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Allyl Protecting Group Mediated Intramolecular Aglycon Delivery (IAD) of Glycosyl Fluorides

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Summary. Stereospecific 1,2-*cis*-glycosylation of 2-O-allyl protected glucosyl and mannosyl fluorides can be achieved *via* a sequence of allyl isomerization, N-iodosuccinimide mediated tethering, and intramolecular aglycon delivery (IAD). Fluoride is advantageous as an anomeric leaving group since extended reaction times can be employed to tether hindered aglycon alcohols without competitive anomeric activation. Tin(II) chloride mediated intramolecular glycosylation furnishes the desired α-glucosides and β-mannosides in an entirely stereoselective manner.

Keywords. Carbohydrates; Glycosides; Glycosylation; Stereoselectivity; Intramolecular aglycon delivery (IAD).

Introduction

Intramolecular aglycon delivery (IAD) is an attractive synthetic approach for the formation of 1,2-*cis*-glycosidic linkages. The technique of temporarily tethering together glycosyl donor and glycosyl acceptor *via* the 2-hydroxyl group of the glycosyl donor was originally pioneered for the synthesis of β-mannosides by *Hindsgaul* [1] and *Stork* [2] and more recently to greater effect by *Ogawa* [3]. The principle of the approach is that the glycosylation reaction, which ensues after tethering, must be intramolecular in nature. This therefore enforces the formation of a 1,2-*cis*-glycosidic linkage since the nucleophile must be delivered to the anomeric centre formally *syn* to the 2-hydroxyl group.

As part of our ongoing interest in the synthesis of oligosaccharides containing 1,2-*cis*-linkages we recently reported the development of an N-iodosuccinimide (*NIS*) mediated one-pot modification of the original *Hindsgaul* methodology [4, 5]. Subsequently we have developed 2-O-allyl protected thioglycosides as glycosyl donors for IAD [6]. Herein, an enol ether at position 2 of the glycosyl donor is accessed in near quantitative yield by isomerization of a 2-O-allyl protecting group. Subsequent tethering and intramolecular glycosylation then yield the 1,2-*cis*-glycoside. However, whereas good yields were obtained for *NIS* mediated

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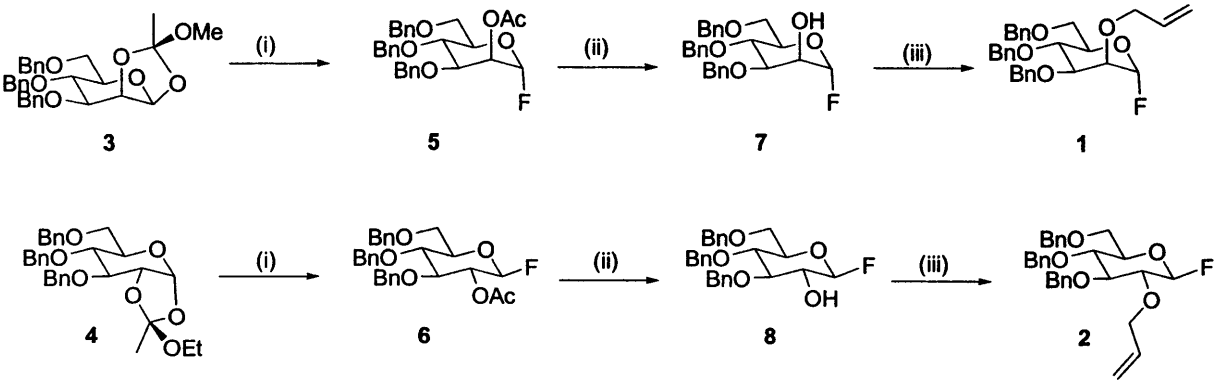
tethering of thioglycoside donors with a variety of simple aglycon alcohols, in the cases of more hindered carbohydrate alcohols where tethering occurred more slowly, limitations arose due to competitive activation of the anomeric leaving group. The use of an orthogonal anomeric leaving group which cannot be activated during tethering could provide a solution to this problem. Reported herein are full details of investigations into the use of glycosyl fluorides as donors for allyl mediated IAD [7].

Results and Discussion

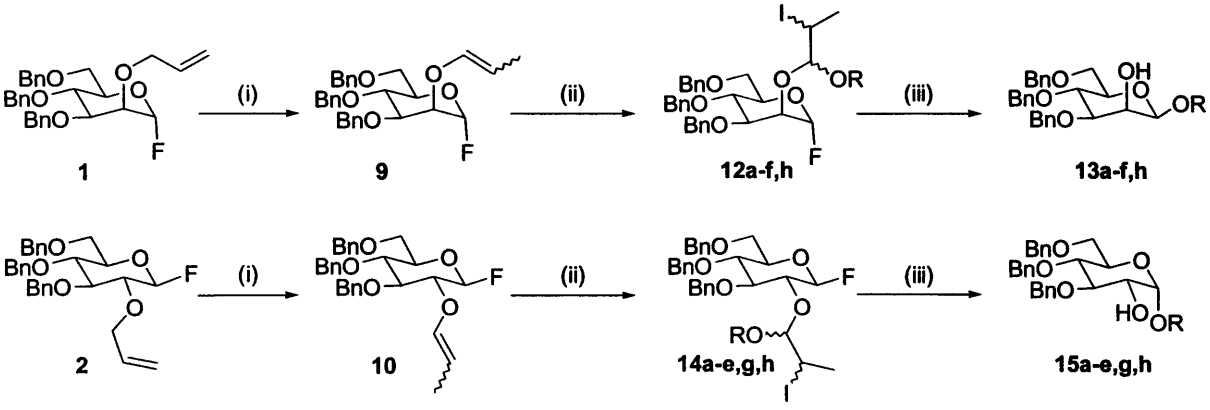
As substrates for IAD investigations the manno (**1**) and gluco glycosyl (**2**) fluorides bearing allyl protection of the 2-hydroxyl were prepared from their respective orthoesters. Thus, *DAST* opening of **3** [8] and **4** [9] followed by an *n*-propylamine mediated deacetylation of acetates **5** and **6** gave alcohols **7** and **8** [10]. Finally, reprotection of the 2-hydroxyl group by treatment with allyl bromide and sodium hydride in *DMF* furnished the desired donors **1** and **2** in excellent overall yields (**1**: 78% yield over three steps from **3**; **2**: 84% yield over three steps from **4**; Scheme 1).

The extremely efficient allyl isomerization following *Boons*' protocol [11] proceeded as smoothly as had been previously observed in the cases of 2-O-allyl protected thioglycosides [6]; thus, enol ethers **9** and **10** were furnished in excellent yields (96% and 98%, respectively; Scheme 2).

Studies then turned to an investigation of tethering reactions of **9** and **10** with a variety of aglycon alcohols. Previous work had demonstrated that N-iodosuccinimide (*NIS*) was a suitable reagent for this type of tethering reaction, whereas attempted acid catalyzed tethering had proved unsuccessful. Therefore, *NIS*-mediated tethering of the manno vinyl ether **9** was carried out with a variety of alcohols **11a–f,h** under our established reaction conditions [12]. Pleasingly, the desired mixed acetals **12a–f,h** were obtained in good to excellent yields (Table 1). The tethering yields for simple non-carbohydrate and primary carbohydrate alcohols are excellent. Also notable are the cases of the secondary carbohydrate alcohols **11e** and **11f** and the steroid **11h**, whereby longer reaction times and thus



Scheme 1. (i) *DAST*, *DCM*, 0°C; **5**: 98%, **6**: 84%; (ii) *n*-$PrNH_2$, MeOH, *THF*, 45°C; **7**: 83%, **8**: 91% from **4**; (iii) allyl bromide, NaH, *DMF*, 0°C; **1**: 96%, **2**: 93%



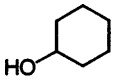
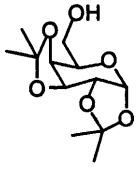
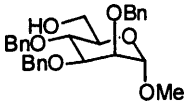
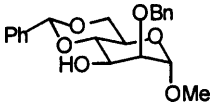
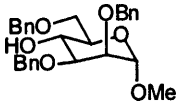
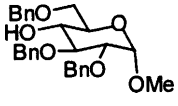
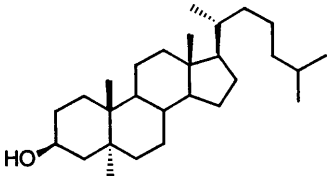
Scheme 2. (i) *Wilkinson*'s catalyst, BuLi, *THF*, 70°C; **9**: 96% from **1**, **10**: 98% from **2**; (ii) *R*OH **13a–h**, *NIS*, *DCE*, −40°C to r.t., 4 Å sieves; (iii) AgO*Tf*, *DTBMP*, $SnCl_2$, *DCE* or MeCN, 50°C; then *TFA*, H_2O or *NIS*, H_2O

more efficient tethering were possible than during previous studies on thioglycosides where competitive anomeric activation occurred. However, it should be noted that in the case of the more hindered alcohols **11d–f,h** an increasing amount of the succinimide trapped material **16** (Fig. 1) was also isolated. Formation of **16** occurs by competitive nucleophilic attack by succinimide rather than the desired alcohol, and therefore indicates a potential limitation of the use of *NIS* as tethering reagent in these cases.

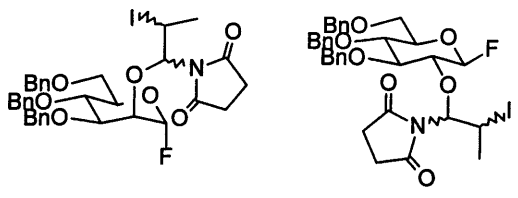
In the gluco series, tethering of enol ether **10** with alcohols **11a–e,g,h** proceeded likewise to give the mixed acetals **14a–e,g,h**. Whereas excellent yields were obtained for alcohols **11a–c**, slightly lower yields were observed than in the manno series for some of the more bulky carbohydrates **11d,e**. Overall it is clear that in general tethering is marginally less efficient in the gluco series. The steroid **11h** was only partially soluble in dichloroethane (*DCE*), but a change of the solvent to *THF* produced an acceptable 68% yield of mixed acetals **14h**. Again some succinimide trapped material, in the gluco series compound **17**, was observed in the cases of the more hindered alcohols.

Attention then turned to activation of the glycosyl fluorides and intramolecular glycosylation. Although activation of glycosyl fluorides can be carried out by the use of any number of different *Lewis* acids [13], in order to ensure complete stereoselectivity it is crucial that the mixed acetal tether, which itself could be susceptible to *Lewis* acid catalyzed cleavage, remains intact so that IAD can operate. Therefore, a series of several different reaction conditions often employed for the activation of glycosyl fluorides were investigated, including $Cp_2HfCl_2/AgClO_4/DTBMP$ [14], $BF_3 \cdot OEt_2$ [15], and $BF_3 \cdot OEt_2$/2,6-di-*tert*-butyl-4-methylpyridine (*DTBMP*). Whereas some of the desired products were usually observed, in these cases product formation was either accompanied by hydrolysis of the tether to various extents, the formation of α/β mixtures of products (presumably arising from intermolecular glycosylation following the hydrolysis of the tether), or occasionally the formation of an intractable mixture of products. Optimum results were obtained using the *Mukaiyama* activation

Table 1. Tethering and glycosylation yields

	Alcohol	Product/yield of mixed acetals[a]	Product/yield of glycosylation[c]
11a	MeOH	**12a**/97% **14a**/99%	**13a**/76%[e] **15a**/89%[e]
11b		**12b**/99% **14b**/99%	**13b**/70%[e] **15b**/66%[e]
11c		**12c**/98% **14c**/91%	**13c**/61%[d,f] **15c**/63%[d]
11d		**12d**/80% **14d**/79%	**13d**/49%,[e] 75%[d] **15d**/44%,[e] 46%[d]
11e		**12e**/83% **14e**/52%	**13e**/55%[d,f] **15e**/66%[d,g]
11f		**12f**/37%	**13f**/50%[d]
11g		**14g**/39%	**15g**/45%[d]
11h		**12h**/72% **14h**/68%[b]	**13h**/59%[d] **15h**/87%[d]

[a] Isolated yields; reactions carried out in *DCE* except where otherwise stated; [b] reaction carried out in *THF*; [c] isolated yields, acid treatment with *TFA* except where otherwise stated; [d] reaction carried out in *DCE*; [e] reaction carried out in acetonitrile; [f] no acid treatment; [g] treatment with *NIS*, H_2O



16 **17**

Fig. 1. Succinimide trapped materials

conditions [16], *i.e.* tin(II) chloride in combination with silver triflate, addition of the hindered base *DTBMP*, and heating to 50°C so that the reaction proceeded at an efficient rate. Under these conditions all mixed acetals furnished the desired β-mannosides **13a–f,h** and α-glucosides **15a–e,g,h** stereospecifically as the pure 1,2-*cis*-anomers in all cases in good to excellent yields (Table 1).

Two features of the intramolecular glycosylation reaction are worth mentioning. The first is that the efficiency of glycosylation is solvent dependent. For example, it was observed that whereas the glycosylation of the manno mixed acetals **12c** was slow in acetonitrile and occurred at the same time as partial hydrolysis of the tether, an otherwise identical experiment employing *DCE* as solvent proceeded very quickly (*ca.* 2 h) and without hydrolysis. Subsequent glycosylation reactions were therefore carried out with *DCE* as the solvent.

The second important feature worthy of special consideration is the potential formation of side-products by nucleophilic trapping of the oxonium ion produced subsequent to the intramolecular glycosylation reaction. Indeed the question as to the possible fate of this type of oxonium ion has recently arisen in the *Ogawa/Ito para*-methoxybenzyl (*PMB*) IAD system [17]. In our earlier work on thioglycosides [5], byproducts were observed after glycosylation that were identified as mixed acetals such as **18** (Fig. 2). These presumably arose from trapping of the oxonium ion produced subsequent to the glycosylation reaction by an external alcohol acting as a nucleophile. In the thioglycoside cases, treatment of the crude reaction mixture with trifluoroacetic acid (*TFA*) during work-up resulted in the hydrolysis of any such mixed acetals and in an increased the yield of the desired 1,2-*cis*-glycoside.

Analysis of the intramolecular glycosylation reactions of the tethered glycosyl fluorides by TLC revealed that varying amounts of byproducts were also sometimes produced. Interestingly, the formation of these byproducts was generally more prevalent in the gluco rather than the manno series. Treatment of these materials with *TFA* following the standard procedure developed earlier always yielded further 1,2-*cis*-glycoside product, but it was notable that by-product hydrolysis was much faster than had previously been observed in the thioglycoside work. Therefore, in the case of alcohol **11e**, which possesses an acid sensitive protecting group which could be cleaved by acid treatment, rather than adopting this acid work-up procedure in order to optimize the yield of disaccharide product, the identity of this by-product was investigated. Rather surprisingly, the minor byproducts were identified as the enol ethers **19** [18]. Treatment of these enol ethers **19** with *NIS*/H_2O proved an excellent alternative to the standard acidic work-up procedure since it rapidly resulted in the formation of the desired glycoside **15e**, without any cleavage of the acid sensitive 4,6-benzylidene protecting group (Scheme 3).

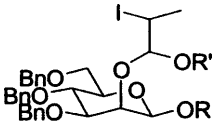


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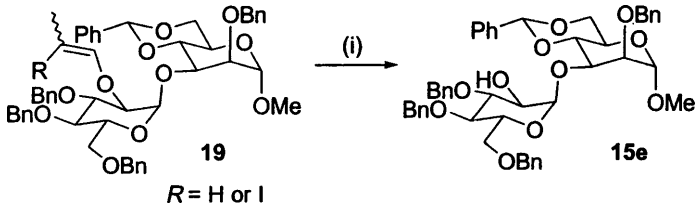
Fig. 2. Trapping after glycosylation



Scheme 3. (i) *NIS*, *THF*, H_2O; then Et_3N, $\sim 70\%$

In summary it has been demonstrated that glycosyl fluorides are excellent glycosyl donors for the allyl mediated IAD approach to 1,2-*cis*-glycosides, and that tethering and stereospecific intramolecular glycosylation may be achieved for a variety of primary and secondary carbohydrate alcohols. In particular, the use of glycosyl fluorides is advantageous in that tethering efficiency can be increased in the case of bulky secondary carbohydrate alcohols by the use of extended reaction times. Comparison with alternative methods of IAD indicates that allyl mediated IAD is superior to the original approaches of *Stork* and *Hindsgaul* in terms of both simplicity of application and yield and can therefore be considered as complementary to the *Ogawa PMB* approach. Although tethering is more efficient in the *PMB* system, the allyl system has the advantages that there is no requirement for cyclic 4,6-protection of the glycosyl donor in order to produce good yields for the glycosylation step and that the technique is also applicable for the formation of α-gluco linkages. The current disadvantages of allyl IAD are competitive trapping by succinimide during attempted tethering with the most hindered alcohol acceptors and the formation of mixed acetal or enol ether side products by further reaction of the oxonium ion produced after intramolecular glycosylation has occurred. 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

General

Melting points were recorded on a Kofler hot block and are uncorrected. Proton nuclear magnetic resonance spectra were recorded on Bruker DPX 400 (400 MHz) or Bruker AMX 500 (500 MHz) spectrometers. Carbon nuclear magnetic resonance spectra were recorded on Bruker AC 200 (50.3 MHz), Bruker DPX 400 (100.6 MHz), or Bruker AMX 500 (125.7 MHz) spectrometers. Multiplicities were assigned using the DEPT sequence. All chemical shifts are quoted on the δ-scale in ppm. Infrared spectra were recorded on a Perkin-Elmer 150 *Fourier* transform spectrophotometer. Low resolution mass spectra were recorded on a Micromass Platform 1 APCI using atmospheric pressure chemical ionisation (APCI). High resolution mass spectra (electrospray) were performed on a Waters 2790-Micromass LCT electrospray ionization mass spectrometer or by the EPSRC Mass Spectrometry Service Centre, Department of Chemistry, University of Wales, Swansea, on a MAT900 XLT electrospray ionization mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in $g/100\,cm^3$. Microanalyses were performed by the microanalytical services of Elemental Microanalysis Ltd, Devon; the results agreed with the calculated values within experimental error. 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* H_2SO_4. 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; MeOH was distilled from NaH, CH_3CN and CH_2Cl_2 were distilled from CaH_2, and *THF* was distilled from a solution of sodium benzophenone ketyl immediately before use. Anhydrous *DMF* and anhydrous dichloroethane (*DCE*) were purchased from Aldrich. Petrol refers to the fraction of light petroleum ether boiling in the range of 40–60°C. All procedures requiring anhydrous conditions were performed under an Ar atmosphere in glassware which was flame-dried before use.

2-O-Allyl-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**1**; $C_{30}H_{33}FO_5$)

Alcohol **7** (960 mg, 2.12 mmol) was dissolved in anhydrous *DMF* (5 cm^3) and cooled to 0°C. Allyl bromide (0.36 cm^3, 4.24 mmol) was added; then, NaH (60% in mineral oil, 170 mg, 4.24 mmol) was added portionwise. After 1 h, TLC (ethyl acetate:petrol = 1:3) indicated formation of a single product ($R_f = 0.5$) and complete consumption of starting material ($R_f = 0.2$). The reaction mixture was quenched with 100 cm^3 H_2O and extracted with 2 × 100 cm^3 CH_2Cl_2. 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 allylated glycosyl fluoride **1** (1.01 g, 96%) as a colourless oil.

$[\alpha]_D^{27} = +35.2$ ($c = 1.4$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.71$ (1H, dd, $J_{5,6} = 1.9$ Hz, $J_{6,6'} = 10.9$ Hz, H-6), 3.67 (1H, dd, $J_{5,6'} = 4.5$ Hz, H-6′), 3.84–3.85 (1H, m, H-2), 3.86–3.98 (2H, m, H-3, H-5), 4.02 (1H, at, $J = 9.5$ Hz, H-4), 4.17 (1H, dd, $J_{gem} = 13.1$ Hz, $J = 6.0$ Hz, OC*H*H′), 4.25 (1H, dd, $J = 5.7$ Hz, OCH*H*′), 4.51, 4.88 (2H, ABq, J_{AB} 10.8 Hz, $PhCH_2$), 4.54, 4.68 (2H, ABq, $J_{AB} = 12.3$ Hz, $PhCH_2$), 4.73 (2H, s, $PhCH_2$), 5.24 (1H, dd, $J_{gem} = 1.5$ Hz, $J_Z = 10.3$ Hz, $OCH_2CH{=}CH_EH_Z$), 5.31 (1H, dd, $J_E = 17.2$ Hz, $OCH_2CH{=}CH_EH_Z$), 5.64 (1H, dd, $J_{1,2} = 1.8$ Hz, $J_{1,F} = 50.6$ Hz, H-1), 5.93 (1H, ddat, $OCH_2CH{=}CH_2$), 7.16–7.41 (15H, m, Ar–H); ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 68.5$ (t, C-6), 72.6, 72.6 (2 × t, $PhCH_2$, $OCH_2CH{=}CH_2$), 73.3 (dd, $^2J_{C\text{-}2,F} = 35.3$ Hz, C-2), 73.4, 75.2 (2 × t, 2 × $PhCH_2$), 73.9 (d, C-4), 74.0 (d, C-5), 79.0 (d, C-3), 106.4 (dd, $^1J_{C\text{-}1,H\text{-}1} = 182.2$ Hz, $^1J_{C\text{-}1,F} = 222.6$ Hz, C-1), 118.1 (t, $OCH_2CH{=}CH_2$), 127.6, 127.7, 127.8, 127.9, 127.9, 128.1, 128.1, 128.3, 128.3, 128.5, 128.7 (11 × d, Ar–CH), 134.5 (d, $OCH_2CH{=}CH_2$), 138.0, 138.0, 138.1 (3 × s, Ar–C); ppm; MS (APCI$^+$): $m/z = 515$ ($M + Na^+$, 100%); HRMS: calcd. for $C_{30}H_{37}NO_5F$ (MNH_4^+): 510.2656, found: 510.2657.

2-O-Allyl-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**2**; $C_{30}H_{33}FO_5$)

Alcohol **8** (3.94 g, 8.70 mmol) was dissolved in anhydrous *DMF* (10 cm^3) and cooled to 0°C. Allyl bromide (1.5 cm^3, 17.4 mmol) was added; then, NaH (60% in mineral oil, 696 mg, 17.4 mmol) was added portionwise. After 1 h, TLC (ethyl acetate:petrol = 1:3) indicated formation of a single product ($R_f = 0.4$) and complete consumption of starting material ($R_f = 0.2$). The reaction was quenched with MeOH (6 cm^3) and concentrated *in vacuo*. The residue was partitioned between CH_2Cl_2 (2 × 100 cm^3) and H_2O (100 cm^3). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 6:1) to afford allylated glycosyl fluoride **2** (3.99 g, 93%) as a colourless oil.

$[\alpha]_D^{22} = +9.2$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.49$ (1H, ddd, $J_{1,2} = 6.9$ Hz, $J_{2,3} = 8.6$ Hz, $J_{2,F} = 12.3$ Hz, H-2), 3.59 (1H, ddd, $J_{4,5} = 9.5$ Hz, $J_{5,6} = 2.6$ Hz, $J_{5,6'} = 3.7$ Hz, H-5), 3.64 (1H, at, $J = 8.7$ Hz, H-3), 3.69–3.77 (3H, m, H-4, H-6, H-6′), 4.20 (1H, dd, $J_{gem} = 12.4$ Hz, $J = 5.8$ Hz, OC*H*H′), 4.34 (1H, dd, $J = 5.7$ Hz, OCH*H*′), 4.54, 4.93 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 4.55, 4.64 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.80, 4.93 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 5.21 (1H, dd, $J_{1,F} = 52.8$ Hz, H-1), 5.22 (1H, dd, $J_{gem} = 1.6$ Hz, $J_Z = 10.3$ Hz, $OCH_2CH{=}CH_EH_Z$), 5.32 (1H, dd, $J_E = 17.3$ Hz, $OCH_2CH{=}CH_EH_Z$), 5.95 (1H, ddt, $OCH_2CH{=}CH_2$), 7.14–7.38 (15H, m,

Ar–H) ppm; ^{13}C NMR δ_C ($CDCl_3$, 100 MHz): $\delta = 68.3$, 73.3, 73.5, 75.0, 75.5 ($5 \times$ t, $3 \times PhCH_2$, $OCH_2CH{=}CH_2$, C-6), 74.7, 76.8, 83.4 ($3 \times$ d, C-3, C-4, C-5), 81.2 (dd, $^2J_{C\text{-}2,F} = 21.5$ Hz, C-2), 109.7 (dd, $^1J_{C\text{-}1,F} = 215.5$ Hz, C-1), 117.6 (t, $OCH_2CH{=}CH_2$), 127.7, 127.8, 127.8, 127.9, 127.9, 128.4, 128.4 ($7 \times$ d, Ar–CH), 134.3 (d, $OCH_2CH{=}CH_2$), 137.8, 137.8, 138.2 ($3 \times$ s, Ar–C) ppm; MS (APCI$^+$): $m/z = 515$ ($M + Na^+$, 10%).

2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**5**; $C_{29}H_{31}FO_6$)

Orthoester **3** (16.7 g, 32.8 mmol) was dissolved in 80 cm^3 freshly distilled CH_2Cl_2. The mixture was cooled to 0°C, and (diethylamino)-sulfur trifluoride (*DAST*, 5.1 cm^3, 37.7 mmol) was added. The reaction mixture was stirred at 0°C. After 7 h, TLC (petrol:ethyl acetate = 3:1) indicated formation of a product ($R_f = 0.5$) and complete consumption of starting material ($R_f = 0.3$). The reaction was diluted with diethyl ether (200 cm^3) and then washed with H_2O (2×200 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 5:1, 1% Et_3N) to afford acetylated glycosyl fluoride **5** (15.8 g, 98%) as a pale yellow oil.

$[\alpha]_D^{23} = +13.3$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\nu = 1751$ (s, C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.17$ (3H, s, CH_3), 3.72 (1H, d, $J_{6,6'} = 10.9$ Hz, H-6), 3.82 (1H, dd, $J_{5,6'} = 2.7$ Hz, H-6′), 3.97–3.99 (3H, m, H-3, H-4, H-5), 4.49, 4.87 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.52, 4.69 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.57, 4.72 (2H, ABq, $J_{AB} = 10.9$ Hz, $PhCH_2$), 5.48 (1H, br s, H-2), 5.62 (1H, dd, $J_{1,2} = 1.9$ Hz, $J_{1,F} = 49.1$ Hz, H-1), 7.15–7.38 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 21.0$ (q, CH_3), 67.0 (dd, $^2J_{C\text{-}2,F} = 39.9$ Hz, C-2), 68.2 (t, C-6), 72.1, 73.5, 75.3 ($3 \times$ t, $3 \times PhCH_2$), 73.3 (d, C-4), 73.8 (dd, $^3J_{C\text{-}5,F} = 2.0$ Hz, C-5), 77.2 (d, C-3), 105.5 (dd, $^1J_{C\text{-}1,H} = 182.6$ Hz, $^1J_{C\text{-}1,F} = 221.0$ Hz, C-1), 127.8, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5 ($7 \times$ d, Ar–CH), 137.6, 138.0, 138.1 ($3 \times$ s, Ar–C), 170.1 (s, C=O) ppm; MS (APCI$^+$) = 517 ($M + Na^+$, 18%); HRMS: calcd. for $C_{29}H_{35}NO_6F$ (MNH_4^+): 512.2448, found: 512.2451.

2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**6**; $C_{29}H_{31}FO_6$)

Orthoester **4** (1.0 g, 1.92 mmol) was dissolved in 8 cm^3 freshly distilled CH_2Cl_2. The mixture was cooled to 0°C, and *DAST* (0.33 cm^3, 2.50 mmol) was added. The reaction mixture was stirred at 0°C. After 3.5 h, TLC (CH_2Cl_2: ether = 14:1) indicated formation of a product ($R_f = 0.8$) and complete consumption of starting material ($R_f = 0.7$). The reaction was quenched with ice-water (200 cm^3) and extracted with diethyl ether (2×200 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 4:1) to afford acetylated glycosyl fluoride **6** (796 mg, 84%) as a colourless oil.

$[\alpha]_D^{22} = +15.3$ ($c = 1.25$, $CHCl_3$); IR (thin film): $\nu = 1750$ (s, C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.02$ (3H, s, CH_3), 3.67–3.75 (4H, m, H-3, H-5, H-6, H-6′), 3.86 (1H, at, $J = 9.0$ Hz, H-4), 4.56, 4.78 (2H, ABq, $J_{AB} = 11.2$ Hz, $PhCH_2$), 4.56, 4.63 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.71, 4.78 (2H, ABq, $J_{AB} = 11.6$ Hz, $PhCH_2$), 5.09–5.15 (1H, m, H-2), 5.27 (1H, dd, $J_{1,2} = 6.1$ Hz, $J_{1,F} = 52.9$ Hz, H-1), 7.16–7.36 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 20.8$ (q, CH_3), 68.4, 73.6, 74.4, 74.9 ($4 \times$ t, C-6, $3 \times PhCH_2$), 72.5 (dd, C-2), 75.0, 81.5, 81.6 ($3 \times$ d, C-3, C-4, C-5), 106.7 (dd, C-1), 127.7, 127.8, 127.8, 127.9, 128.0, 128.4, 128.4, 128.9 ($8 \times$ d, Ar–CH), 137.6, 137.8 ($2 \times$ s, Ar–C), 169.4 (s, C=O) ppm; ^{19}F NMR ($CDCl_3$, 376 MHz): $\delta = -136.8$ (dd, $J_{1,F} = 52.9$ Hz, $J_{2,F} = 10.2$ Hz) ppm; MS (APCI$^+$): $m/z = 533$ ($M + K^+$, 100%), 517 ($M + Na^+$, 15%), 475 (M-F, 5%).

3,4,6-Tri-O-benzyl-α-D-mannopyranosyl fluoride (**7**; $C_{27}H_{29}FO_5$)

Acetate **5** (2.0 g, 4.04 mmol) was dissolved in MeOH (5 cm^3), *THF* (10 cm^3), and *n*-propylamine (5 cm^3), and the reaction mixture was stirred at 45°C. After 15 h, TLC (ethyl acetate:petrol = 1:3)

indicated formation of a product ($R_f = 0.2$) and complete consumption of starting material ($R_f = 0.4$). The mixture was concentrated *in vacuo* and purified by flash column chromatography (petrol:ethyl acetate = 3:1, 1% Et_3N) to afford alcohol **7** (1.56 g, 83%) as a colourless oil.

$[\alpha]_D^{23} = +34.2$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.70$ (1H, dd, $J_{5,6} = 1.6$ Hz, $J_{6,6'} = 10.8$ Hz, H-6), 3.78 (1H, dd, $J_{5,6'} = 3.5$ Hz, H-6′), 3.87–3.90 (1H, m, H-3), 3.94–3.96 (2H, m, H-4, H-5), 4.12–4.13 (1H, m, H-2), 4.54, 4.67 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.54, 4.83 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 4.71, 4.74 (2H, ABq, $J_{AB} = 11.4$ Hz, $PhCH_2$), 5.68 (1H, dd, $J_{1,2} = 1.7$ Hz, $J_{1,F} = 49.5$ Hz, H-1), 7.17–7.37 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 67.1$ (dd, $^2J_{C\text{-}2,F} = 39.0$ Hz, C-2), 68.2 (d, C-6), 72.4, 73.5, 75.2 (3 × t, 3 × $PhCH_2$), 73.2 (d, C-4), 73.4 (dd, $^3J_{C\text{-}5,F} = 2.7$ Hz, C-5), 79.1 (dd, $^3J_{C\text{-}3,F} = 1.8$ Hz, C-3), 107.2 (dd, $^1J_{C\text{-}1,H\text{-}1} = 181.9$ Hz, $^1J_{C\text{-}1,F} = 217.7$ Hz, C-1), 127.7, 127.8, 127.9, 127.9, 128.0, 128.1, 128.4, 128.6 (8 × d, Ar–CH), 137.6, 137.9, 138.0 (3 × s, Ar–C) ppm.

3,4,6-Tri-O-benzyl-β-D-glucopyranosyl fluoride (**8**; $C_{27}H_{29}FO_5$)

Orthoester **4** (5.00 g, 9.62 mmol) was dissolved in 20 cm^3 freshly distilled CH_2Cl_2 in a flame-dried flask, cooled to 0°C under Ar, and *DAST* (1.65 cm^3, 12.5 mmol) was added. After 7.5 h, TLC (ethyl acetate:petrol = 1:3) indicated formation of a product ($R_f = 0.45$) and complete consumption of starting material ($R_f = 0.5$). The reaction was quenched with water (200 cm^3) and extracted with diethyl ether (2 × 150 cm^3). The organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was dissolved in *THF* (10 cm^3), MeOH (5 cm^3), and *n*-propylamine (5 cm^3) and stirred at 45°C. After 16.5 h, TLC (ethyl acetate:petrol = 1:3) indicated formation of a single product ($R_f = 0.2$). The mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 4:1) to afford alcohol **8** (3.94 g, 91%) as a white crystalline solid.

M.p.: 84°C (diethyl ether/petrol; Ref. [10]: 80–82°C); $[\alpha]_D^{22} = +31.5$ ($c = 0.55$ in $CHCl_3$; Ref. [10]: $[\alpha]_D^{22} = +25.2$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.59$–3.80 (6H, m, H-2, H-3, H-4, H-5, H-6, H-6′), 4.54, 4.62 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.57, 4.78 (2H, ABq, $J_{AB} = 11.1$ Hz, $PhCH_2$), 4.81, 4.85 (2H, ABq, $J_{AB} = 11.5$ Hz, $PhCH_2$), 5.17 (1H, d, $J_{1,2} = 6.5$ Hz, $J_{1,F} = 53.0$ Hz, H-1), 7.17–7.40 (15H, m, Ar–H) ppm.

2-O-Prop-1′-enyl-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**9**; $C_{30}H_{33}FO_5$)

Wilkinson's catalyst (185 mg, 0.20 mmol) was dissolved in 4 cm^3 freshly distilled *THF*, and the solution was degassed. *n*-Butyllithium (1.6 *M* solution in hexanes, 0.19 cm^3, 0.30 mmol) was added, and the mixture was stirred for 1 h. Allylated mannosyl fluoride **1** (975 mg, 1.98 mmol) was dissolved in 4 cm^3 freshly distilled *THF* and heated to 70°C. The catalyst solution was added *via* a cannular under Ar. After 1 h, TLC (ethyl acetate:petrol = 1:3) indicated formation of a single product ($R_f = 0.51$) and complete consumption of starting material ($R_f = 0.49$). The reaction was allowed to cool, diluted with CH_2Cl_2 (20 cm^3), and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 6:1, 1% Et_3N) to afford vinyl ethers **9** (934 mg, 96%) as a pale yellow oil.

Partial data: ^{1}H NMR (400 MHz, $CDCl_3$): *Z*:*E* = 2.7:1; *E*-isomer: $\delta = 1.55$ (3H, dd, $J = 1.7$ Hz, $J = 6.8$ Hz, OCH=CHCH_3), 5.02 (1H, dq, $J_E = 12.4$ Hz, OCH=C*H*CH_3), 5.66 (1H, dd, $J_{1,2} = 1.9$ Hz, $J_{1,F} = 50.2$ Hz, H-1), 6.12 (1H, dq, OC*H*=$CHCH_3$) ppm; *Z*-isomer: $\delta = 1.63$ (3H, dd, $J = 1.6$ Hz, $J = 6.9$ Hz, OCH=CHCH_3), 5.62 (1H, dd, $J_{1,2} = 2.0$ Hz, $J_{1,F} = 50.5$ Hz, H-1), 5.97 (1H, dq, $J_Z = 6.0$ Hz, OC*H*=$CHCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): *E*-isomer: $\delta = 12.3$ (q, OCH=CH*C*H_3), 102.4 (d, OCH=*C*HCH_3), 105.6 (dd, $^1J_{C\text{-}1,F} = 221.7$ Hz, C-1), 145.5 (d, O*C*H=$CHCH_3$) ppm; *Z*-isomer: $\delta = 9.4$ (q, OCH=CH*C*H_3), 104.2 (d, OCH=*C*HCH_3), 106.1 (dd, $^1J_{C\text{-}1,F} = 220.7$ Hz, C-1), 144.5 (d, O*C*H=$CHCH_3$) ppm; MS (APCI$^+$): $m/z = 515$ ($M + Na^+$, 100%); HRMS: calcd. for $C_{30}H_{37}NO_5F$ (MNH_4^+): 510.2656, found: 510.2663.

2-O-Prop-1′-enyl-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**10**; $C_{30}H_{33}FO_5$)

Wilkinson's catalyst (390 mg, 0.42 mmol) was dissolved in 8 cm^3 freshly distilled *THF*, and the solution was degassed. *n*-Butyl lithium (1.6 *M* solution in hexanes, 0.4 cm^3, 0.63 mmol) was added, and the mixture was stirred for 1 h. Allylated glucosyl fluoride **2** (2.06 g, 4.19 mmol) was dissolved in 8 cm^3 freshly distilled *THF* and heated to 70°C. The catalyst solution was added *via* a cannular under Ar. After 45 min, the reaction was allowed to cool, diluted with 20 cm^3 CH_2Cl_2, and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol:ethyl acetate = 5:1, 1% Et_3N) to afford vinyl ethers **10** (2.02 g, 98%) as a pale yellow oil.

Partial data: ^{1}H NMR (400 MHz, $CDCl_3$): *E*:*Z* = 1:2.3; *E*-isomer: $\delta = 1.58$ (3H, dd, $J = 1.6$ Hz, $J = 7.0$ Hz, OCH=CHCH_3), 5.08 (1H, dq, $J_E = 12.2$ Hz, OCH=C*H*CH_3), 5.23 (1H, dd, $J_{1,2} = 6.3$ Hz, $J_{1,F} = 52.5$ Hz, H-1), 6.23 (1H, d, OC*H*=$CHCH_3$) ppm; *Z*-isomer: $\delta = 1.65$ (3H, dd, $J = 1.7$ Hz, $J = 6.8$ Hz, OCH=CHCH_3), 4.51 (1H, aquin, $J = 6.6$ Hz, OCH=C*H*CH_3), 5.25 (1H, m, $J_{1,2} = 6.4$ Hz, $J_{1,F} = 52.7$ Hz, H-1), 6.16 (1H, dd, $J_Z = 6.1$ Hz, OC*H*=$CHCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): *E*-isomer: $\delta = 12.2$ (q, OCH=CH*C*H_3), 102.1 (d, OCH=*C*HCH_3), 108.4 (dd, $^1J_{C\text{-}1,F} = 217.0$ Hz, C-1), 146.4 (d, O*C*H=$CHCH_3$) ppm; *Z*-isomer: $\delta = 9.3$ (q, OCH=CH*C*H_3), 101.5 (d, OCH=*C*HCH_3), 108.5 (dd, $^1J_{C\text{-}1,F} = 213.3$ Hz, C-1), 145.6 (d, O*C*H=$CHCH_3$) ppm; MS (ES^+): $m/z = 510$ ($M + NH_4^+$, 100%); HRMS: calcd. for $C_{30}H_{37}NO_5F$ (MNH_4^+): 510.2656, found: 510.2663.

General procedure for NIS mediated tethering

NIS (3 equiv.) and powdered molecular sieves (4 Å) were stirred in 1 cm^3 dry *DCE* under Ar at −40°C. The alcohol (1.5–3 equiv.) was added *via* a cannular under Ar in 1.5 cm^3 dry *DCE*. The vinyl ether (0.1 mmol) was added *via* a cannular under Ar in 1.5 cm^3 dry *DCE*, and the mixture was allowed to warm slowly to room temperature. After 1–24 h, the mixture was diluted with *DCM*, washed with aqueous $Na_2S_2O_3$ solution, dried, filtered and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography to give the mixed acetals.

2-O-(2-Iodo-1-methoxypropyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12a**; $C_{31}H_{36}FIO_6$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11a** (0.010 ml, 0.24 mmol) gave mixed acetals **12a** (102 mg, 97%) as a colourless oil; MS ($APCI^+$): $m/z = 673$ ($M + Na^+$, 15%).

2-O-(1-Cyclohexyloxy-2-iodopropyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12b**; $C_{36}H_{44}FIO_6$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11b** (0.034 cm^3, 0.33 mmol) gave mixed acetals **12b** (115 mg, 99%) as a colourless oil; MS ($APCI^+$): $m/z = 741$ ($M + Na^+$, 5%).

2-O-(1-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-O-yl)-2-iodopropyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12c**; $C_{42}H_{52}FIO_{11}$)

Vinyl ethers **9** (178 mg, 0.36 mmol), *NIS* (243 mg, 1.1 mmol), and **11c** (212 mg, 0.82 mmol) gave mixed acetals **12c** (311 mg, 98%) as a colourless oil; MS (ES^+): $m/z = 917$ ($M + K^+$, 25%), 901 ($M + Na^+$, 100%), 896 ($M + NH_4^+$, 32%).

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-α-D-mannopyranosyl fluoride (**12d**; $C_{58}H_{64}FIO_{11}$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11d** (151 mg, 0.33 mmol) gave mixed acetals **12d** (140 mg, 80%) as a colourless oil; MS ($APCI^-$): $m/z = 1117$ ($M + Cl^-$, 92%).

2-O-(2-Iodo-1-(methyl 2-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosid-3-O-yl)-propyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12e**; $C_{51}H_{56}FIO_{11}$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11e** (121 mg, 0.33 mmol) gave mixed acetals **12e** (134 mg, 83%) as a colourless oil; MS (APCI$^-$): $m/z = 1025$ (M + Cl$^-$, 15%).

2-O-(2-Iodo-1-(methyl 2,3,6-tri-O-benzyl-α-D-mannopyranosid-4-O-yl)-propyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12f**; $C_{58}H_{64}FIO_{11}$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11f** (226 mg, 0.49 mmol) gave mixed acetals **12f** (65 mg, 37%) as a colourless oil; MS (APCI$^-$): $m/z = 1117$ (M + Cl$^-$, 8%).

2-O-(1-(Cholestan-3-β-yloxy)-2-iodopropyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**12h**; $C_{57}H_{80}FIO_6$)

Vinyl ethers **9** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11h** (136 mg, 0.33 mmol) gave mixed acetals **12h** (118 mg, 72%) as a colourless oil; MS (APCI$^-$): $m/z = 1041$ (M + Cl$^-$, 18%).

General procedure for intramolecular glycosylation

2,6-Di-*tert*-butyl-4-methylpyridine (*DTBMP*, 2 equiv.), silver triflate (2 equiv.), anhydrous tin(II) chloride (2 equiv.), and powdered molecular sieves (4 Å) were stirred in 1 cm^3 dry *DCE* under Ar at 50°C. The mixed acetals (0.1 mmol) were added *via* a cannular under argon in 3 cm^3 dry *DCE*, and the reaction was stirred at 50°C until TLC indicated disappearance of starting material. *TFA* (2 cm^3) and H_2O (1 cm^3) were added, and the solution was stirred for further 30 min. Diethyl ether was added, and the mixture filtered through Celite®, washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography to give the pure 1,2-*cis*-glycoside.

Methyl 3,4,6-tri-O-benzyl-β-D-mannopyranoside (**13a**; $C_{28}H_{32}O_6$)

Mixed acetals **12a** (102 mg, 0.157 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (64 mg, 0.314 mmol), silver trifluoromethanesulfonate (81 mg, 0.314 mmol), and anhydrous tin(II) chloride (60 mg, 0.314 mmol) gave β-mannoside **13a** (55 mg, 76%) as a colourless oil.

$[\alpha]_D^{24} = -13$ ($c = 0.75$, $CHCl_3$; Ref. [4]: $[\alpha]_D = -13$ ($c = 1.0$, $CHCl_3$)); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.47$ (1H, ddd, $J_{4,5} = 9.5$ Hz, $J_{5,6} = 5.0$ Hz, $J_{5,6'} = 1.3$ Hz, H-5), 3.57 (3H, s, OCH_3), 3.57–3.60 (1H, m, H-3), 3.74 (1H, dd, $J_{6,6'} = 10.8$ Hz, H-6), 3.80 (1H, dd, H-6′), 3.88 (1H, at, $J = 9.4$ Hz, H-4), 4.11 (1H, d, $J_{2,3} = 3.0$ Hz, H-2), 4.35 (1H, s, H-1), 4.55, 4.90 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 4.58, 4.65 (2H, ABq, $J_{AB} = 12.3$ Hz, $PhCH_2$), 4.69, 4.78 (2H, ABq, $J_{AB} = 11.7$ Hz, $PhCH_2$), 7.22–7.40 (15H, m, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $^1J_{C\text{-}1,H\text{-}1} = 156.7$ Hz.

Cyclohexyl 3,4,6-tri-O-benzyl-β-D-mannopyranoside (**13b**; $C_{33}H_{40}O_6$)

Mixed acetals **12b** (112 mg, 0.156 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (64 mg, 0.312 mmol), silver trifluoromethanesulfonate (80 mg, 0.312 mmol), and anhydrous tin(II) chloride (59 mg, 0.312 mmol) gave β-mannoside **13b** (50 mg, 60% plus a further 8 mg (10%) by subsequent acid treatment of the combined minor products; overall yield: 58 mg, 70%) as a colourless oil.

$[\alpha]_D^{24} = -20$ ($c = 0.4$, $CHCl_3$; Ref. [4]: $[\alpha]_D = -19$ ($c = 1.6$, $CHCl_3$)); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.20$–2.02 (10H, m, cyclohexyl-H), 2.50 (1H, br s, OH-2), 3.43–3.45 (1H, m, H-5), 3.58 (1H, br d, $J_{3,4} = 8.6$ Hz, H-3), 3.61–3.81 (3H, m, H-6, H-6′, OCH), 3.86 (1H, at, $J = 9.3$ Hz, H-4),

4.08 (1H, br s, H-2), 4.56 (1H, s, H-1), 4.58, 4.63 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.58, 4.91 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.69, 4.80 (2H, ABq, $J_{AB} = 11.7$ Hz, $PhCH_2$), 7.23–7.41 (15H, m, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $^1J_{C\text{-}1,H\text{-}1} = 155.3$ Hz.

3,4,6-Tri-O-benzyl-β-D-mannopyranosyl-(1 → 6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**13c**; $C_{39}H_{48}O_{11}$)

Mixed acetals **12c** (124 mg, 0.14 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (57 mg, 0.28 mmol), silver trifluoromethanesulfonate (72 mg, 0.28 mmol), and anhydrous tin(II) chloride (53 mg, 0.28 mmol) gave β-manno disaccharide **13c** (60 mg, 61%) as a colourless oil.

$[\alpha]_D^{22} = -50.7$ ($c = 0.55$, $CHCl_3$; Ref. [4]: $[\alpha]_D = -53$ ($c = 1.3$, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.32$, 1.34, 1.44, 1.54 (12H, 4 × s, 4 × CH_3), 3.42 (1H, ddd, $J_{4,5} = 9.8$ Hz, $J_{5,6} = 2.2$ Hz, $J_{5,6'} = 4.6$ Hz, H-5_b), 3.56 (1H, dd, $J_{2,3} = 3.1$ Hz, $J_{3,4} = 9.2$ Hz, H-3_b), 3.70–3.78 (3H, m, H-6_a, H-6_b, H-$6'_b$), 3.92 (1H, at, $J = 9.5$ Hz, H-4_b), 4.03 (1H, dat, $J = 2.2$ Hz, $J_{5,6} = 7.8$ Hz, H-5_a), 4.13 (1H, dd, $J_{5,6'} = 2.7$ Hz, $J_{6,6'} = 11.2$ Hz, H-$6'_a$), 4.22 (1H, dd, $J_{3,4} = 7.9$ Hz, $J_{4,5} = 1.9$ Hz, H-4_a), 4.22 (1H, d, H-2_b), 4.32 (1H, dd, $J_{1,2} = 5.0$ Hz, $J_{2,3} = 2.4$ Hz, H-2_a), 4.5 (1H, s, H-1_b), 4.52, 4.90 (2H, ABq, J_{AB} 10.8 Hz, $PhCH_2$), 4.54, 4.64 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.60 (1H, dd, H-3_a), 4.66, 4.78 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 5.55 (1H, d, H-1_a), 7.18–7.39 (15H, m, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $^1J_{C\text{-}1b,H\text{-}1b} = 160.0$ Hz.

Methyl 3,4,6-tri-O-benzyl-β-D-mannopyranosyl-(1 → 6)-2,3,4-tri-O-benzyl-α-D-mannopyranoside (**13d**; $C_{55}H_{60}O_{11}$)

Mixed acetals **12d** (136 mg, 0.126 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (52 mg, 0.25 mmol), silver trifluoromethanesulfonate (65 mg, 0.312 mmol), and anhydrous tin(II) chloride (48 mg, 0.312 mmol) gave β-manno disaccharide **13d** (125 mg, 75%) as a colourless oil.

$[\alpha]_D^{24} = +16.0$ ($c = 1.1$ in $CHCl_3$; Ref. [2]: $[\alpha]_D = +16.5$ ($c = 1.0$, $CHCl_3$)); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.30$ (3H, s, CH_3), 3.40 (1H, ddd, $J_{4,5} = 9.7$ Hz, $J_{5,6} = 4.7$ Hz, $J_{5,6'} = 2.4$ Hz, H-5_b), 3.52 (1H, dd, $J_{2,3} = 3.0$ Hz, $J_{3,4} = 9.2$ Hz, H-3_b), 3.70–3.76 (3H, m, H-6_b, H-$6'_b$, H-6_a), 3.78–3.81 (3H, m, H-2_a, H-4_a, H-5_a), 3.90–3.92 (1H, m, H-3_a), 3.92 (1H, at, $J = 9.4$ Hz, H-4_b), 4.06 (1H, d, H-2_b), 4.23 (1H, dd, $J_{6,6'} = 10.0$ Hz, H-$6'_a$), 4.37 (1H, s, H-1_b), 4.56, 4.93 (2H, ABq, $J_{AB} = 11.4$ Hz, $PhCH_2$), 4.56, 4.63 (2H, ABq, $J_{AB} = 13.0$ Hz, $PhCH_2$), 4.57, 4.91 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 4.62 (2H, s, $PhCH_2$), 4.69, 4.79 (2H, ABq, $J_{AB} = 12.3$ Hz, $PhCH_2$), 4.71, 4.76 (2H, ABq, $J_{AB} = 12.7$ Hz, $PhCH_2$), 4.72 (1H, d, $J_{1,2} = 1.7$ Hz, H-1_a), 7.22–7.41 (30H, m, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $^1J_{C\text{-}1b,H\text{-}1b} = 157.9$ Hz.

Methyl 3,4,6-tri-O-benzyl-β-D-mannopyranosyl-(1 → 3)-2-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside (**13e**; $C_{48}H_{52}O_{11}$)

Mixed acetals **12e** (126 mg, 0.127 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (52 mg, 0.25 mmol), silver trifluoromethanesulfonate (65 mg, 0.25 mmol), and anhydrous tin(II) chloride (48 mg, 0.25 mmol) gave β-manno disaccharide **13e** (56 mg, 55%) as a colourless oil.

$[\alpha]_D^{22} = +5.1$ ($c = 0.35$, $CHCl_3$); IR (thin film): $\nu = 3479$ (br, OH) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.27$ (1H, dt, $J_{4,5} = 9.6$ Hz, $J_{5,6} = 3.5$ Hz, H-5_b), 3.32 (3H, s, OCH_3), 3.39 (1H, dd, $J_{2,3} = 3.1$ Hz, $J_{3,4} = 9.0$ Hz, H-3_b), 3.70 (2H, d, H-6_b, H-$6'_b$), 3.79–3.87 (3H, m, H-2_a, H-5_a, H-6_a), 3.89 (1H, at, $J = 9.1$ Hz, H-4_b), 3.94 (1H, d, H-2_b), 4.19 (1H, at, $J = 9.7$ Hz, H-4_a), 4.26 (1H, s, H-1_b), 4.28 (1H, dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 9.6$ Hz, H-$6'_a$), 4.49, 4.58 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.49 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 10.2$ Hz, H-3_a), 4.55, 4.87 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 4.62, 4.77 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.63, 4.73 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.77 (1H, d, $J_{1,2} = 1.4$ Hz, H-1_a), 5.61 (1H, s, PhCH), 7.21–7.49 (25H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$,

100 MHz): $\delta = 54.9$ (q, OCH_3), 64.0, 68.4, 71.8, 74.0, 75.1, 75.9, 77.2, 80.8 (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), 68.8, 68.9, 71.1, 73.0, 73.5, 75.1 (6 × t, C-6_b, C-6_a, 4 × $PhCH_2$), 96.4 (d, $^1J_{C\text{-}1,H\text{-}1} = 158.9$ Hz, C-1_b), 99.7 (d, $^1J_{C\text{-}1,H\text{-}1} = 168.6$ Hz, C-1_a), 101.8 (d, PhCH), 126.0, 127.4, 127.6, 127.7, 127.7, 127.8, 128.0, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4, 128.4, 129.0 (15 × d, Ar–CH), 137.3, 137.6, 138.1, 138.3, 138.5 (5 × s, Ar–C); MS ($APCI^-$): $m/z = 839$ ($M + Cl^-$, 100%); MS (ES^+): $m/z = 822$ ($M + NH_4^+$, 100%); HRMS: calcd. for $C_{48}H_{56}NO_{11}$ (MNH_4^+): 822.3853, found: 822.3864.

Methyl 3,4,6-tri-O-benzyl-β-D-mannopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-α-D-mannopyranoside (**13f**; $C_{55}H_{60}O_{11}$)

Mixed acetals **12f** (65 mg, 0.06 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (25 mg, 0.12 mmol), silver trifluoromethanesulfonate (31 mg, 0.12 mmol), and anhydrous tin(II) chloride (23 mg, 0.12 mmol) gave β-manno disaccharide **13f** (27 mg, 50%) as a colourless oil.

$[\alpha]_D^{22} = +21.4$ ($c = 0.35$, $CHCl_3$); IR (thin film): $\nu = 3416$ (br, OH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.29$ (1H, ddd, $J_{4,5} = 9.7$ Hz, $J_{5,6} = 2.2$ Hz, $J_{5,6'} = 4.5$ Hz, H-5_b), 3.34 (3H, s, OCH_3), 3.39 (1H, dd, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.2$ Hz, H-3_b), 3.62 (1H, dd, $J_{6,6'} = 11.2$ Hz, H-6_b), 3.65 (1H, dd, H-$6'_b$), 3.75–3.80 (3H, m, H-2_a, H-5_a, H-6_a), 3.86 (1H, at, $J = 9.5$ Hz, H-4_b), 3.88 (1H, dd, $J_{5,6'} = 3.7$ Hz, $J_{6,6'} = 11.0$ Hz, H-$6'_a$), 3.97 (1H, dd, $J_{2,3} = 3.2$ Hz, H-3_a), 4.01 (1H, d, H-2_b), 4.32 (1H, at, $J = 9.2$ Hz, H-4_a), 4.43, 4.56 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.48, 4.54 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.51, 4.86 (2H, ABq, $J_{AB} = 11.1$ Hz, $PhCH_2$), 4.57, 4.71 (2H, ABq, $J_{AB} = 11.7$ Hz, $PhCH_2$), 4.59, 4.70 (2H, ABq, $J_{AB} = 11.8$ Hz, $PhCH_2$), 4.68, 4.72 (2H, ABq, $J_{AB} = 12.9$ Hz, $PhCH_2$), 4.69 (1H, s, H-1_b), 4.77 (1H, d, $J_{1,2} = 1.9$ Hz, H-1_a), 7.19–7.36 (30H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 54.7$ (q, OCH_3), 67.4 (d, C-2_b), 69.0 (t, C-6_b), 69.4 (t, C-6_a), 70.9 (d, C-5_a), 70.8, 72.2, 72.5, 73.2, 73.3, 75.0 (6 × t, 6 × $PhCH_2$), 72.9 (d, C-4_a), 73.8 (d, C-4_b), 74.8 (d, C-2_a), 75.5 (d, C-5_b), 79.0 (d, C-3_a), 81.8 (d, C-3_b), 98.9 (d, $^1J_{C\text{-}1,H\text{-}1} = 172.5$ Hz, C-1_a), 100.0 (d, $^1J_{C\text{-}1,H\text{-}1} = 161.5$ Hz, C-1_b), 127.3, 127.4, 127.4, 127.5, 127.5, 127.5, 127.5, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 128.2 (14 × d, Ar–CH), 137.9, 138.1, 138.2, 138.2, 138.3, 138.4 (6 × s, Ar–C) ppm; MS ($APCI^-$): $m/z = 931$ ($M + Cl^-$, 100%); MS (ES^+): $m/z = 914$ ($M + NH_4^+$, 100%); HRMS: calcd. for $C_{55}H_{64}NO_{11}$ (MNH_4^+): 914.4479, found: 914.4473.

Cholestan-3′-β-yl 3,4,6-tri-O-benzyl-β-D-mannopyranoside (**13h**; $C_{54}H_{76}O_6$)

Mixed acetals **12h** (121 mg, 0.12 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (49 mg, 0.24 mmol), silver trifluoromethanesulfonate (61 mg, 0.24 mmol), and anhydrous tin(II) chloride (46 mg, 0.24 mmol) gave β-mannoside **13h** (58 mg, 59%) as colourless crystals.

M.p.: 100–102°C (EtOH); $[\alpha]_D^{24} = -4.9$ ($c = 0.75$, $CHCl_3$); IR (thin film): $\nu = 3435$ (br, OH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.58$–2.00 (31H, m, steroid CH, CH_2), 0.66, 0.81 (6H, 2 × s, 2 × CH_3), 0.87 (3H, d, $J = 6.6$ Hz, CH_3), 0.88 (3H, d, $J = 6.8$ Hz, CH_3), 0.91 (3H, d, $J = 6.5$ Hz, CH_3), 2.11 (1H, br s, OH-2), 3.43 (1H, ddd, $J_{4,5} = 9.7$ Hz, $J_{5,6} = 5.6$ Hz, $J_{5,6'} = 1.9$ Hz, H-5), 3.57 (1H, dd, $J_{2,3} = 3.2$ Hz, $J_{3,4} = 9.1$ Hz, H-3), 3.69 (1H, dd, $J_{6,6'} = 10.7$ Hz, H-6), 3.70–3.77 (1H, m, steroid OCH), 3.80 (1H, dd, H-6′), 3.84 (1H, at, $J = 9.3$ Hz, H-4), 4.06 (1H, d, H-2), 4.56, 4.91 (2H, ABq, $J_{AB} = 10.9$ Hz, $PhCH_2$), 4.57 (1H, s, H-1), 4.58, 4.63 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.68, 4.79 (2H, ABq, $J_{AB} = 11.9$ Hz, $PhCH_2$), 7.21–7.40 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 12.0$, 12.2, 18.7, 22.5, 22.8 (5 × q, 5 × steroid CH_3), 21.2, 23.8, 24.2, 28.2, 28.8, 29.2, 32.1, 34.2, 36.2, 37.0, 39.5, 40.0 (12 × t, 12 × steroid CH_2), 28.0, 35.6, 35.8, 44.6, 54.4, 56.2, 56.5 (7 × d, 7 × steroid CH), 35.4, 42.6 (2 × s, 2 × steroid C), 68.8 (d, C-2), 69.4 (t, C-6), 71.3, 73.4, 75.2 (3 × t, 3 × $PhCH_2$), 74.3 (d, C-4), 75.1 (d, C-5), 77.5 (d, steroid OCH), 81.7 (d, C-3), 97.2 (d, $^1J_{C\text{-}1,H\text{-}1} = 155.6$ Hz, C-1), 127.5, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5 (8 × d, Ar–CH), 137.9, 138.2, 138.3 (3 × s, Ar–C) ppm.

2-O-(2-Iodo-1-methoxypropyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14a**; $C_{31}H_{36}FIO_6$)

Vinyl ethers **10** (300 mg, 0.61 mmol), *NIS* (410 mg, 1.83 mmol), and **11a** (0.037 cm^3, 0.92 mmol) gave mixed acetals **14a** (399 mg, >99%) as a colourless oil; MS (APCI$^+$): $m/z = 673$ ($M + Na^+$, 15%).

2-O-(1-Cyclohexyloxy-2-iodopropyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14b**; $C_{36}H_{44}FIO_6$)

Vinyl ethers **10** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11b** (0.034 cm^3, 0.33 mmol) gave mixed acetals **14b** (116 mg, 99%) as a colourless oil; MS (APCI$^+$): $m/z = 741$ ($M + Na^+$, 5%).

2-O-(1-(1,2:3,4-Di-O-isopropylidene-D-galactopyranos-6-O-yl)-2-iodopropyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14c**; $C_{42}H_{52}FIO_{11}$)

Vinyl ethers **10** (80 mg, 0.36 mmol), *NIS* (109 mg, 0.49 mmol), **11c** (84 mg, 0.82 mmol) gave mixed acetals **14c** (130 mg, 91%) as a colourless oil; MS (APCI$^-$): $m/z = 913$ ($M + Cl^-$, 4%); MS (APCI$^+$): $m/z = 901$ ($M + Na^+$, 5%).

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-β-D-glucopyranosyl fluoride (**14d**; $C_{58}H_{64}FIO_{11}$)

Vinyl ethers **10** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11d** (151 mg, 0.33 mmol) gave mixed acetals **14d** (139 mg, 79%) as a colourless oil; MS (APCI$^-$): $m/z = 1117$ ($M + Cl^-$, 92%).

2-O-(2-Iodo-1-(methyl 2-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosid-3-O-yl)propyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14e**; $C_{51}H_{56}FIO_{11}$)

Vinyl ethers **10** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11e** (121 mg, 0.33 mmol) gave mixed acetals **14e** (83 mg, 52%) as a colourless oil; MS (ES$^+$): $m/z = 1029$ ($M + K^+$, 74%), 1013 ($M + Na^+$, 100%), 1008 ($M + NH_4^+$, 15%).

2-O-(2-Iodo-1-(methyl 2,3,6-tri-O-benzyl-α-D-glucopyranosid-4-O-yl)propyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14g**; $C_{58}H_{65}FIO_{11}$)

Vinyl ethers **10** (80 mg, 0.16 mmol), *NIS* (109 mg, 0.49 mmol), and **11g** (221 mg, 0.48 mmol) gave mixed acetals **14g** (69 mg, 39%) as a colourless oil; MS (ES$^+$): $m/z = 1121$ ($M + K^+$, 22%), 1105 ($M + Na^+$, 100%), 1100 ($M + NH_4^+$, 21%).

2-O-(1-(Cholestan-3-β-yloxy)-2-iodopropyl)-3,4,6-tri-O-benzyl-β-D-glucopyranosyl fluoride (**14h**; $C_{57}H_{80}FIO_6$)

Vinyl ethers **10** (71 mg, 0.13 mmol), *NIS* (103 mg, 0.40 mmol), and **11h** (84 mg, 0.82 mmol) in *THF* (3 cm^3) gave mixed acetals **14h** (99 mg, 68%) as a colourless oil; MS (ES$^+$): $m/z = 1045$ ($M + K^+$, 100%), 1029 ($M + Na^+$, 90%).

Methyl 3,4,6-tri-O-benzyl-α-D-glucopyranoside (**15a**; $C_{28}H_{32}O_6$)

Mixed acetals **14a** (77 mg, 0.118 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (48 mg, 0.236 mmol), silver trifluoromethanesulfonate (61 mg, 0.236 mmol), and anhydrous tin(II) chloride (45 mg,

0.236 mmol) gave α-methyl glucoside **15a** (49 mg, 89%) as a white solid which was recrystallized from diethyl ether/petrol.

M.p.: 78–81°C (diethyl ether/petrol; Ref. [4]: 83–84°C); $[\alpha]_D^{22} = +70.8$ ($c = 1.2$, $CHCl_3$; Ref. [4]: $[\alpha]_D = +90$ ($c = 1.1$, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.11$ (1H, d, $J_{OH,2} = 7.4$ Hz, OH-2), 3.40 (3H, s, OCH_3), 3.60–3.76 (6H, m, H-2, H-3, H-4, H-5, H-6, H-6′), 4.47, 4.79 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.49, 4.62 (2H, ABq, $J_{AB} = 12.1$ Hz, $PhCH_2$), 4.78 (1H, d, $J_{1,2} = 3.2$ Hz, H-1), 4.83, 4.88 (2H, ABq, $J_{AB} = 11.2$ Hz, $PhCH_2$), 7.11–7.36 (15H, m, Ar–H) ppm.

Cyclohexyl 3,4,6-tri-O-benzyl-α-D-glucopyranoside (**15b**; $C_{33}H_{40}O_6$)

Mixed acetals **14b** (77 mg, 0.118 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (65 mg, 0.318 mmol), silver trifluoromethanesulfonate (82 mg, 0.318 mmol), and anhydrous tin(II) chloride (60 mg, 0.318 mmol) gave α-glucoside **15b** (56 mg, 66%) as a white solid which was recrystallized from diethyl ether/petrol.

M.p.: 92–94°C (diethyl ether/petrol); $[\alpha]_D^{22} = +90.0$ ($c = 0.3$, $CHCl_3$; Ref. [4]: $[\alpha]_D = +60$ ($c = 0.6$, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.24$–1.92 (10H, m, cyclohexyl-H), 2.06 (1H, d, $J = 2.7$ Hz, OH-2), 3.61–3.75 (5H, m, H-2, H-3, H-4, H-6, cyclohexyl OCH), 3.77 (1H, dd, $J_{5,6'} = 3.9$ Hz, $J_{6,6'} = 10.7$ Hz, H-6′), 3.87–3.90 (1H, m, H-5), 4.49, 4.83 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.51, 4.65 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.84, 4.99 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 5.03 (1H, d, $J_{1,2} = 3.5$ Hz, H-1), 7.14–7.42 (15H, m, Ar–H) ppm.

3,4,6-Tri-O-benzyl-α-D-glucopyranosyl-(1 → 6)-1,2:3,4-di-O-isopropylidene-D-galactopyranose (**15c**; $C_{39}H_{48}O_{11}$)

Mixed acetals **14c** (124 mg, 0.14 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (58 mg, 0.28 mmol), silver trifluoromethanesulfonate (73 mg, 0.28 mmol), and anhydrous tin(II) chloride (54 mg, 0.28 mmol) gave α-gluco disaccharide **15c** (62 mg, 63%) as a colourless oil.

$[\alpha]_D^{22} = +27.7$ ($c = 0.35$, $CHCl_3$; Ref. [4]: $[\alpha]_D = +29$ ($c = 0.9$, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.34, 1.35, 1.45, 1.54$ (12H, $4 \times$ s, $4 \times CH_3$), 3.63–3.79 (6H, m, H-2_b, H-3_b, H-4_b, H-6_b, H-$6'_b$, H-6_a), 3.85 (1H, ddd, $J_{4,5} = 9.9$ Hz, $J_{5,6} = 2.2$ Hz, $J_{5,6'} = 3.0$ Hz, H-5_b), 3.91 (1H, dd, $J_{5,6'} = 6.7$ Hz, $J_{6,6'} = 10.2$ Hz, H-$6'_a$), 4.00 (1H, atd, $J = 6.7$ Hz, $J_{4,5} = 1.9$ Hz, H-5_a), 4.25 (1H, dd, $J_{3,4} = 7.8$ Hz, H-4_a), 4.34 (1H, dd, $J_{1,2} = 4.9$ Hz, $J_{2,3} = 2.2$ Hz, H-2_a), 4.49, 4.83 (2H, ABq, $J_{AB} = 10.3$ Hz, $PhCH_2$), 4.50, 4.64 (2H, ABq, $J_{AB} = 11.7$ Hz, $PhCH_2$), 4.63 (1H, dd, H-3_a), 4.82, 4.98 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.93 (1H, d, H-1_b), 5.53 (1H, d, H-1_a), 7.12–7.41 (15H, m, Ar–H) ppm.

Methyl 3,4,6-tri-O-benzyl-α-D-glucopyranosyl-(1 → 6)-3,4,6-tri-O-benzyl-α-D-mannopyranoside (**15d**; $C_{55}H_{60}O_{11}$)

Mixed acetals **14d** (49 mg, 0.045 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (19 mg, 0.09 mmol), silver trifluoromethanesulfonate (23 mg, 0.09 mmol), and anhydrous tin(II) chloride (17 mg, 0.09 mmol) gave α-gluco disaccharide **15d** (18 mg, 44%) as a colourless oil.

$[\alpha]_D^{22} = +65.5$ ($c = 1.1$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.30$ (3H, s, OCH_3), 3.59–3.80 (8H, m, 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 (1H, dd, $J_{1,2} = 2.0$ Hz, $J_{2,3} = 3.0$ Hz, H-2_a), 3.91 (1H, dd, $J_{3,4} = 9.4$ Hz, H-3_a), 4.04–4.10 (2H, m, H-4_a, H-$6'_a$), 4.47, 4.84 (2H, ABq, $J_{AB} = 10.8$ Hz, $PhCH_2$), 4.48, 4.61 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.62 (2H, s, $PhCH_2$), 4.62, 4.98 (2H, ABq, $J_{AB} = 11.1$ Hz, $PhCH_2$), 4.70 (1H, d, H-1_a), 4.71, 4.92 (2H, ABq, $J_{AB} = 11.1$ Hz, $PhCH_2$), 4.72 (2H, s, $PhCH_2$), 5.00 (1H, d, $J_{1,2} = 2.9$ Hz, H-1_b), 7.14–7.39 (30H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 54.9$ (q, CH_3), 67.7, 68.4, 72.0, 72.8, 73.4, 75.0, 75.1, 75.2 ($8 \times$ t, $6 \times PhCH_2$, C-6_b, C-6_a), 70.7, 71.3, 73.8, 74.1, 74.2, 77.0, 79.9, 83.3 ($8 \times$ 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), 98.9, 100.6 ($2 \times$ d, C-1_b, C-1_a), 127.4, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 128.0, 128.1, 128.3, 128.3, 128.4 ($13 \times$ d, Ar–CH), 138.0, 138.2, 138.3, 138.4, 138.9

(5 × s, Ar–C) ppm; MS (APCI$^+$): $m/z = 919$ (M + Na$^+$, 55%); MS (APCI$^-$): $m/z = 931$ (M + Cl$^-$, 10%); HRMS: calcd. for $C_{55}H_{61}O_{11}$ (MH$^+$): 897.4214, found: 897.4229.

Methyl 3,4,6-tri-O-benzyl-α-D-glucopyranosyl-(1 → 3)-2-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside (**15e**; $C_{48}H_{52}O_{11}$)

Mixed acetals **14e** (77 mg, 0.078 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (32 mg, 0.16 mmol), silver trifluoromethanesulfonate (40 mg, 0.16 mmol), and anhydrous tin(II) chloride (30 mg, 0.16 mmol) gave α-gluco disaccharide **15e** (23 mg, 37%) as white crystals.

M.p.: 145–147°C (diethyl ether/petrol); $[\alpha]_D^{22} = +42.4$ ($c = 0.25$, $CHCl_3$); IR (thin film): $\nu = 3462$ (br, OH) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.65$ (1H, d, $J_{OH,2} = 9.8$ Hz, OH-2), 3.34 (3H, s, OCH_3), 3.56 (1H, at, $J = 9.2$ Hz, H-4$_b$), 3.65–3.68 (2H, m, H-6$_b$, H-6′$_b$), 3.71 (1H, atd, $J_{1,2} = 3.4$ Hz, $J = 9.6$ Hz, H-2$_b$), 3.75 (1H, at, $J = 9.3$ Hz, H-3$_b$), 3.81–3.88 (3H, m, H-2$_a$, H-5$_a$, H-6$_a$), 3.90–3.94 (1H, m, H-5$_b$), 4.22–4.24 (2H, m, H-4$_a$, H-6′$_a$), 4.28 (1H, dd, $J_{2,3} = 3.7$ Hz, $J_{3,4} = 9.2$ Hz, H-3$_a$), 4.47, 4.85 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 4.48, 4.57 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.66, 4.76 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.69, 4.82 (2H, ABq, $J_{AB} = 10.9$ Hz, $PhCH_2$), 4.69 (1H, d, $J_{1,2} = 1.4$ Hz, H-1$_a$), 5.21 (1H, d, H-1$_b$), 5.63 (1H, s, PhCH), 7.14–7.49 (25H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 54.9$ (q, OCH_3), 63.9, 71.5, 73.8, 76.1, 77.0, 77.6, 78.2, 83.4 (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$_b$), 68.7, 68.8, 73.4, 73.5, 74.8, 75.2 (6 × t, C-6$_a$, C-6$_b$, 4 × $PhCH_2$), 100.0, 100.8, 101.8 (3 × d, C-1$_a$, C-1$_b$, PhCH), 125.6, 127.5, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.2, 128.3, 128.3, 128.3, 128.5, 129.1 (15 × d, Ar–CH), 137.0, 137.8, 137.9, 138.4, 138.7 (5 × s, Ar–C) ppm; MS (ES$^+$): $m/z = 843$ (M + K$^+$, 50%), 827 (M + Na$^+$, 100%); HRMS: calcd. for $C_{48}H_{56}NO_{11}$ (MNH_4^+): 822.3853, found: 822.3842.

Methyl 3,4,6-tri-O-benzyl-α-D-glucopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**15g**; $C_{55}H_{60}O_{11}$)

Mixed acetals **14g** (65 mg, 0.06 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (25 mg, 0.12 mmol), silver trifluoromethanesulfonate (31 mg, 0.12 mmol), and anhydrous tin(II) chloride (23 mg, 0.12 mmol) gave α-gluco disaccharide **15g** (24 mg, 45%) as a colourless oil.

$[\alpha]_D^{22} = +35.1$ ($c = 1.05$, $CHCl_3$); IR (thin film): $\nu = 3418$ (br, OH) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.38$ (3H, s, OCH_3), 3.45 (1H, br d, $J_{OH,2} = 9.1$ Hz, OH-2$_b$), 3.55 (1H, at, $J = 9.1$ Hz, H-3$_b$), 3.55 (1H, dd, $J_{5,6} = 1.8$ Hz, $J_{6,6'} = 10.6$ Hz, H-6$_a$), 3.61–3.66 (4H, m, H-2$_b$, H-2$_a$, H-3$_a$, H-6′$_a$), 3.68 (1H, dd, $J_{5,6} = 1.9$ Hz, $J_{6,6'} = 11.0$ Hz, H-6$_b$), 3.69–3.71 (1H, m, H-5$_b$), 3.86–3.90 (1H, m, H-5$_a$), 3.88 (1H, at, $J = 9.5$ Hz, H-4$_b$), 3.93 (1H, dd, $J_{5,6'} = 3.9$ Hz, H-6′$_b$), 3.99 (1H, at, $J = 9.3$ Hz, H-4$_a$), 4.44, 4.57 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.49, 4.83 (2H, ABq, $J_{AB} = 10.6$ Hz, $PhCH_2$), 4.49, 4.59 (2H, ABq, $J_{AB} = 11.6$ Hz, $PhCH_2$), 4.57, 4.69 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 4.59, 4.70 (2H, ABq, $J_{AB} = 12.0$ Hz, $PhCH_2$), 4.61 (1H, d, $J_{1,2} = 3.6$ Hz, H-1$_b$), 4.79, 5.18 (2H, ABq, $J_{AB} = 10.6$ Hz, $PhCH_2$), 5.19 (1H, d, $J_{1,2} = 3.1$ Hz, H-1$_a$), 7.16–7.36 (30H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 55.2$ (q, OCH_3), 68.4 (t, C-6$_b$), 68.7 (t, C-6$_a$), 70.0 (d, C-5$_b$), 71.5 (d, C-5$_a$), 73.0, 73.2, 73.3, 74.9, 75.1, 75.2 (6 × t, 6 × $PhCH_2$), 74.0, 80.2, 83.6 (3 × d, C-2$_b$, C-2$_a$, C-3$_a$), 76.9 (d, C-3$_b$), 77.6 (d, C-4$_b$), 80.5 (d, C-4$_a$), 97.7 (d, C-1$_b$), 101.2 (d, C-1$_a$), 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.8, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4 (13 × d, Ar–CH), 137.5, 137.7, 137.7, 137.9, 138.2, 138.7 (6 × s, Ar–C) ppm; MS (ES$^+$): $m/z = 935$ (M + K$^+$, 14%), 919 (M + Na$^+$, 100%), 916 (2M + K$^+$ + H$^+$, 21%), 914 (M + NH_4^+, 14%); HRMS: calcd. for $C_{55}H_{64}NO_{11}$ (MNH_4^+): 914.4479, found: 914.4476.

Cholestan-3′-β-yl 3,4,6-tri-O-benzyl-α-D-glucopyranoside (**15h**; $C_{54}H_{76}O_6$)

Mixed acetals **14h** (41 mg, 0.04 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (16 mg, 0.08 mmol), silver trifluoromethanesulfonate (21 mg, 0.08 mmol), and anhydrous tin(II) chloride (15 mg, 0.08 mmol) gave α-glucoside **15h** (29 mg, 87%) as white crystals.

M.p.: 108–109°C; $[\alpha]_D^{24} = +98.5$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\nu = 3487$ (br, OH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.59$–1.99 (31H, m, steroid CH, CH_2), 0.66, 0.81 (6H, 2 × s, 2 × CH_3), 0.88 (3H, d, $J = 6.5$ Hz, CH_3), 0.89 (3H, d, $J = 6.5$ Hz, CH_3), 0.91 (3H, d, $J = 6.6$ Hz, CH_3), 2.10 (1H, br d, $J_{OH,2} = 8.0$ Hz, OH-2), 3.57–3.79 (4H, m, H-2, H-3, H-4, OCH), 3.68 (1H, dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 10.5$ Hz, H-6), 3.77 (1H, dd, $J_{5,6'} = 4.0$ Hz, H-6′), 3.89–3.92 (1H, m, H-5), 4.49, 4.84 (2H, ABq, $J_{AB} = 10.7$ Hz, $PhCH_2$), 4.51, 4.65 (2H, ABq, $J_{AB} = 11.9$ Hz, $PhCH_2$), 4.84, 4.99 (2H, ABq, $J_{AB} = 11.2$ Hz, $PhCH_2$), 5.04 (1H, d, $J_{1,2} = 3.6$ Hz, H-1), 7.14–7.41 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 12.0$, 12.3, 18.6, 22.6, 22.8 (5 × q, 5 × steroid CH_3), 21.2, 23.8, 24.2, 27.8, 28.2, 28.7, 32.0, 36.0, 36.1, 36.8, 39.5, 40.0 (12 × t, 12 × steroid CH_2), 28.0, 35.5, 35.8, 44.9, 54.2, 56.2, 56.4 (7 × d, 7 × steroid CH), 35.4, 42.6 (2 × s, 2 × steroid C), 68.6, 73.4, 75.0, 75.3 (4 × t, 3 × $PhCH_2$, C-6), 70.4, 73.0, 77.3, 77.3, 83.8 (5 × d, C-2, C-3, C-4, C-5, steroid OCH), 96.9 (d, C-1), 127.6, 127.7, 127.7, 127.9, 127.9, 128.3, 128.3 (7 × d, Ar–CH), 137.9, 138.2, 138.8 (3 × s, Ar–C) ppm.

Hydrolsis of vinyl ethers **19**

Vinyl ethers **19** (30 mg, 0.04 mmol) were dissolved in 2 cm^3 *THF* and 0.2 cm^3 H_2O. *NIS* (9 mg, 0.04 mmol) was added to the stirred mixture at room temperature. After 50 min, the mixture was partitioned between 30 cm^3 $CHCl_2$ and 30 cm^3 of a 10% aqueous solution of $Na_2S_2O_3$. Triethylamine (2 cm^3) was added to the organic layer which was then concentrated *in vacuo* and purified by flash column chromatography (petrol:ethyl acetate = 3:1) to give α-gluco disaccharide **15e** (18 mg, ~70%) as a white solid, identical to that described previously.

Data for succinimide trapped material: 2-O-(2-Iodo-1-(succinimid-N-yl)-propyl)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl fluoride (**16**; $C_{34}H_{37}FINO_7$)

Isolated in varying amounts during manno tethering reactions as single diastereomer as a colourless oil; $[\alpha]_D^{22} = +60.0$ ($c = 0.75$, $CHCl_3$); IR (thin film): $\nu = 1709$ (s, C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.98$ (3H, d, $J = 6.8$ Hz, CH_3), 2.76 (4H, s, $COCH_2CH_2CO$), 3.66–3.73 (2H, m, H-6, H-6′), 3.90 (3H, br s, H-3, H-4, H-5), 3.99 (1H, br s, H-2), 4.51, 4.62 (2H, ABq, $J_{AB} = 12.2$ Hz, $PhCH_2$), 4.51, 4.82 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 4.68, 4.90 (2H, ABq, $J_{AB} = 11.0$ Hz, $PhCH_2$), 5.12 (1H, dq, $J = 10.2$ Hz, CHI), 5.39 (1H, dd, $J_{1,2} = 2.0$ Hz, $J_{1,F} = 50.5$ Hz, H-1), 5.72 (1H, d, CHN), 7.15–7.47 (15H, m, Ar–H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 23.2$, 25.0 (d, q, CH_3, CHI), 27.9 (t, $COCH_2CH_2CO$), 68.4, 73.0, 73.4, 75.1 (4 × t, C-6, 3 × $PhCH_2$), 72.7 (dd, $^2J_{C\text{-}2,F} = 6.6$ Hz, C-2), 73.6, 74.2, 78.9 (3 × d, C-3, C-4, C-5), 86.4 (d, CHN), 106.3 (dd, $^1J_{C\text{-}1,F} = 221.0$ Hz, C-1), 127.6, 127.8, 127.8, 128.0, 128.0, 128.3, 128.4, 128.5, 128.6 (9 × d, Ar–CH), 137.5, 137.8, 138.0 (3 × s, Ar–C) ppm; MS (ES^+): $m/z = 735$ ($M + NH_4^+$, 100%); HRMS: calcd. for $C_{34}H_{41}N_2O_7FI$ (MNH_4^+): 735.1943, found: 725.1949.

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[18] It is not yet entirely clear exactly how **19** ($R = \mathrm{H}$) is formed, since this formally requires loss of I^+ from the oxonium ion produced subsequently to intramolecular glycosylation

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