), 2.00, 2.07, 2.13 (9H, 3×s, 3×$COCH_3$), 2.32 (3H, s, $ArCH_3$), 4.36 (1H, dq, $J_{4,5}=9.7$ Hz, H-5), 5.13 (1H, at, $J=10.0$ Hz, H-4), 5.28 (1H, dd, $J_{2,3}=3.5$ Hz, $J_{3,4}=10.1$ Hz, H-3), 5.32 (1H, d, $J_{1,2}=1.3$ Hz, H-1), 5.48 (1H, dd, H-2), 7.11, 7.35 (4H, 2× d, $J=8.1$ Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 17.3 (q, C-6),

20.6, 20.8, 20.9, 21.1 (4×q, $ArCH_3$, 3×$COCH_3$), 67.6, 69.3, 71.1, 71.2 (4×d, C-2, C-3, C-4, C-5), 86.0 (d, $^1J_{C\text{-}1,H\text{-}1}$= 168.2 Hz, C-1), 129.3, 138.2 (2×s, Ar-C), 129.9, 132.4 (2×d, Ar-CH), 169.9, 170.0, 170.0 (3×s, 3×C=O); *m/z* (CI^+) 414 ($M+NH_4^+$, 76), 273 (M-STol, 100%). (HRMS calcd for $C_{19}H_{28}NO_7S$ (MNH_4^+) 414.1586. Found 414.1581). (Found: C, 57.49; H, 6.27. $C_{19}H_{24}O_7S$ requires C, 57.56; H, 6.10%); and pure β-thioglycoside **3β** as white crystals, mp 103–107 °C (ether/petrol); $[\alpha]_D^{25}=+23.5$ (*c*, 1.5 in $CHCl_3$); ν_{max} 1749 (s, C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, d, $J_{5,6}$=6.1 Hz, CH_3-6), 1.98, 2.04, 2.21 (9H, 3×s, 3×$COCH_3$), 2.34 (3H, s, $ArCH_3$), 3.52 (1H, dq, $J_{4,5}$=9.6 Hz, H-5), 4.83 (1H, d, $J_{1,2}$=1.2 Hz, H-1), 4.99 (1H, dd, $J_{2,3}$=3.5 Hz, $J_{3,4}$=10.1 Hz, H-3), 5.11 (1H, at, *J*= 9.8 Hz, H-4), 5.64 (1H, dd, H-2), 7.13, 7.40 (4H, 2×d, *J*= 8.0 Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 17.7 (q, C-6), 20.6, 20.6, 20.7, 21.1 (4×q, $ArCH_3$, 3×$COCH_3$), 70.2, 70.9, 71.8, 74.9 (4×d, C-2, C-3, C-4, C-5), 85.7 (d, $^1J_{C\text{-}1,H\text{-}1}$= 153.4 Hz, C-1), 129.4, 138.4 (2×s, Ar-C), 129.9, 132.7 (2×d, Ar-CH) 169.8, 170.2, 170.3 (3×s, 3×C=O); *m/z* (CI^+) 414 ($M+NH_4^+$, 100), 273 (M-STol, 96%). (HRMS calcd for $C_{19}H_{28}NO_7S$ (MNH_4^+) 414.1586. Found 414.1586). (Found: C, 57.65; H, 6.30. $C_{19}H_{24}O_7S$ requires C, 57.56; H, 6.10%).

4.1.2. *para*-Tolyl 1-thio-α-L-rhamnopyranoside 4. Pure α-thioglycoside **3α** (9.4 g 23.7 mmol) was suspended in methanol (70 ml). Sodium (60 mg, 2.6 mmol) was dissolved in methanol (10 ml) and then added to the sugar solution. The reaction mixture was stirred at rt. After 1 h 40 min, TLC (petrol/ethyl acetate, 1:1) indicated formation of a major product (R_f 0.1) and no remaining starting material (R_f 0.7). The reaction mixture was concentrated in vacuo and the residue purified by flash column chromatography (ethyl acetate/methanol, 9:1) to afford the triol **4** (6.23 g, 97%) as a white solid which was recrystallised from ether to give white crystals, mp 95–96 °C (ether); $[\alpha]_D^{25}=-207$ (*c*, 0.25 in $CHCl_3$); ν_{max} 3342 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, $J_{5,6}$=6.2 Hz, CH_3-6), 2.34 (3H, s, $ArCH_3$), 3.57 (1H, at, *J*=9.4 Hz, H-4), 3.81 (1H, dd, $J_{2,3}$=2.9 Hz, $J_{3,4}$= 9.3 Hz, H-3), 4.12–4.19 (1H, m, H-5), 4.22 (1H, d, H-2), 5.41 (1H, s, H-1), 7.04, 7.30 (4H, 2×d, *J*=8.0 Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 17.5 (q, C-6), 21.0 (q, $ArCH_3$), 69.3, 72.1, 72.5, 73.2 (4×d, C-2, C-3, C-4, C-5), 88.2 (d, C-1), 129.8, 131.9 (2×d, Ar-CH), 130.1, 137.4 (2×s, Ar-C); *m/z* (CI^+) 288 ($M+NH_4^+$, 42), 271 ($M+H^+$, 4%). (HRMS calcd for $C_{13}H_{22}NO_4S$ (MNH_4^+) 288.1270. Found 288.1269). (Found: C, 57.61; H, 6.71. $C_{13}H_{18}O_4S$ requires C, 57.76; H, 6.71%).

4.1.3. (2′*S*, 3′*S*) *para*-Tolyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-α-L-rhamnopyranoside 5. Triol **4** (145 mg 0.54 mmol) was suspended in anhydrous methanol (5 ml). 2,3-Butanedione (0.15 ml, 1.72 mmol), trimethyl orthoformate (0.50 ml, 4.62 mmol) and camphorsulfonic acid (15 mg, 0.064 mmol) were added and the reaction mixture stirred under Ar at 75 °C. After 16 h, TLC (petrol/ethyl acetate, 1:1) indicated formation of a major product (R_f 0.6) and no remaining starting material (R_f 0.1). Triethylamine (4 ml) was added and the mixture was concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 3:1) to afford alcohol **5** (153 mg, 74%) as a colourless oil; $[\alpha]_D^{25}=-262$ (*c*, 1.0 in $CHCl_3$); ν_{max} 3410 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, d, $J_{5,6}$=6.5 Hz, CH_3-6), 1.32, 1.34 (6H, 2×s, 2×$C(O)_2CH_3$), 2.33 (3H, s, $ArCH_3$), 2.69 (1H, d, $J_{OH,2}$=1.8 Hz, OH-2), 3.25, 3.31 (6H, 2×s, 2×OCH_3), 3.78 (1H, at, *J*=9.7 Hz, H-4), 3.99 (1H, dd, $J_{2,3}$=3.1 Hz, $J_{3,4}$=10.0 Hz, H-3), 4.18 (1H, br s, H-2), 4.26–4.30 (1H, m, H-5), 5.43 (1H, s, H-1), 7.11, 7.35 (4H, 2×d, *J*=8.0 Hz, Ar-H); δ_C (125.7 MHz, $CDCl_3$) 16.3, 17.5, 17.7 (3×q, 2×$C(O)_2CH_3$, C-6), 21.0 (q, $ArCH_3$), 47.6, 48.0 (2×q, 2×OCH_3), 67.5, 68.5, 68.6, 71.2 (4×d, C-2, C-3, C-4, C-5), 88.0 (d, C-1), 99.7, 100.1 (2×s, 2×$C(O)_2CH_3$), 129.7, 131.9 132.0 (3×d, Ar-CH), 130.2, 137.5 (2×s, Ar-C); *m/z* (ES^+) 786 ($2M+NH_4^+$, 5), 402 ($M+NH_4^+$, 41), 353 (M−OMe, 100%). (HRMS calcd for $C_{19}H_{32}NO_6S$ (MNH_4^+) 402.1950. Found 402.1949).

4.1.4. (2′*S*, 3′*S*) *para*-Tolyl 2-*O*-allyl-3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-α-L-rhamnopyranoside 1. Alcohol **5** (118 mg 0.31 mmol) was dissolved in anhydrous DMF (2 ml) and cooled to 0 °C. Allyl bromide (0.053 ml, 0.62 mmol) then sodium hydride (60% in mineral oil) (25 mg, 0.62 mmol) were added. After 2 h, TLC (petrol/ethyl acetate, 3:1) indicated formation of a single product (R_f 0.6) and almost complete consumption of starting material (R_f 0.3). The reaction was quenched with water (50 ml) and extracted with ether (50 ml). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 8:1) to afford the BDA protected donor **1** (108 mg, 83%) as a colourless oil; $[\alpha]_D^{25}=-289$ (*c*, 0.25 in $CHCl_3$); ν_{max} no significant peaks; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, $J_{5,6}$=6.3 Hz, CH_3-6), 1.32, 1.33 (6H, 2×s, 2×$C(O)_2CH_3$), 2.33 (3H, s, $ArCH_3$), 3.26, 3.31 (6H, 2×s, 2×OCH_3), 3.81 (1H, at, *J*=9.9 Hz, H-4), 3.89 (1H, dd, $J_{1,2}$=1.3 Hz, $J_{2,3}$=3.0 Hz, H-2), 3.97 (1H, dd, $J_{3,4}$=10.2 Hz, H-3), 4.16 (1H, ddat, J_{gem}= 13.5 Hz, *J*=5.8, 1.4 Hz, $OCHH'CH=CH_2$), 4.20–4.29 (2H, m, H-5, $OCHH'CH=CH_2$), 5.16 (1H, dd, J_{gem}= 1.7 Hz, J_Z=10.4 Hz, $CH=CH_EH_Z$), 5.29 (1H, daq, *J*= 1.7 Hz, J_E=17.3 Hz, $CH=CH_EH_Z$), 5.42 (1H, d, H-1), 5.92 (1H, ddat, $CH=CH_2$), 7.11, 7.34 (4H, 2×d, *J*=8.1 Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 16.6, 17.7, 17.8 (3×q, 2×$C(O)_2CH_3$, C-6), 21.1 (q, $ArCH_3$), 47.6, 47.9 (2×q, 2×OCH_3), 67.9, 68.9, 68.9, 77.5 (4×d, C-2, C-3, C-4, C-5), 71.7 (t, $OCH_2CH=CH_2$), 87.2 (d, C-1), 99.5, 99.8 (2×s, 2×$C(O)_2CH_3$), 117.1 (t, $CH=CH_2$), 129.7, 131.7 (2×d, Ar-CH), 131.0, 135.0 (2×s, Ar-C) 137.4 (d, $CH=CH_2$); *m/z* (ES^+) 483 ($M+NH_4^+$ +MeCN, 15), 442 ($M+NH_4^+$, 40), 425 ($M+H^+$, 100), 393 (M−OMe, 81%). (HRMS calcd for $C_{22}H_{36}NO_6S$ (MNH_4^+) 442.2263. Found 442.2265).

4.1.5. (2′*S*, 3′*S*) *para*-Tolyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-2-*O*-prop-1″-enyl-1-thio-α-L-rhamnopyranoside 6. Wilkinson's catalyst (471 mg, 0.51 mmol) was dissolved in freshly distilled THF (6 ml) and degassed. Butyl lithium (1.6 M solution in hexanes) (0.48 ml, 0.76 mmol) was added and the mixture stirred for 10 min. BDA protected donor **1** (2.16 g, 5.09 mmol) was dissolved in freshly distilled THF (6 ml) and heated to 70 °C. The catalyst solution was added by cannula under Ar. After 30 min, TLC (petrol/ether, 8:1) indicated formation of two products (R_f 0.2 and R_f 0.25) and complete consumption of

starting material (R_f 0.1). The reaction was allowed to cool then diluted with CH_2Cl_2 (20 ml) and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 8:1) to afford enol ethers **6** (2.04 g, 95%) as a colourless oil. (*Z*/*E*, 1.8:1). The isomers were separated by flash column chromatography (petrol/ether, 8:1) for characterisation purposes. *E* isomer, a colourless oil; $[\alpha]_D^{25}=-254$ (*c*, 0.5 in $CHCl_3$); ν_{max} 1673 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, $J_{5,6}=6.3$ Hz, CH_3-6), 1.32, 1.35 (6H, 2×s, $2\times C(O)_2CH_3$), 1.52 (3H, dd, $J=1.5$, 6.8 Hz, OCH=CHCH_3), 2.34 (3H, s, $ArCH_3$), 3.27, 3.31 (6H, 2×s, $2\times OCH_3$), 3.80 (1H, at, $J=9.9$ Hz, H-4), 4.03 (1H, dd, $J_{2,3}=3.1$ Hz, $J_{3,4}=10.1$ Hz, H-3), 4.18 (1H, d, H-2), 4.25 (1H, dq, $J_{4,5}=9.6$ Hz, H-5), 4.88 (1H, dq, $J_E=12.7$ Hz, OCH=C*H*), 5.49 (1H, s, H-1), 6.14 (1H, dd, OC*H*=CH), 7.12, 7.36 (4H, 2×d, $J=8.1$ Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 12.4 (q, CH=CH*C*H_3), 16.6, 17.7, 17.8 (3×q, $2\times C(O)_2CH_3$, C-6), 21.0 (q, $ArCH_3$), 47.6, 47.9 (2×q, $2\times OCH_3$), 67.7, 67.8, 68.8, 77.6 (4×d, C-2, C-3, C-4, C-5), 85.6 (d, C-1), 99.6, 100.2 ($2\times$s, $2\times C(O)_2CH_3$), 102.5 (d, OCH=*C*H), 129.8, 131.9 (2×d, Ar-CH), 130.6, 137.6 (2×s, Ar-C) 144.7 (d, O*C*H=CH); *Z* isomer, a colourless oil; $[\alpha]_D^{25}=-366$ (*c*, 1.0 in $CHCl_3$); ν_{max} 1668 (C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, d, $J_{5,6}=6.1$ Hz, CH_3-6), 1.32, 1.34 (6H, 2×s, $2\times C(O)_2CH_3$), 1.61 (3H, dd, $J=1.7$ Hz, $J=6.7$ Hz, OCH=CHCH_3), 2.33 (3H, s, $ArCH_3$), 3.27, 3.32 (6H, 2×s, $2\times OCH_3$), 3.86 (1H, at, $J=9.9$ Hz, H-4), 4.03 (1H, dd, $J_{2,3}=3.1$ Hz, $J_{3,4}=10.1$ Hz, H-3), 4.08 (1H, d, H-2), 4.26 (1H, dq, $J_{4,5}=9.6$ Hz, H-5), 4.58 (1H, aquint, $J=6.7$ Hz, OCH=C*H*), 5.38 (1H, s, H-1), 5.96 (1H, dd, $J_Z=6.0$ Hz, OC*H*=CH), 7.12, 7.35 (4H, 2×d, $J=8.1$ Hz, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 9.5 (q, CH=CH*C*H_3), 16.7, 17.7, 17.8 (3×q, $2\times C(O)_2CH_3$, C-6), 21.1 (q, $ArCH_3$), 47.6, 48.0 (2×q, $2\times OCH_3$), 67.9, 68.1, 68.9, 79.5 (4×d, C-2, C-3, C-4, C-5), 86.8 (d, C-1), 99.6, 100.0 ($2\times$s, $2\times C(O)_2CH_3$), 105.6 (d, OCH=*C*H), 129.8, 132.1 (2×d, Ar-CH), 130.5, 137.7 (2×s, Ar-C) 143.8 (d, O*C*H=CH); For the *E*/*Z* mixture; *m*/*z* (ES^+) 483 ($M+NH_4^+$ + MeCN, 27), 442 ($M+NH_4^+$, 29), 425 ($M+H^+$, 64), 393 (M−OMe, 100%). (HRMS calcd for $C_{22}H_{36}NO_6S$ (MNH_4^+) 442.2263. Found 442.2261).

4.1.6. *para*-Tolyl 2-*O*-allyl-1-thio-α-L-rhamnopyranoside 8. The BDA protected donor **1** (159 mg 0.38 mmol) was dissolved in trifluoroacetic acid (1.8 ml) and water (0.2 ml) and stirred at rt. After 10 min, TLC (petrol/ethyl acetate, 3:1) indicated formation of a single product (R_f 0.2) and disappearance of starting material (R_f 0.7). The reaction mixture was concentrated in vacuo and the residue purified by flash column chromatography (petrol/ethyl acetate, 5:2→1:1) to afford the triol **8** (110 mg, 95%) as a colourless oil; $[\alpha]_D^{25}=-289$ (*c*, 0.25 in $CHCl_3$); ν_{max} 3392 (br, OH), 1646 (w, C=C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.34 (3H, d, $J_{5,6}=6.2$ Hz, CH_3-6), 2.34 (3H, s, $ArCH_3$), 2.70 (2H, br s, OH), 3.50 (1H, at, $J=9.5$ Hz, H-4), 3.77 (1H, dd, $J_{2,3}=3.7$ Hz, $J_{3,4}=9.5$ Hz, H-3), 3.92 (1H, dd, $J_{1,2}=1.2$ Hz, H-2), 4.00 (1H, ddat, $J_{gem}=12.6$ Hz, $J=6.2$ Hz, $J=1.2$ Hz, OC*H*H′CH=CH_2), 4.12 (1H, dq, $J_{4,5}=9.4$ Hz, H-5), 4.19 (1H, ddat, $J=5.5$, 1.4 Hz, OCH*H*′CH=CH_2), 5.21 (1H, dd, $J_{gem}=1.4$ Hz, $J_Z=10.3$ Hz, CH=CH_EH_Z), 5.29 (1H, daq, $J=1.5$ Hz, $J_E=17.3$ Hz, CH=CH_EH_Z), 5.50 (1H, d, H-1), 5.90 (1H, ddat, C*H*=CH_2), 7.13, 7.36 (4H, 2×d, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 17.4 (q, C-6), 21.1 (q, $ArCH_3$), 68.9, 71.9, 74.2, 79.2 (4×d, C-2, C-3, C-4, C-5), 71.3 (t, $OCH_2CH=CH_2$), 85.1 (d, C-1), 118.3 (t, CH=*C*H_2), 129.8, 132.0, 133.8 (3×d, Ar-CH, *C*H=CH_2), 130.4, 137.7 (2×s, Ar-C); *m*/*z* (TOF FI^+) 310 (M^+, 100%). (HRMS calcd for $C_{16}H_{22}O_4S$ (M^+) 310.1239. Found 310.1237).

4.1.7. *para*-Tolyl 2-*O*-allyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside 7. The triol **8** (500 mg 1.61 mmol) was dissolved in anhydrous DMF (15 ml) and cooled to 0 °C. Benzyl bromide (0.57 ml, 4.84 mmol) then sodium hydride (60% in mineral oil) (258 mg, 6.44 mmol) were added. After 14 h 30 min, TLC (petrol/ethyl acetate, 4:1) indicated formation of a single product (R_f 0.6) and complete consumption of starting material (R_f 0.1). The reaction mixture was quenched with methanol (4 ml) and partitioned between ether (100 ml) and water (100 ml). The aqueous layer was re-extracted with ether (50 ml) and the combined organic extracts were washed with brine (50 ml), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 8:1) to afford the benzylated donor **7** (693 mg, 88%) as a colourless oil; $[\alpha]_D^{25}=-120.7$ (*c*, 0.75 in $CHCl_3$); ν_{max} no significant peaks; δ_H (400 MHz, $CDCl_3$) 1.35 (3H, d, $J_{5,6}=6.3$ Hz, CH_3-6), 2.34 (3H, s, $ArCH_3$), 3.63 (1H, at, $J=9.4$ Hz, H-4), 3.85 (1H, dd, $J_{2,3}=3.2$ Hz, $J_{3,4}=9.3$ Hz, H-3), 3.95 (1H, dd, $J_{1,2}=1.6$ Hz, H-2), 4.09–4.20 (3H, m, OCH_2CH=CH_2, H-5), 4.65, 4.97 (2H, ABq, $J_{AB}=10.9$ Hz, $PhCH_2$), 4.73 (2H, s, $PhCH_2$), 5.20 (1H, dd, $J_{gem}=1.6$ Hz, $J_Z=10.2$ Hz, CH=CH_EH_Z), 5.28 (1H, daq, $J=1.5$ Hz, $J_E=17.2$ Hz, CH=CH_EH_Z), 5.43 (1H, d, H-1), 5.92 (1H, ddat, C*H*=CH_2), 7.11–7.42 (14H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 17.8 (q, C-6), 21.1 (q, $ArCH_3$), 69.1, 76.4, 77.2, 79.8 (4×d, C-2, C-3, C-4, C-5), 71.5, 72.2, 75.5 (3×t, $OCH_2CH=CH_2$, $2\times PhCH_2$), 86.1 (d, C-1), 118.0 (t, CH=*C*H_2), 127.6, 127.7, 127.9, 128.0, 128.3, 128.4, 129.8, 131.8, 134.7 (9×d, Ar-CH, *C*H=CH_2), 130.9, 137.4, 138.1, 138.5 (4×s, Ar-C); *m*/*z* ($APCI^+$) 546 (M+56, 100), 508 ($M+NH_4^+$, 5), 491 ($M+H^+$, 10%); (CI^+) 508 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{30}H_{38}NO_4S$ (MNH_4^+) 508.2522. Found 508.2524). (Found: C, 73.60; H, 7.12. $C_{30}H_{34}O_4S$ requires C, 73.44; H, 6.98%).

4.1.8. *para*-Tolyl 3,4-di-*O*-benzyl-2-*O*-prop-1′-enyl-1-thio-α-L-rhamnopyranoside 9. Wilkinson's catalyst (120 mg, 0.13 mmol) was dissolved in freshly distilled THF (3 ml) and degassed. Butyl lithium solution in hexanes (0.12 ml, 0.20 mmol) was added and the mixture stirred for 10 min. Benzylated donor **7** (640 mg, 1.31 mmol) was dissolved in freshly distilled THF (3 ml) and heated to 75 °C. The catalyst solution was added by cannula under Ar. After 1 h 30 min, TLC (petrol/ether, 4:1) indicated formation of two products (R_f 0.5 and R_f 0.55) and complete consumption of starting material (R_f 0.45). The reaction was allowed to cool then diluted with CH_2Cl_2 (4 ml) and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 8:1) to afford the enol ethers **9** (513 mg, 80%) as a colourless oil; ν_{max} 1671 (C=C) cm^{-1}; partial data: δ_H (400 MHz, $CDCl_3$) (*E*/*Z*, 1.4:1), *E* isomer 1.35 (3H, d, $J_{5,6}=6.1$ Hz, CH_3-6), 1.54 (3H, dd, $J=1.6$, 6.9 Hz, OCH=CHCH_3), 3.63 (1H, at, $J=9.3$ Hz, H-4), 4.92 (1H, dq, $J_E=12.5$ Hz, OCH=C*H*CH_3), 5.45 (1H, d, $J_{1,5}=1.5$ Hz, H-1), 6.09 (1H, dq, OC*H*=CHCH_3); *Z* isomer 1.36 (3H, d, $J_{5,6}=6.2$ Hz, CH_3-6), 1.65 (3H, dd, $J=1.5$,

6.7 Hz, OCH=CHCH_3), 3.67 (1H, at, J=9.3 Hz, H-4), 4.10 (1H, dd, $J_{1,2}$=1.8 Hz, $J_{2,3}$=2.8 Hz, H-2), 4.58 (1H, aquin, J=6.6 Hz, OCH=CHCH$_3$), 5.37 (1H, d, H-1), 5.91 (1H, dq, J_Z=6.1 Hz, OCH=CHCH$_3$); δ_C (100.6 MHz, $CDCl_3$) *E* isomer 12.4 (q, OCH=CHCH$_3$), 17.8 (q, C-6), 21.1 (q, ArCH_3), 72.2, 75.5 (2×t, 2×PhCH_2), 85.4 (d, C-1), 102.4 (d, OCH=CHCH$_3$), 144.0 (d, OCH=CHCH$_3$); Z isomer 9.5 (q, OCH=CHCH$_3$), 17.9 (q, C-6), 21.1 (q, ArCH_3), 72.2, 75.5 (2×t, 2×PhCH_2), 86.3 (d, C-1), 104.8 (d, OCH=CHCH$_3$), 144.9 (d, OCH=CHCH$_3$); *m/z* (APCI$^+$) 546 (M+56, 100), 491 (M+H$^+$, 11%); (CI$^+$) 508 (M+NH_4^+, 100), 491 (M+H$^+$, 17%). (HRMS calcd for $C_{30}H_{38}NO_4S$ (MNH_4^+) 508.2522. Found 508.2526). (Found: C, 73.56; H, 7.11. $C_{30}H_{34}O_4S$ requires C, 73.44; H, 6.98%).

4.1.9. (2′*S*, 3′*S*) para-Tolyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-2-*O*-(2-iodo-1-methoxypropyl)-1-thio-α-L-rhamnopyranoside 10. *N*-Iodosuccinimide (239 mg, 1.1 mmol) and 4 Å molecular sieves were added to anhydrous dichloroethane (2 ml) and cooled to −40 °C under Ar. (2′S, 3′S) Enol ethers **6** (150 mg, 0.35 mmol, *E*/*Z*, 68:32) and methanol (0.022 ml, 0.53 mmol) were dissolved in anhydrous dichloroethane (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to 0 °C over 55 min. After this time, the reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2× 30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 8:1) to afford mixed acetals **10** (197 mg, 96%) as a colourless oil. *m/z* (ES$^+$) 641 (M+NH_4^++MeCN, 12), 600 (M+NH_4^+, 3), 583 (M+H$^+$, 3%). (HRMS calcd for $C_{23}H_{39}NO_7SI$ (MNH_4^+) 600.1492. Found 600.1496). Data for the individual 4 diastereomers (relative %): Diastereomer 1 (17%): δ_H (400 MHz, $CDCl_3$) 1.27 (3H, d, $J_{5,6}$=6.0 Hz, CH_3-6), 1.31, 1.34 (6H, 2×s, 2×C(O)$_2$CH$_3$), 1.87 (3H, d, J=6.9 Hz, CHICH_3), 2.33 (3H, s, ArCH_3), 3.24, 3.32, 3.37 (9H, 3×s, 3×OCH_3), 3.74 (1H, at, J=10.0 Hz, H-4), 3.99 (1H, dd, $J_{2,3}$=2.5 Hz, $J_{3,4}$=10.3 Hz, H-3), 4.07 (1H, dd, $J_{1,2}$=1.4 Hz, H-2), 4.24 (1H, dq, $J_{4,5}$=9.6 Hz, H-5), 4.65 (1H, d, J=2.6 Hz, (O)$_2$CHCHI), 4.67 (1H, dq, CHI), 5.46 (1H, d, H-1), 7.11–7.13, (2H, m, Ar-H), 7.34–7.36 (2H, m, Ar-H); Diastereomer 2 (8%): δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, $J_{5,6}$=6.2 Hz, CH_3-6), 1.29, 1.31 (6H, 2×s, 2×C(O)$_2$CH$_3$), 1.92 (3H, d, J=6.8 Hz, CHICH_3), 2.33 (3H, s, ArCH_3), 3.27, 3.31, 3.33 (9H, 3×s, 3×OCH_3), 3.79 (1H, at, J=10.0 Hz, H-4), 3.98 (1H, dd, $J_{2,3}$=2.6 Hz, $J_{3,4}$=10.4 Hz, H-3), 4.17 (1H, dd, $J_{1,2}$=1.3 Hz, H-2), 4.24 (1H, dq, $J_{4,5}$=9.7 Hz, H-5), 4.42 (1H, d, J=5.7 Hz, (O)$_2$CHCHI), 4.51 (1H, dq, CHI), 5.44 (1H, d, H-1), 7.11–7.13, (2H, m, Ar-H), 7.34–7.36 (2H, m, Ar-H); Diastereomer 3 (25%): δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, $J_{5,6}$=6.2 Hz, CH_3-6), 1.28, 1.30 (6H, 2×s, 2×C(O)$_2$CH$_3$), 1.88 (3H, d, J=7.2 Hz, CHICH_3), 2.34 (3H, s, ArCH_3), 3.23, 3.31, 3.50 (9H, 3×s, 3×OCH_3), 3.82 (1H, at, J=9.9 Hz, H-4), 3.98 (1H, dd, $J_{2,3}$=3.0 Hz, $J_{3,4}$=10.3 Hz, H-3), 4.18 (1H, dd, $J_{1,2}$=1.2 Hz, H-2), 4.20 (1H, dq, J=5.8 Hz, CHI), 4.25 (1H, dq, $J_{4,5}$=9.7 Hz, H-5), 4.31 (1H, d, (O)$_2$CHCHI), 5.41 (1H, s, H-1), 7.11–7.14, (2H, m, Ar-H), 7.34–7.37 (2H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 16.5, 17.6, 17.8 (3×q, 2×C(O)$_2$$CH_3$, C-6), 21.1 (q, Ar$CH_3$), 23.0 (q, CHI$CH_3$), 27.1 (q, CHICH$_3$), 47.6, 47.9 (2×q, 2×OCH_3), 54.8 (q, OCH_3), 68.0, 68.4, 68.7, (3×d, C-3, C-4, C-5), 74.4 (d, C-2), 88.0 (d, C-1), 99.6, 99.9 (2×s, 2×C(O)$_2$CH$_3$), 105.1 (d, (O)$_2$$C$HCHI), 129.9, 132.3 (2×d, Ar-CH), 130.5, 137.8 (2×s, Ar-C); Diastereomer 4 (50%): δ_H (400 MHz, $CDCl_3$) 1.28 (3H, d, $J_{5,6}$=6.0 Hz, CH_3-6), 1.29, 1.31 (6H, 2×s, 2×C(O)$_2$CH$_3$), 1.81 (3H, d, J=6.8 Hz, CHICH_3), 2.34 (3H, s, ArCH_3), 3.24, 3.32, 3.55 (9H, 3×s, 3×OCH_3), 3.85 (1H, at, J=9.5 Hz, H-4), 3.98–4.02 (2H, m, H-2, H-3), 4.06 (1H, dq, J=4.0 Hz, CHI), 4.24 (1H, dq, $J_{4,5}$=9.7 Hz, H-5), 4.78 (1H, d, (O)$_2$CHCHI), 5.36 (1H, s, H-1), 7.12–7.14, (2H, m, Ar-H), 7.34–7.36 (2H, m, Ar-H).

4.1.10. (2′*S*, 3′*S*) Methyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-β-L-rhamnopyranoside 11. Mixed acetals **10** (114 mg, 0.25 mmol), were dissolved in anhydrous dichloroethane (9 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (138 mg, 0.67 mmol), *N*-iodosuccinimide (227 mg, 1.0 mmol) and silver trifluoromethanesulfonate (87 mg, 0.34 mmol) were added. The reaction mixture was stirred at 50 °C under Ar. After 19 h, TLC (petrol/ethyl acetate, 1:1) indicated the formation of a product (R_f 0.2). The reaction mixture was partitioned between CH_2Cl_2 (60 ml) and $Na_2S_2O_3$ (50 ml of a 10% aqueous solution). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 1:2) to afford the β-rhamnoside **11** (21 mg, 29%) as a colourless oil; $[\alpha]_D^{25}$=−122.7 (*c*, 1.0 in $CHCl_3$); ν_{max} 3472 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.30, 1.35 (6H, 2×s, 2×C(O)$_2$CH$_3$), 1.33 (3H, d, $J_{5,6}$=6.1 Hz, CH_3-6), 2.46 (1H, br s, OH-2), 3.25, 3.27 (6H, 2×s, 2×OCH_3), 3.46 (1H, dq, $J_{4,5}$=9.3 Hz, H-5), 3.55 (3H, s, OCH_3-1), 3.66 (1H, dd, $J_{2,3}$=3.0 Hz, $J_{3,4}$=10.1 Hz, H-3), 4.01 (1H, br s, H-2), 3.75 (1H, at, J=9.6 Hz, H-4), 4.41 (1H, d, $J_{1,2}$=0.8 Hz, H-1); δ_C (125.7 MHz, $CDCl_3$) 16.4, 17.5, 17.7 (3×q, 2×C(O)$_2$$CH_3$, C-6), 47.5, 47.9 (2×q, 2×OCH_3), 56.8 (q, OCH_3-1), 67.8, 69.4, 70.0, 70.4 (4×d, C-2, C-3, C-4, C-5), 99.6, 100.1 (2×s, 2×C(O)$_2$CH$_3$), 100.8 (d, $^1J_{C\text{-}1,H\text{-}1}$=156.6 Hz, C-1); *m/z* (ES$^+$) 315 (M+Na$^+$, 14), 310 (M+NH_4^+, 62), 261 (M−OMe, 100%). (HRMS calcd for $C_{13}H_{28}NO_7$ (MNH_4^+) 310.1866. Found 310.1867).

4.1.11. Phenyl 4,6-*O*-benzylidene-2-*O*-(2-iodo-1-(methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosid-3-*O*-yl)propyl)-3-*O*-pivaloyl-1-thio-β-D-glucopyranoside 14. *N*-Iodosuccinimide (163 mg, 0.23 mmol), 2,6-di-*tert*-butyl-4-methyl pyridine (99 mg, 0.48 mmol), methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (90 mg, 0.282 mmol) and 4 Å molecular sieves were added to anhydrous dichloromethane (2 ml) and cooled to −40 °C under Ar. Phenyl 4,6-*O*-benzylidene-3-*O*-pivaloyl-2-*O*-prop-1′-enyl-1-thio-β-D-glucopyranoside **13** (234 mg, 0.484 mmol) was dissolved in anhydrous dichloromethane (2 ml) and added to the reaction vessel by cannula under N_2. The reaction was allowed to warm to rt. After 16 h, TLC (cyclohexane/ethyl acetate, 4:1) indicated the complete consumption of starting material (R_f 0.7). After a further 24 h, the solvent had all evaporated off. TLC (cyclohexane/ethyl acetate, 4:1) indicated the formation of two major products (R_f 0.45 and 0.5), plus some remaining starting alcohol (R_f 0.4). The reaction was quenched with Et_3N (2 ml) and stirred for 5 min. Sodium thiosulfate (50 ml of a

10% aqueous solution) was added and the mixture extracted with CH_2Cl_2 (2×50 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (cyclohexane/ethyl acetate, 6:1) to afford mixed acetals **14**. (142 mg, 60%) as a white foam. *m/z* (ES^+) 1000 ($M+NH_4^+$, 53%), which was used directly in the next step without further characterisation.

4.1.12. Methyl 4,6-*O*-benzylidene-3-*O*-pivaloyl-α-D-glucopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside 15. The mixed acetals **14** prepared above (133 mg, 0.136 mmol) were dissolved in anhydrous dichloroethane (4 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (56 mg, 0.272 mmol), silver trifluoromethanesulfonate (35 mg, 0.136 mmol) and *N*-iodosuccinimide (92 mg, 0.409 mmol) were added. After 14 h 30 min, TLC (petrol/ethyl acetate, 4:1) indicated the formation of a major product (R_f 0.3) and the absence of starting material (R_f 0.4). The reaction mixture was partitioned between CH_2Cl_2 (2× 50 ml) and $Na_2S_2O_3$ (50 ml of a 10% aqueous solution). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 3:1) to afford the α-*gluco* disaccharide **15** (67 mg, 70%) as a colourless oil; $[\alpha]_D^{22}=+40.6$ (*c*, 0.65 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.23 (9H, s, $C(CH_3)_3$), 2.56 (1H, d, $J_{OH,2}=11.5$ Hz, OH-2_b), 3.37 (3H, s, OCH_3), 3.59 (1H, at, $J=9.6$ Hz, H-4_b), 3.67 (1H, ddd, $J_{1,2}=3.8$ Hz, $J_{2,3}=9.7$ Hz, H-2_b), 3.72 (1H, at, $J=10.3$ Hz, H-6_b), 3.79–3.90 (3H, m, H-2_a, H-5_a, H-5_b), 3.89 (1H, at, $J=10.3$ Hz, H-6_a), 4.20–4.26 (3H, m, H-3_a, H-4_a, H-$6'_b$), 4.28 (1H, dd, $J_{5,6'}=4.5$ Hz, $J_{6,6'}=9.9$ Hz, H-$6'_a$), 4.74 (1H, d, $J_{1,2}=1.4$ Hz, H-1_a), 4.77 (2H, s, PhC*H*$_2$), 5.28 (1H, d, H-1_b), 5.42 (1H, at, $J=9.7$ Hz, H-3_b), 5.50, 5.62 (2H, 2×s, 2×PhC*H*), 7.27–7.48 (15H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 27.6 (q, $C(CH_3)_3$), 37.8 (s, $C(CH_3)_3$), 55.4 (q, OCH_3), 63.9, 64.3, 72.1, 72.2, 75.7, 77.8, 78.9, 79.3 (8×d, C-2_a, C-3_a, C-4_a, C-5_a, C-2_b, C-3_b, C-4_b, C-5_b), 69.1, 69.3, (2×t, C-6_a, C-6_b), 73.9 (t, PhC*H*$_2$), 100.1, 101.2, 101.5, 101.9 (4×d, C-1_a, C-1_b, 2×PhC*H*), 126.4, 126.7, 127.9, 128.4, 128.5, 128.7, 129.1, 129.3, 129.5 (9×d, Ar-CH), 136.4 (s, Ar-C), 176.9 (s, C=O); *m/z* (ES^+) 729 ($M+Na^+$, 30), 724 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{39}H_{50}NO_{12}$ (MNH_4^+) 724.3333. Found 724.3331).

4.1.13. *para*-Tolyl 3,4-di-*O*-benzyl-2-*O*-(2-iodo-1-methoxypropyl)-1-thio-α-L-rhamnopyranoside 16a. *N*-Iodosuccinimide (138 mg, 0.61 mmol) and 4 Å molecular sieves were added to anhydrous dichloroethane (2 ml) and cooled to −40 °C under Ar. Vinyl ethers **9** (100 mg, 0.20 mmol) and methanol (0.013 ml, 0.30 mmol) were dissolved in anhydrous dichloroethane (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt over 1 h. After this time, the reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 8:1) to afford mixed acetals **16a** (117 mg, 88%) as a colourless oil; *m/z* ($APCI^+$) 704 (M+56, 100), 666 ($M+NH_4^+$, 10%); (ES^+) 671 ($M+Na^+$, 100%). (HRMS calcd for $C_{31}H_{41}NO_5SI$ (MNH_4^+) 666.1750. Found 666.1760).

4.1.14. *para*-Tolyl 3,4-di-O-benzyl-2-*O*-(2-iodo-1-(methyl 2,3,4-tri-O-benzyl-α-D-glucopyranosid-6-*O*-yl)propyl)-1-thio-α-L-rhamnopyranoside 16b. *N*-Iodosuccinimide (138 mg, 0.61 mmol) and 4 Å molecular sieves were added to anhydrous dichloroethane (2 ml) and cooled to −40 °C under Ar. Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (189 mg, 0.41 mmol) was dissolved in anhydrous dichloroethane (2 ml) and added to the reaction vessel by cannula under Ar. Vinyl ethers **9** (99 mg, 0.20 mmol) were dissolved in anhydrous dichloroethane (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt. After 21 h, TLC (petrol/ether, 4:1) indicated complete consumption of the enol ether (R_f 0.5). TLC (petrol/ethyl acetate, 3:1) indicated formation of a major (R_f 0.7) and two minor (R_f 0.6 and 0.4) products and remaining aglycon (R_f 0.3). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 3:1) to afford mixed acetals **16b** (164 mg, 75%) as a colourless oil; *m/z* ($APCI^+$) 1136 (M+56, 20%); (ES^+) 1139 ($M+NH_4^+$+MeCN, 11), 1098 ($M+NH_4^+$, 14%). (HRMS calcd for $C_{58}H_{69}NO_{10}SI$ (MNH_4^+) 1098.3687. Found 1098.3678).

4.1.15. *para*-Tolyl 3,4-di-*O*-benzyl-2-*O*-(2-iodo-1-(methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosid-3-*O*-yl)propyl)-1-thio-α-L-rhamnopyranoside 16c. Iodine (61 mg, 0.24 mmol), silver trifluoromethanesulfonate (61 mg, 0.24 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (100 mg, 0.48 mmol), methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (72 mg, 0.19 mmol) and 4 Å molecular sieves were added to freshly distilled CH_2Cl_2 (2 ml) and cooled to −78 °C under Ar. Vinyl ethers **9** (90 mg, 0.18 mmol) were dissolved in freshly distilled CH_2Cl_2 (3 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt. After 6 h 30 min, TLC (petrol/ethyl acetate, 4:1) indicated complete consumption of starting material (R_f 0.8) and formation of a major product (R_f 0.7). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 3:1) to afford mixed acetals **16c** (148 mg, 82%) as a white foam; *m/z* (ES^+) 1027 ($M+K^+$, 62), 1011 ($M+Na^+$, 100), 1006 ($M+NH_4^+$, 65%).

4.1.16. *para*-Tolyl 3,4-di-*O*-benzyl-2-*O*-(1-(cholestan-3-β-yloxy)-2-iodopropyl)-1-thio-α-L-rhamnopyranoside 16d. Iodine (57 mg, 0.22 mmol), silver trifluoromethanesulfonate (57 mg, 0.22 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (91 mg, 0.44 mmol), cholestan-3-β-ol (70 mg, 0.18 mmol) and 4 Å molecular sieves were added to freshly distilled CH_2Cl_2 (1 ml) and cooled to −78 °C under Ar. Vinyl ethers **9** (90 mg, 0.18 mmol) were dissolved in freshly distilled CH_2Cl_2 (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt. After 6 h 45 min, TLC (petrol/ethyl acetate, 4:1) indicated complete consumption of starting material (R_f 0.8) and formation of a major product (R_f 0.9). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous

solution) then extracted with CH_2Cl_2 (2×30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 11:1) to afford mixed acetals **16d** (118 mg, 69%) as a white foam; *m/z* (ES^+) 1027 ($M+Na^+$, 22%).

4.1.17. Methyl 3,4-di-*O*-benzyl-β-L-rhamnopyranoside 17a. Mixed acetals **16a** (114 mg, 0.18 mmol) was dissolved in anhydrous dichloroethane (3 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (73 mg, 0.35 mmol), *N*-iodosuccinimide (119 mg, 0.53 mmol) and silver trifluoromethanesulfonate (46 mg, 0.18 mmol) were added. The reaction mixture was stirred at rt for 30 min under Ar and then heated to 50 °C. After 3 h, TLC (petrol/ether, 4:1) indicated the absence of starting material (R_f 0.5). TLC (petrol/ethyl acetate, 3:1) indicated formation of several products (R_f 0.55, 0.5 and 0.1). The reaction mixture was allowed to cool and then trifluoroacetic acid (2 ml) and water (1 ml) were added, and the mixture stirred further. After 2 h, TLC (petrol/ethyl acetate, 3:1) indicated formation of a major product (R_f 0.1). The reaction mixture was partitioned between $NaHCO_3$ (30 ml of a saturated aqueous solution) and CH_2Cl_2 (2× 30 ml). The combined organic extracts were washed with sodium thiosulfate (30 ml of a 10% aqueous solution) dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 2:1) to afford β-rhamnoside **17a** (34 mg, 54%) as a colourless oil; $[\alpha]_D^{25}=+27.0$ (*c*, 1.5 in $CHCl_3$); ν_{max} 3480 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, $J_{5,6}=$ 6.2 Hz, CH_3-6), 2.39 (1H, br s, OH-2), 3.33 (1H, dq, $J_{4,5}=$ 9.2 Hz, H-5), 3.51–3.60 (2H, m, H-3, H-4), 3.55 (3H, s, OCH_3), 4.11 (1H, br s, H-2), 4.31 (1H, d, $J_{1,2}=1.0$ Hz, H-1), 4.66, 4.95 (2H, ABq, $J_{AB}=10.9$ Hz, PhCH_2), 4.69, 4.78 (2H, ABq, $J_{AB}=12.2$ Hz, PhCH_2), 7.28–7.41 (10H, m, Ar-H); δ_C (125.7 MHz, $CDCl_3$) 17.7 (q, C-6), 56.7 (q, OCH_3), 68.2, 71.3, 79.6, 81.3 (4×d, C-2, C-3, C-4, C-5), 71.3, 75.3 (2×t, $PhCH_2$), 100.5 (d, $^1J_{C\text{-}1,H\text{-}1}=156.0$ Hz, C-1), 127.6, 127.7, 127.8, 128.0, 128.3, 128.4 (6×d, Ar-CH), 137.7, 138.2 (2×s, Ar-C); *m/z* (ES^+) 739 ($2M+Na^+$, 7), 734 ($2M+NH_4^+$, 11), 417 ($M+MeCN+NH_4^+$, 46), 381 ($M+Na^+$, 15), 376 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{21}H_{30}NO_5$ (MNH_4^+) 376.2124. Found 376.2124).

4.1.18. Methyl 3,4-di-*O*-benzyl-β-L-rhamnopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside 17b. Mixed acetals **16b** (70 mg, 0.065 mmol) were dissolved in anhydrous dichloroethane (3 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (27 mg, 0.13 mmol), *N*-iodosuccinimide (44 mg, 0.20 mmol) and silver trifluoromethanesulfonate (17 mg, 0.065 mmol) were added and the mixture stirred under Ar at rt. After 17 h 30 min, TLC (petrol/ethyl acetate, 3:1) indicated the complete consumption of starting material (R_f 0.6) and the formation of a major product (R_f 0.1). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) and extracted with CH_2Cl_2 (2× 30 ml). The organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 3:1→1:1) to afford β-*rhamno* disaccharide **17b** (32 mg, 62%) as a colourless oil; $[\alpha]_D^{24}=+32.6$ (*c*, 1.4 in $CHCl_3$); ν_{max} 3452 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, $J_{5,6}=$ 6.4 Hz CH_3-6_b), 2.26 (1H, br s, OH-2_b), 3.32 (1H, dq, $J_{4,5}=$ 8.7 Hz, H-5_b), 3.37 (3H, s, OCH_3), 3.49–3.56 (3H, m, H-2_a, H-3_b, H-4_b), 3.64 (1H, at, $J=9.5$ Hz, H-4_a), 3.71–3.76 (2H, m, H-5_a, H-6_a), 4.00 (1H, at, $J=9.3$ Hz, H-3_a), 4.14 (1H, br d, $J=1.9$ Hz, H-2_b), 4.23 (1H, dd, $J_{5,6'}=3.6$ Hz, $J_{6,6'}=$ 11.5 Hz, H-$6'_a$), 4.44 (1H, s, H-1_b), 4.61 (1H, d, $J_{1,2}=$ 3.5 Hz, H-1_a), 4.64, 4.96 (2H, ABq, $J_{AB}=10.8$ Hz, PhCH_2), 4.66, 4.82 (2H, ABq, $J_{AB}=12.5$ Hz, PhCH_2), 4.69, 4.77 (2H, ABq, $J_{AB}=11.5$ Hz, PhCH_2), 4.76, 4.87 (2H, ABq, $J_{AB}=10.3$ Hz, PhCH_2), 4.87, 5.00 (2H, ABq, $J_{AB}=$ 10.7 Hz, PhCH_2), 7.27–7.40 (25H, m, Ar-H); δ_C (125.7 MHz, $CDCl_3$) 17.8 (q, C-6_b), 55.1 (q, OCH_3), 66.9, 71.0, 73.3, 75.0, 75.4, 75.6 (6×t, 5×PhCH_2, C-6_a), 68.2, 69.7, 71.4, 77.2, 79.5, 79.6, 81.0, 81.9 (8×d, C-2_a, C-3_a, C-4_a, C-5_a, C-2_b, C-3_b, C-4_b, C-5_b), 98.1 (d, $^1J_{C\text{-}1,H\text{-}1}=$ 167.9 Hz, C-1_a), 99.3 (d, $^1J_{C\text{-}1,H\text{-}1}=157.1$ Hz, C-1_b), 127.5, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.3 (13×d, Ar-CH), 137.7, 138.0, 138.2, 138.3, 138.7 (5×s, Ar-C); *m/z* ($APCI^+$) 846 (M+ 56, 12), 808 ($M+NH_4^+$, 7%); ($APCI^-$) 825 ($M+Cl^-$, 32), 699 (M−Bn, 95%). (HRMS calcd for $C_{48}H_{58}NO_{10}$ (MNH_4^+) 808.4061. Found 808.4069).

4.1.19. Cholestan-3′-β-yl 3,4-di-*O*-benzyl-β-L-rhamnopyranoside 17d. Mixed acetals **16d** (102 mg, 0.10 mmol) were dissolved in anhydrous dichloroethane (9 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (42 mg, 0.20 mmol), *N*-iodosuccinimide (69 mg, 0.31 mmol) and silver trifluoromethanesulfonate (26 mg, 0.10 mmol) were added and the mixture stirred under Ar at rt. After 2 h 20 min, TLC (petrol/ethyl acetate, 3:1) indicated the absence of starting material (R_f 0.9) and the formation of a various products (R_f 0.5–0.9). The reaction mixture was partitioned between CH_2Cl_2 (2× 40 ml) and sodium thiosulfate (40 ml of a saturated aqueous solution). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 4:1) to afford β-rhamnosyl steroid **17d** (21 mg, 29%) as a colourless oil; $[\alpha]_D^{24}=+25.4$ (*c*, 0.8 in $CHCl_3$); ν_{max} 3469 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.65, 0.80 (6H, 2×s, 2×steroid CH_3), 0.86 (3H, d, $J=6.3$ Hz, steroid CH_3), 0.90 (3H, d, $J=6.9$ Hz, steroid CH_3), 0.90 (3H, d, $J=$ 6.4 Hz, steroid CH_3), 0.93–1.99 (31H, m, steroid CH, CH_2), 1.34 (3H, d, $J_{5,6}=6.2$ Hz, CH_3-6), 2.44 (1H, br s, OH-2), 3.30 (1H, dq, $J_{4,5}=8.8$ Hz, H-5), 3.51–3.57 (2H, m, H-3, H-4), 3.63–3.69 (1H, m, steroid OCH), 4.05 (1H, br s, H-2), 4.52 (1H, s, H-1), 4.65, 4.95 (2H, ABq, $J_{AB}=10.9$ Hz, PhCH_2), 4.68, 4.78 (2H, ABq, $J_{AB}=11.9$ Hz, PhCH_2), 7.27–7.40 (10H, m, Ar-H); δ_C (125.7 MHz, $CDCl_3$) 12.0, 12.3, 18.6, 22.5, 22.8 (5×q, 5×steroid CH_3), 17.9 (q, C-6), 21.2, 23.8, 24.2, 27.7, 28.2, 28.7, 32.1, 35.8, 36.1, 36.8, 39.5, 40.0 (12×t, 12×steroid CH_2), 28.0, 35.5, 35.8, 44.9, 54.4, 56.3, 56.5 (7×d, 7×steroid CH), 35.6, 42.6 (2×s, 2×steroid C), 69.0, 71.3, 77.7, 79.6, 81.5 (5×d, C-2, C-3, C-4, C-5, steroid O*C*H), 71.2, 75.5 (2×t, 2×PhCH_2), 97.2 (d, $^1J_{C\text{-}1,H\text{-}1}=158.3$ Hz, C-1), 127.7, 127.8, 127.9, 128.1, 128.4, 128.4 (6×d, Ar-CH), 137.9, 138.6 (2×s, Ar-C); *m/z* (ES^+) 737 ($M+Na^+$, 24), 732 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{47}H_{74}NO_5$ (MNH_4^+) 732.5567. Found 732.5563).

4.1.20. *para*-Tolyl 2-*O*-acetyl-3,5,6-tri-*O*-benzyl-1-thio-α-D-glucofuranoside 19α and *para*-tolyl 2-*O*-acetyl-3,5,6-tri-*O*-benzyl-1-thio-β-D-glucofuranoside 19β. *Method 1 (reaction carried out at 0 °C).* Diacetate **18**

(1.0 g, 1.87 mmol) and *para*-thiocresol (348 mg, 2.81 mmol) were dissolved in freshly distilled CH_2Cl_2 (5 ml) and cooled to 0 °C. $BF_3{\cdot}OEt_2$ (0.3 ml, 2.43 mmol) was added and the mixture stirred under Ar. After 45 min, TLC (petrol/ethyl acetate, 2:1) indicated complete consumption of starting material (R_f 0.5) and formation of two major products (R_f 0.6 and 0.65). After a further 2 h, the reaction mixture was partitioned between CH_2Cl_2 (2× 100 ml) and $NaHCO_3$ (100 ml of a saturated aqueous solution). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 5:1) to afford α-thioglycoside **19α** (154 mg, 13%) as a colourless oil; $[\alpha]_D^{24}=+60.5$ (*c*, 1.0 in $CHCl_3$); ν_{max} 1749 (s, C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.16 (3H, s, $COCH_3$), 2.34 (3H, s, $ArCH_3$), 3.71 (1H, dd, $J_{5,6}=5.5$ Hz, $J_{6,6'}=10.6$ Hz, H-6), 3.91 (1H, dd, $J_{5,6'}=1.8$ Hz, H-6′), 4.06 (1H, ddd, $J_{4,5}=9.3$ Hz, H-5), 4.15 (1H, dd, $J_{2,3}=0.6$ Hz, $J_{3,4}=3.4$ Hz, H-3), 4.42 (1H, dd, H-4), 4.49, 4.80 (2H, ABq, $J_{AB}=11.2$ Hz, $PhCH_2$), 4.56, 4.76 (2H, ABq, $J_{AB}=11.6$ Hz, $PhCH_2$), 4.62 (2H, s, $PhCH_2$), 5.54 (1H, dd, $J_{1,2}=4.6$ Hz, H-2), 5.72 (1H, d, H-1), 7.09–7.40 (19H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 20.7, 21.1 (2×q, $ArCH_3$, $COCH_3$), 71.0, 72.0, 72.7, 73.4 (4×t, 3×$PhCH_2$, C-6), 75.5, 77.2, 78.8, 81.5 (4×d, C-2, C-3, C-4, C-5), 89.6 (d, C-1), 127.4, 127.5, 127.6, 127.7, 127.7, 127.7, 127.8, 128.3, 128.3, 128.4, 129.7, 131.9 (12×d, Ar-CH), 131.1, 137.3, 137.4, 138.4, 138.6 (5×s, Ar-C), 169.8 (s, C=O); *m/z* (ES^+) 657 ($M+NH_4^+$ +MeCN, 34), 621 ($M+Na^+$, 21), 616 ($M+NH_4^+$, 100), 599 ($M+H^+$, 3%). (HRMS calcd for $C_{36}H_{42}NO_6S$ (MNH_4^+) 616.2733. Found 616.2727); and β-thioglycoside **19β** (213 mg, 18%) as a colourless oil; $[\alpha]_D^{24}=-88.9$ (*c*, 1.0 in $CHCl_3$); ν_{max} 1748 (s, C=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.09 (3H, s, $COCH_3$), 2.33 (3H, s, $ArCH_3$), 3.73 (1H, dd, $J_{5,6}=4.8$ Hz, $J_{6,6'}=10.7$ Hz, H-6), 3.90 (1H, dd, $J_{5,6'}=1.9$ Hz, H-6′), 4.11 (1H, d, $J_{3,4}=3.8$ Hz, H-3), 4.18 (1H, ddd, $J_{4,5}=9.3$ Hz, H-5), 4.30 (1H, dd, H-4), 4.44, 4.71 (2H, ABq, $J_{AB}=11.1$ Hz, $PhCH_2$), 4.53, 4.85 (2H, ABq, $J_{AB}=11.5$ Hz, $PhCH_2$), 4.61, 4.65 (2H, ABq, $J_{AB}=12.4$ Hz, $PhCH_2$), 5.34 (1H, d, $J_{1,2}=1.4$ Hz, H-1), 5.44 (1H, d, H-2), 7.09–7.42 (19H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 20.9, 21.1 (2×q, $ArCH_3$, $COCH_3$), 70.1, 71.8, 72.5, 73.7 (4×t, 3×$PhCH_2$, C-6), 75.8, 80.2, 80.7, 81.2 (4×d, C-2, C-3, C-4, C-5), 91.0 (d, C-1), 127.4, 127.5, 127.6, 127.7, 127.8, 128.2, 128.3, 128.3, 129.6, 129.7, 131.9 (11×d, Ar-CH), 131.5, 137.4, 137.5, 138.5, 138.6 (5×s, Ar-C), 169.8 (s, C=O); *m/z* (ES^+) 657 ($M+NH_4^+$ +MeCN, 33), 616 ($M+NH_4^+$, 60%). (HRMS calcd for $C_{36}H_{42}NO_6S$ (MNH_4^+) 616.2733. Found 616.2732), together with a further α/β mixture (223 mg, 19%) as a colourless oil.

Method 2 (reaction carried out at −30 °C). Diacetate **18** (2.99 g, 5.61 mmol) and *para*-thiocresol (836 mg, 6.74 mmol) were dissolved in freshly distilled CH_2Cl_2 (15 ml) in a flame-dried flask and cooled to −30 °C under Ar. $BF_3{\cdot}OEt_2$ (1.04 ml, 8.42 mmol) was added and the mixture stirred under Ar. After 40 min, the mixture had warmed to −20 °C. At this time, TLC (petrol/ethyl acetate, 2:1) indicated little remaining starting material (R_f 0.5) and formation of a major product (R_f 0.6). The reaction was quenched with Et_3N (2 ml), and the mixture partitioned between CH_2Cl_2 (120+60 ml) and water (100 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, 5:1) to afford α-thioglycoside **19α** (37 mg, 1%) as a colourless oil identical to that described above, and β-thioglycoside **19β** (1.93 g, 58%) as a colourless oil identical to that described above.

4.1.21. *para*-Tolyl 3,5,6-tri-*O*-benzyl-1-thio-β-D-glucofuranoside 20. β-Thioglycoside **19β** (195 mg, 0.33 mmol) was dissolved in methanol (5 ml), THF (10 ml) and *n*-propylamine (5 ml) and stirred at rt. After 14 h, TLC (petrol/ethyl acetate, 2:1) indicated complete consumption of starting material (R_f 0.7) and formation of a major product (R_f 0.6). The reaction mixture was concentrated in vacuo and the residue purified by flash column chromatography (petrol/ethyl acetate, 4:1→3:1) to afford alcohol **20** (2.10 g, 91%) as a colourless oil; $[\alpha]_D^{25}=-132.2$ (*c*, 1.25 in $CHCl_3$); ν_{max} 3406 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.34 (3H, s, $ArCH_3$), 2.40 (1H, d, $J_{OH,2}=3.8$ Hz, OH-2), 3.75 (1H, dd, $J_{5,6}=5.2$ Hz, $J_{6,6'}=10.7$ Hz, H-6), 3.91 (1H, dd, $J_{5,6'}=2.0$ Hz, H-6′), 4.04 (1H, dd, $J_{2,3}=1.2$ Hz, $J_{3,4}=4.3$ Hz, H-3), 4.17 (1H, ddd, $J_{4,5}=9.0$ Hz, H-5), 4.37 (1H, br s, H-2), 4.39 (1H, dd, H-4), 4.46, 4.62 (2H, ABq, $J_{AB}=11.6$ Hz, $PhCH_2$), 4.50, 4.76 (2H, ABq, $J_{AB}=11.2$ Hz, $PhCH_2$), 4.61 (2H, s, $PhCH_2$), 5.19 (1H, d, $J_{1,2}=2.4$ Hz, H-1), 7.09–7.40 (19H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 21.1 (q, $ArCH_3$), 70.6 (t, C-6), 72.0, 72.6, 73.4 (3×t, 3×$PhCH_2$), 76.3 (d, C-5), 79.5 (d, C-2), 80.7 (d, C-4), 83.2 (d, C-3), 93.2 (d, C-1), 127.4, 127.6, 127.7, 128.2, 128.3, 128.4, 129.7, 131.4 (8×d, Ar-CH), 131.8, 137.1, 137.7, 138.5, 138.7 (5×s, Ar-C); *m/z* (ES^+) 615 ($M+NH_4^+$ +MeCN, 8), 574 ($M+NH_4^+$, 18), 557 ($M+H^+$, 6%). (HRMS calcd for $C_{34}H_{40}NO_5S$ (MNH_4^+) 574.2627. Found 574.2627).

4.1.22. *para*-Tolyl 2-*O*-allyl-3,5,6-tri-*O*-benzyl-1-thio-β-D-glucofuranoside 21. Alcohol **20** (2.1 g, 3.78 mmol) was dissolved in anhydrous DMF (10 ml) and cooled to 0 °C. Allyl bromide (0.65 ml, 7.55 mmol) then sodium hydride (60% in mineral oil) (300 mg, 7.55 mmol) were added. After 1 h, TLC (petrol/ethyl acetate, 3:1) indicated formation of a single product (R_f 0.5) and little remaining starting material (R_f 0.2). The reaction mixture was partitioned between ether (100+50 ml) and water (100 ml). The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ether, 4:1) to afford glycosyl donor **21** (2.12 g, 94%) as a colourless oil; $[\alpha]_D^{23}=-99.9$ (*c*, 2.0 in $CHCl_3$); ν_{max} no significant peaks; δ_H (400 MHz, $CDCl_3$) 2.34 (3H, s, $ArCH_3$), 3.74 (1H, dd, $J_{5,6}=5.3$ Hz, $J_{6,6'}=10.7$ Hz, H-6), 3.93 (1H, dd, $J_{5,6'}=2.0$ Hz, H-6′), 3.97–4.00 (2H, m, $OCHH'CH=CH_2$), 4.10–4.12 (2H, m, H-2, H-3), 4.20 (1H, ddd, $J_{4,5}=9.1$ Hz, H-5), 4.31 (1H, dd, $J_{3,4}=3.8$ Hz, H-4), 4.52, 4.62 (2H, ABq, $J_{AB}=11.6$ Hz, $PhCH_2$), 4.52, 4.80 (2H, ABq, $J_{AB}=11.6$ Hz, $PhCH_2$), 4.62 (2H, s, $PhCH_2$), 5.20 (1H, dq, $J_Z=10.4$ Hz, $J=1.5$ Hz, $CH=CH_EH_Z$), 5.26 (1H, dq, $J_E=17.3$ Hz, $J=1.7$ Hz, $CH=CH_EH_Z$), 5.30 (1H, d, $J_{1,2}=1.7$ Hz, H-1), 5.84 (1H, ddt, $J=5.5$ Hz, $CH=CH_2$), 7.09–7.42 (19H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 21.1 (q, $ArCH_3$), 70.6, 70.8, 72.0, 72.5, 73.4 (5×t, C-6, 3×$PhCH_2$, $OCH_2CH=CH_2$), 76.2, 81.2, 81.3, 86.3 (4×d, C-2, C-3, C-4, C-5), 91.0 (d, C-1), 117.6 (t, $CH=CH_2$), 127.4, 127.4,

127.6, 127.6, 127.7, 127.8, 128.2, 128.3, 128.4, 129.6, 131.4, 133.9 (12×d, Ar-CH, *C*H=CH_2), 131.9, 137.0, 137.7, 138.6, 138.9 (5×s, Ar-C); *m/z* (ES^+) 619 ($M+Na^+$, 33), 614 ($M+NH_4^+$, 100), 597 ($M+H^+$, 7%). (HRMS calcd for $C_{37}H_{44}NO_5S$ (MNH_4^+) 614.2940. Found 614.2938).

4.1.23. *para*-Tolyl 3,5,6-tri-*O*-benzyl-2-*O*-prop-1′-enyl-1-thio-β-D-glucofuranoside 22. Wilkinson's catalyst (320 mg, 0.35 mmol) was dissolved in anhydrous THF (6 ml) and degassed. Butyl lithium (1.6 M solution in hexanes) (0.32 ml, 0.52 mmol) was added and the mixture stirred for 10 min. Glycosyl donor **21** (2.07 g, 3.47 mmol) was dissolved in anhydrous THF (6 ml) and heated to 70 °C. The catalyst solution was added by cannula under Ar. After 2 h, TLC (CH_2Cl_2/petrol, 4:1) indicated formation of a two products (R_f 0.45 and 0.5) and complete consumption of starting material (R_f 0.4). The reaction was allowed to cool then diluted with CH_2Cl_2 (*ca* 5 ml) and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 8:1) to afford enol ethers **22** (1.99 g, 96%) as a colourless oil. Partial data: δ_H (400 MHz, $CDCl_3$) (*E*/*Z*, 1:1.7), *E* isomer 1.50 (3H, dd, $J=1.5$ Hz, $J=6.7$ Hz, OCH=CHCH_3), 2.33 (3H, s, $ArCH_3$), 4.83 (1H, dq, $J_E=12.5$ Hz, OCH=C*H*), 5.31 (1H, d, $J_{1,2}=1.2$ Hz, H-1), 5.97 (1H, daq, $J=1.5$ Hz, OC*H*=CH); *Z* isomer 1.53 (3H, dd, $J=1.9$ Hz, $J=6.7$ Hz, OCH=CHCH_3), 2.33 (3H, s, $ArCH_3$), 5.30 (1H, d, $J_{1,2}=1.8$ Hz, H-1), 5.84 (1H, daq, $J_Z=6.2$ Hz, $J=1.7$ Hz, OC*H*=CH); δ_C (100.6 MHz, $CDCl_3$) *E* isomer 12.4 (q, OCH=CH*C*H_3), 21.1 (q, $ArCH_3$), 90.8 (d, C-1), 102.6 (d, OCH=*C*H), 143.8 (d, O*C*H=CH); *Z* isomer 9.3 (q, OCH=CH*C*H_3), 21.1 (q, $ArCH_3$), 91.1 (d, C-1), 104.4 (d, OCH=*C*H), 142.9 (d, O*C*H=CH); *m/z* (ES^+) 619 ($M+Na^+$, 100), 614 ($M+NH_4^+$, 67), 597 ($M+H^+$, 23%). (HRMS calcd for $C_{37}H_{41}O_5S$ (MH^+) 597.2675. Found 597.2674).

4.1.24. *para*-Tolyl 3,5,6-tri-*O*-benzyl-2-O-(1-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl)-2-iodopropyl)-1-thio-β-D-glucofuranoside 23a. *N*-Iodosuccinimide (68 mg, 0.30 mmol), and 4 Å molecular sieves were added to anhydrous dichloroethane (1 ml) and cooled to −40 °C under Ar. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (52 mg, 0.20 mmol) was dissolved in anhydrous dichloroethane (1.5 ml) and added to the reaction vessel by cannula under Ar. Vinyl ethers **22** (60 mg, 0.1 mmol) were dissolved in anhydrous dichloroethane (1.5 ml) and added to the reaction vessel by cannula under Ar. The reaction was stirred and allowed to warm to rt. After 1 h 35 min, TLC (petrol/ethyl acetate, 6:1) indicated formation of a major product (R_f 0.2), and complete consumption of starting material (R_f 0.5). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×30 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, 5:1 with 1% Et_3N) to afford mixed acetals **23a** (107 mg, 75%) as a colourless oil. *m/z* (ES^+) 1005 ($M+Na^+$, 41), 1000 ($M+NH_4^+$, 5), 877 (M-STol+NH_4^+, 25%). (HRMS calcd for $C_{49}H_{63}NO_{11}SI$ (MNH_4^+) 1000.3167. Found 1000.3170).

4.1.25. *para*-Tolyl 3,5,6-tri-O-benzyl-2-*O*-(2-iodo-1-(methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranosid-6-*O*-yl)propyl)-1-thio-β-D-glucofuranoside 23b. Iodine (55 mg, 0.22 mmol), silver trifluoromethanesulfonate (56 mg, 0.22 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (116 mg, 0.57 mmol) and 4 Å molecular sieves were added to freshly distilled CH_2Cl_2 (1 ml) and cooled to −78 °C under Ar. Methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (82 mg, 0.18 mmol) was dissolved in freshly distilled CH_2Cl_2 (2 ml) and added by cannula under Ar. Enol ethers **22** (100 mg, 0.17 mmol) were dissolved in freshly distilled CH_2Cl_2 (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt. After 18 h, TLC (petrol/ethyl acetate, 6:1) indicated formation of a single major product (R_f 0.7), and little remaining starting material (R_f 0.8). The reaction was quenched with sodium thiosulfate (40 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×40 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, 7:1) to afford mixed acetals **23b** (128 mg, 64%) as a colourless oil; *m/z* (ES^+) 1245 ($M+NH_4^+$+MeCN, 55), 1209 ($M+Na^+$, 100), 1204 ($M+NH_4^+$, 92%).

4.1.26. *para*-Tolyl 3,5,6-tri-*O*-benzyl-2-*O*-(2-iodo-1-(methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosid-3-*O*-yl)propyl)-1-thio-β-D-glucofuranoside 23c. Iodine (55 mg, 0.22 mmol), silver trifluoromethanesulfonate (56 mg, 0.22 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (116 mg, 0.57 mmol) and 4 Å molecular sieves were added to freshly distilled CH_2Cl_2 (1 ml) and cooled to −78 °C under Ar. Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (65 mg, 0.18 mmol) was dissolved in freshly distilled CH_2Cl_2 (2 ml) and added by cannula under Ar. Enol ethers **22** (100 mg, 0.17 mmol) were dissolved in freshly distilled CH_2Cl_2 (2 ml) and added to the reaction vessel by cannula under Ar. The reaction was allowed to warm to rt. After 17 h, TLC (petrol/ethyl acetate, 3:1) indicated formation of a two major products (R_f 0.55 and 0.5), and little remaining starting material (R_f 0.6). The reaction was quenched with sodium thiosulfate (40 ml of a 10% aqueous solution) then extracted with CH_2Cl_2 (2×40 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, 7:1→3:1) to afford mixed acetals **23c** (161 mg, 88%) as a colourless oil; *m/z* (ES^+) 1153 ($M+NH_4^+$+MeCN, 22), 1117 ($M+Na^+$, 58%).

4.1.27. 3,5,6-Tri-*O*-benzyl-α-D-glucofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 24a. Mixed acetals **23a** (85 mg, 0.087 mmol) were dissolved in anhydrous dichloroethane (7 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (35 mg, 0.17 mmol), *N*-iodosuccinimide (59 mg, 0.26 mmol) and silver trifluoromethanesulfonate (22 mg, 0.087 mmol) were added and the mixture stirred under Ar at rt. After 6 h, TLC (petrol/ethyl acetate, 3:1) indicated the complete consumption of starting material (R_f 0.6) and the formation of a major product (R_f 0.3). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) and extracted with CH_2Cl_2 (2×30 ml). The organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash

column chromatography (petrol/ethyl acetate, 2:1) to afford α-*gluco* disaccharide **24a** (44 mg, 75%) as a colourless oil; $[\alpha]_D^{22} = -18.2$ (*c*, 0.55 in $CHCl_3$); ν_{max} 3467 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.33, 1.34, 1.46, 1.53 (12H, 4×s, 4×CH_3), 3.68 (1H, dd, $J_{5,6}=6.1$ Hz, $J_{6,6'}=10.5$ Hz, H-6_b), 3.79 (1H, dd, $J_{5,6}=7.9$ Hz, $J_{6,6'}=10.0$ Hz, H-6_a), 3.86–3.90 (2H, m, H-$6'_a$, H-$6'_b$), 4.03 (1H, ddd, $J_{4,5}=8.4$ Hz, $J_{5,6'}=2.0$ Hz, H-5_b), 4.06–4.11 (2H, m, H-5_a, H-3_b), 4.27–4.29 (2H, m, H-4_a, H-2_b), 4.33 (1H, dd, $J_{1,2}=5.1$ Hz, $J_{2,3}=2.3$ Hz, H-2_a), 4.37 (1H, dd, $J_{3,4}=4.3$ Hz,, H-4_b), 4.52, 4.70 (2H, ABq, $J_{AB}=11.8$ Hz, PhCH_2), 4.54, 4.80 (2H, ABq, $J_{AB}=11.6$ Hz, PhCH_2), 4.58 (2H, s, PhCH_2), 4.58–4.61 (1H, m, H-3_a), 5.21 (1H, d, $J_{1,2}=4.4$ Hz, H-1_b), 5.52 (1H, d, H-1_a), 7.16–7.37 (15H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 24.4, 24.9, 25.9, 26.1 (4×q, 4×CH_3), 65.5 (d, C-5_a), 67.1 (t, C-6_a), 70.5, 70.5, 70.8, 75.5 (4×d, C-2_a, C-3_a, C-4_a, C-2_b), 71.3, 71.7, 72.6, 73.3 (4×t, 3×PhCH_2, C-6_b), 76.0 (d, C-5_b), 78.2 (d, C-4_b), 83.7 (d, C-3_b), 96.3 (d, C-1_a), 102.4 (d, C-1_b), 108.9, 109.3 (2×s, 2×$C(CH_3)_2$), 127.3, 127.4, 127.4, 127.5, 127.5, 127.6, 128.2, 128.3, 128.3 (9×d, Ar-CH), 137.9, 138.6, 138.9 (3×s, Ar-C); *m/z* (ES^+) 751 ($M+NH_4^+$ + MeCN, 22%), 715 ($M+Na^+$, 26), 710 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{39}H_{52}NO_{11}$ (MNH_4^+) 710.3540. Found 710.3541).

4.1.28. Methyl 3,5,6-tri-*O*-benzyl-α-D-glucofuranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside 24b. Mixed acetals **23b** (103 mg, 0.087 mmol) were dissolved in anhydrous dichloroethane (7 ml). 2,6-Di-*tert*-butyl-4-methylpyridine (35 mg, 0.17 mmol), *N*-iodosuccinimide (59 mg, 0.26 mmol) and silver trifluoromethanesulfonate (22 mg, 0.087 mmol) were added and the mixture stirred under Ar at rt. After 5 h, TLC (petrol/ethyl acetate, 3:1) indicated the complete consumption of starting material (R_f 0.7) and the formation of a major product (R_f 0.3). The reaction was quenched with sodium thiosulfate (30 ml of a 10% aqueous solution) and extracted with CH_2Cl_2 (2× 30 ml). The organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 2:1) to afford α-*gluco* disaccharide **24b** (30 mg, 39%) as a colourless oil; $[\alpha]_D^{22} = +35.6$ (*c*, 0.5 in $CHCl_3$); ν_{max} 3383 (br, OH) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.31 (3H, s, OCH_3), 3.63 (1H, dd, $J_{5,6}=6.7$ Hz, $J_{6,6'}=10.5$ Hz, H-6_b), 3.68–3.71 (1H, m, H-5_a), 3.79–3.82 (2H, m, H-2_a, H-6_a), 3.84 (1H, dd, $J_{5,6'}=1.9$ Hz, H-$6'_b$), 3.89 (1H, dd, $J_{2,3}=2.9$ Hz, $J_{3,4}=9.6$ Hz, H-3_a), 4.01–4.07 (2H, m, H-4_a, H-5_b), 4.09 (1H, dd, $J_{2,3}=2.0$ Hz, $J_{3,4}=4.4$ Hz, H-3_b), 4.18 (1H, dd, $J_{5,6'}=3.6$ Hz, $J_{6,6'}=11.3$ Hz, H-$6'_a$), 4.25 (1H, dd, $J_{1,2}=4.3$ Hz, H-2_b), 4.34 (1H, dd, $J_{4,5}=8.0$ Hz, H-4_b), 4.46 (2H, s, PhCH_2), 4.49, 4.67 (2H, ABq, $J_{AB}=12.0$ Hz, PhCH_2), 4.55, 4.81 (2H, ABq, $J_{AB}=11.6$ Hz, PhCH_2), 4.63 (2H, s, PhCH_2), 4.67, 4.93 (2H, ABq, $J_{AB}=10.8$ Hz, PhCH_2), 4.69, 4.77 (2H, ABq, $J_{AB}=12.2$ Hz, PhCH_2), 4.70 (1H, s, H-1_a), 5.28 (1H, d, H-1_b), 7.23–7.38 (30H, m, Ar-H); δ_C (100.6 MHz, $CDCl_3$) 54.8 (q, OCH_3), 67.6 (t, C-6_a), 71.3 (d, C-5_a), 71.7, 72.1, 72.1, 72.7, 72.8, 73.2, 75.1 (7×t, 6×PhCH_2, C-6_b), 74.4, 74.5 (2×d, C-2_a, C-4_a), 75.6 (d, C-2_b), 76.3 (d, C-5_b), 78.4 (d, C-4_b), 79.9 (d, C-3_a), 83.7 (d, C-3_b), 99.0 (d, C-1_a), 102.6 (d, C-1_b), 127.2, 127.3, 127.4, 127.5, 127.5, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.3 (14×d, Ar-CH), 138.0, 138.1, 138.4, 138.4, 138.6, 139.0 (6×s, Ar-C); *m/z* (ES^+) 919 ($M+Na^+$, 54), 914 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{55}H_{64}NO_{11}$ (MNH_4^+) 914.4479. Found 914.4467).

4.1.29. Methyl 3,5,6-tri-*O*-benzyl-α-D-glucofuranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside 24c. Dimethyl disulfide (24 μl, 0.26 mmol) and methyl trifluoromethanesulfonate (30 μl, 0.26 mmol) were dissolved in freshly distilled CH_2Cl_2 (1 ml) and stirred under Ar at rt. After 5 min, 2,6-di-*tert*-butyl-4-methylpyridine (68 mg, 0.33 mmol) was added and the mixture cooled to 0 °C. Mixed acetals **23c** (72 mg, 0.066 mmol) was dissolved in freshly distilled CH_2Cl_2 (2 ml) and added by cannula under Ar. After 5 h, TLC (petrol/ethyl acetate, 3:1) indicated very little remaining starting material (R_f 0.6) and the formation of major (R_f 0.4) and minor (R_f 0.4–0.5) products. The reaction was quenched with Et_3N and the mixture partitioned between ether (40 ml) and brine (40 ml). The aqueous layer was re-extracted with ether (20 ml) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 7:2) to afford α-*gluco* disaccharide **24c** (17 mg, 32%) as a colourless oil; $[\alpha]_D^{22} = +12.8$ (*c*, 0.5 in $CHCl_3$); ν_{max} 3498 (br, OH) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 3.37 (3H, s, OCH_3), 3.67 (1H, dd, $J_{5,6}=5.7$ Hz, $J_{6,6'}=10.8$ Hz, H-6_b), 3.78–3.89 (4H, m, H-2_a, H-5_a, H-6_a, H-$6'_b$), 4.00 (1H, ddd, $J_{4,5}=8.0$ Hz, $J_{5,6'}=2.1$ Hz, H-5_b), 4.04 (1H, dd, $J_{2,3}=2.3$ Hz, $J_{3,4}=4.5$ Hz, H-3_b), 4.14 (1H, at, $J=9.5$ Hz, H-4_a), 4.23–4.28 (3H, m, H-3_a, H-$6'_a$, H-2_b), 4.35 (1H, dd, H-4_b), 4.48, 4.67 (2H, ABq, $J_{AB}=12.0$ Hz, PhCH_2), 4.52, 4.75 (2H, ABq, $J_{AB}=11.6$ Hz, PhCH_2), 4.52, 4.56 (2H, ABq, $J_{AB}=12.0$ Hz, PhCH_2), 4.59, 4.67 (2H, ABq, $J_{AB}=12.0$ Hz, PhCH_2), 4.67 (1H, d, $J_{1,2}=1.3$ Hz, H-1_a), 5.28 (1H, d, $J_{1,2}=4.5$ Hz, H-1_b), 5.59 (1H, s, PhC*H*), 7.23–7.47 (25H, m, Ar-H); δ_C (125.7 MHz, $CDCl_3$) 54.8 (q, OCH_3), 63.8 (d, C-5_a), 68.7 (t, C-6_a), 70.7 (t, C-6_b), 71.4, 72.3, 73.2, 73.8 (4×t, 4×PhCH_2), 75.2 (d, C-3_a), 75.9, 76.0 (2×d, C-2_b, C-5_b), 78.0, (d, C-2_a, C-4_a, C-4_b), 83.4 (d, C-3_b), 100.2 (d, C-1_a), 101.5 (d, PhC*H*), 102.8 (d, C-1_b), 125.9, 127.2, 127.3, 127.3, 127.4, 127.5, 127.7, 128.1, 128.1, 128.2, 128.3, 128.9 (12×d, Ar-CH), 137.2, 137.7, 137.9, 138.5, 138.8 (5×s, Ar-C); *m/z* (ES^+) 827 ($M+Na^+$, 46), 822 ($M+NH_4^+$, 100%). (HRMS calcd for $C_{48}H_{56}NO_{11}$ (MNH_4^+) 822.3853. Found 822.2863).

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21. Studies were in fact also carried out on the minor α-anomer **19α**, which was carried through an analogous reaction sequence to that undertaken for **19β** (Scheme 4). However, all subsequent IAD experiments on tethered materials derived from the α-donor, in which the leaving group is *syn* to the 2-hydroxyl group, revealed that whilst intramolecular glycosylation did occur that this was substantially less efficient than for the epimeric donor, in which the anomeric leaving group is *anti* to the 2-hydroxyl.
22. The anomeric stereochemistry of the α-glucofuranose disaccharides **24a–c** was determined by the $^{3}J_{H1,H2}$ coupling constant, which was between 4.3 and 4.5 Hz in all cases. See Ref. 19.
23. Whilst the desired 1,2-*cis* disaccharide **24c** was formed, as evidenced by ^{1}H NMR spectroscopy, this material could not be efficiently separated from the also-formed *manno* aglycon alcohol. In addition the overall reaction yield was low ($<31\%$), and many other unidentified products were also observed.