Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 8361

www.rsc.org/obc

PAPER

Ready access to a branched Man_5 oligosaccharide based on regioselective glycosylations of a mannose-tetraol with *n*-pentenyl orthoesters†‡

Clara Uriel,[a] Ana M. Gómez,*[a] J. Cristóbal López*[a] and Bert Fraser-Reid[b]

Received 21st July 2012, Accepted 24th August 2012
DOI: 10.1039/c2ob26432c

A branched Man_5 oligosaccharide has been synthesized by sequential regioselective glycosylations on a mannose-tetraol with *n*-pentenyl orthoester glycosyl-donors promoted by NIS/$BF_3{\cdot}Et_2O$, in CH_2Cl_2. An extended *n*-pentenyl chain was incorporated into the tetraol acceptor to facilitate (a) the solubility of the starting tetraol in CH_2Cl_2, and (b) future manipulations at the reducing end of the Man_5 oligosaccharide.

Introduction

High-mannose oligosaccharides are, ubiquitous, biologically important molecules. They are known to participate in quality control and intracellular transportation of glycoproteins.[1] Furthermore, they cover the surface of many pathogenic microorganisms and are the targets of the immune system cells, including macrophages and dendritic cells, through their mannose receptors, as well as of soluble circulating proteins such as collectins.[2] High-mannose oligosaccharides belong to the *N*-linked family of carbohydrates, which are conjugated to glycoproteins *via* an *N*-acetyl-glucosamine unit to the amide group of an asparagine residue on the polypeptide backbone. Chemically, they are characterized by the presence of a variable number of mannose residues linked to the common core Manα(1–6)[Manα(1–3)]Manβ(1–4)GlcNAcb(1–4)GlcNAc. Functionally, these mannose oligosaccharides have been investigated as recognition moieties in drug delivery,[3] in targeting antigens to dendritic cells[4,5] and in carbohydrate-based vaccines.[6]

The discovery of a broadly neutralizing human antibody 2G12,[7] which was able to recognize oligomannose epitope $Man_9GlcNAc_2$ (**1**, Fig. 1) present on the gp120 receptor-binding glycoprotein of the HIV-1 virus,[8] has given the confidence that the glycan shield defense of the virus can be breached, and that these structures under the right circumstances can act as potential targets for vaccine development.[9–12] In this context, early studies seemed to indicate that the *N*-acetylglucosamine residues in gp120 are not essential for specific binding of the mannan moiety to target systems, and that they might be replaced with other groups which present the opportunity for linking the glycan to a protein or a solid support to give a number of desirable biological tools. Consequently, synthetic efforts have been devoted to the total synthesis of high mannose glycans of the gp120[13,14] as well as to the preparation of an assortment of partial structures that exhibit affinity to human antibody 2G12 with potential immunogenic applications.[15]

Our group has been involved in recent years in exploring the potential of *n*-pentenyl orthoesters (NPOEs) in the design of synthetic strategies towards complex oligosaccharides.[16] One aspect appealing to us has been the advantages associated with regiochemically-driven methodologies, which might minimize the number of protection–deprotection steps involved in standard oligosaccharide synthesis.[17] In this paper, we wish to describe the effective application of sequential, regioselective, NPOE glycosylations on a mannose-tetraol to target a branched pentasaccharide moiety incorporated into HIV glycoprotein gp120.

Results and discussion

Synthetic strategy

In previous studies, we have found that NPOEs displayed an excellent regioselectivity in glycosylations in CH_2Cl_2 [18] of some

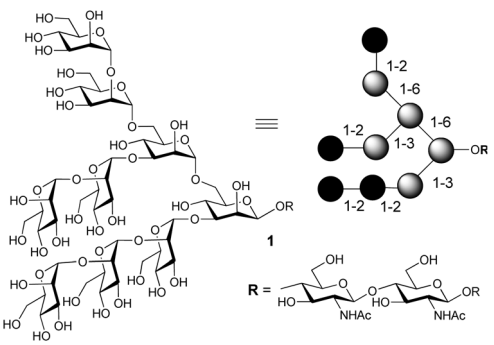


Fig. 1 Structure of $Man_9GlcNAc_2$, **1**.

[a]*Instituto de Química Orgánica General (IQOG-CSIC), Juan de la Cierva 3, 28006 Madrid, Spain. E-mail: jc.lopez@csic.es; Fax: +34 91 5644853; Tel: +34 91 5622900 Ext 320*
[b]*Natural Products and Glycotechnology Research Institute Inc., (NPG), 595F, Weathersfield Road, Pittsboro, NC, USA, 27312. E-mail: dglucose@aol.com; Fax: +1 9195427111; Tel: +1 9195427111*
†Electronic supplementary information (ESI) available: Copies of ^1H and ^{13}C NMR spectra of all compounds. See DOI: 10.1039/c2ob26432c
‡In memoriam of Professor Kostas Antonakis

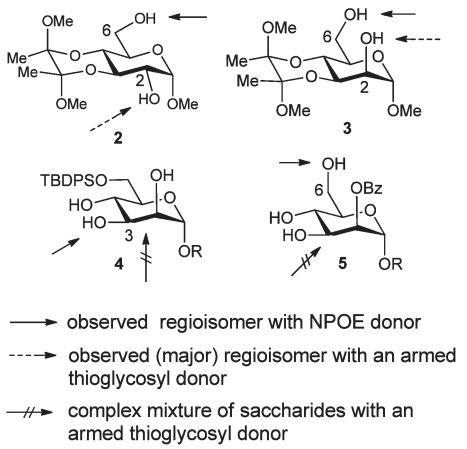
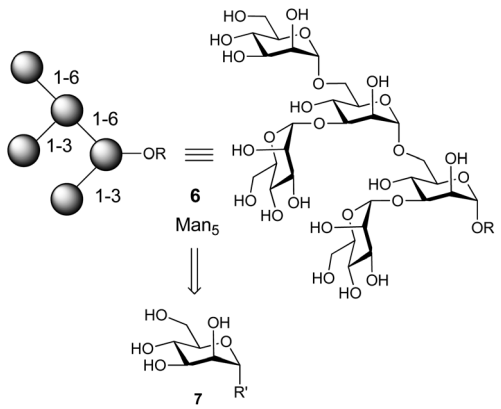


Fig. 2 Regioselective glycosylation with NPOEs.



Scheme 1 Projected synthesis of Man_5 unit **6**, from tetraol **7**.

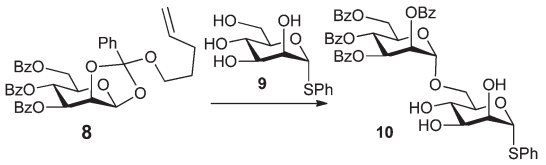
mannose-derived diols (**2**, **3**, Fig. 2)[19] and triols (**4**, **5**, Fig. 2).[20] The same diols, when confronted with a phenyl 2,3,4,6-tetra-*O*-benzyl 1-thio-mannopyranoside donor, displayed opposite regioselectivity.[19] Mannose-derived triols **4** and **5** also underwent regioselective glycosylation with NPOEs whereas the use of phenyl 2,3,4,6-tetra-*O*-benzyl 1-thio-mannoside as a donor gave rise to complex reaction mixtures containing several saccharides (Fig. 2)[20]

In this manuscript we describe a concise approach to the 3,6-branched Man_5 saccharide, **6**, component of the $Man_9GlcNAc_2$,[21–25] from an unprotected tetraol acceptor **7**, and entirely based on NPOE-mediated regioselective glycosyl couplings. In our strategy, the anomeric substituent of the unprotected tetraol **7** (Scheme 1) might play a dual role as (i) a solubility enhancer to facilitate its reaction in common glycosylation solvents and (ii) a leaving group for future manipulations, including glycosylation.

Glycosylation of thioglycosidic tetraol acceptors

For our initial experiments we selected phenyl 1-thiomannopyranoside **9** as the tetraol acceptor and NPOE **8** as the glycosyl donor (Table 1). Since compound **9** showed low solubility in CH_2Cl_2, CH_2Cl_2–dioxane mixtures were initially used in the

Table 1 Glycosylation of mannose tetraol **9** with NPOE **8**



Entry	Orthoester (equiv.)	Reaction conditions (equiv.)	Yield (%)
i	(2)	CH_2Cl_2/dioxane NIS (2)/$BF_3{\cdot}OEt_2$, −30 °C to r.t., overnight[a]	—
ii	(2)	Dioxane NIS(1 + 1)/$BF_3{\cdot}OEt_2$[b] r.t., 10 min + 20 min	36
iii	(4)	Dioxane NIS(2 + 2)/$Yb(OTf)_3$[b] r.t., 10 min + 20 min	35
iv	(1 + 1 + 1 + 1)[c]	Dioxane NIS(1 + 1 + 1 + 1)/$Yb(OTf)_3$[c] r.t., 90 min	74

[a] NIS added in one portion. [b] NIS added in two portions. [c] Orthoester and NIS added in several portions over 90 min.

glycosylation experiments. However, the use of CH_2Cl_2–dioxane (1 : 1.3) as a solvent did not result in the formation of disaccharide **10** (Table 1, entry *i*). Conversely, when dioxane was used as a solvent, the reaction of tetraol **9** with NPOE **8**, mediated by either NIS/$BF_3{\cdot}Et_2O$ or NIS/$Yb(OTf)_3$,[26] led to the formation of disaccharide **10** (Table 1, entries *ii–iv*). In the first case, the stepwise addition[27] of NIS (1 equiv. + 1 equiv.) allowed us to obtain disaccharide **10** in 36% yield by reaction with NPOE **8** (2 equiv., Table 1, entry *ii*). The glycosylation of tetraol **9** with 4 equiv. of donor **8** could produce a 35% or a 74% yield of disaccharide **10** by switching from a 2 + 2 equiv. addition of NIS to a stepwise 1 + 1 + 1 + 1 addition of NIS and **8**, all together, to the reaction mixture (Table 1, entries *iii* and *iv*). However, the fact that 4 equiv. of NPOE were required to obtain disaccharide **10** in good yield made us search for alternative anomeric substituents in the tetraol.

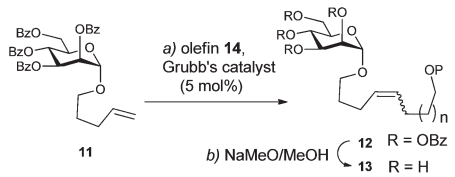
Synthesis and glycosylation of tetraols based on "chain extended" NPGs

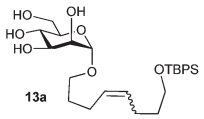
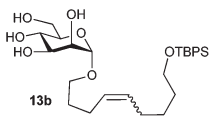
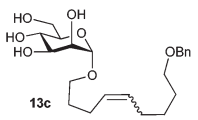
Our previous success with regioselective NPOE glycosylations of polyols in CH_2Cl_2 made us consider a second generation of tetraol acceptors based on *n*-pentenyl glycosides (NPGs) with enhanced lipophilicity that could facilitate their solubility in that solvent. Our experience with "chain extended" NPGs[28] led us to consider tetraols **13** as acceptor candidates. The modified *n*-pentenyl chain in these derivatives could, in principle, be derivatized or oxidatively removed as needed in future endeavors. Accordingly, cross-metathesis[29–31] of NPG **11**, readily formed by acid-mediated rearrangement of **8**,[32] with pentenyl silyl ether **14a**, or with hexenyl ethers **14b,c** (1st generation Grubbs catalyst, bis (tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride,[33] CH_2Cl_2, reflux, 12 h) followed by saponification (NaOMe/MeOH) led to tetraols **13a–c** (*E*/*Z* mixtures, *E* very major isomer), respectively, in good overall yields (Table 2).[34]

Glycosylation of tetraols **13** with NPOE **8** was then studied, and our results are displayed in Table 3. Normally, a mixture of

di- (**15**) and trisaccharides (**16**) was obtained, and better yields of the corresponding derivatives occurred when benzyl substituted tetraol **13c** was used as the glycosyl acceptor, when compared to silyl derivative **13b** (Table 3, compare entries *i*, *ii* with entries *iii*, *iv*). The use of 1.2 equiv. of NPOE **8** led to acceptable yields of disaccharide **15c** (Table 3, entry *iii*, 46%), whereas excess (4.0 equiv.) of NPOE donor led to acceptable yields of 3,6-trisaccharide **16c** (Table 3, entry *iv*, 38%). In contrast, attempted glycosylation of **13a** with 3.0 equiv. of NPOE **8** led to trisaccharide **17**, with the anomeric tether modified, as the major compound. The formation of the halo-furanosyl moiety in **17** is undoubtedly due to a NIS-triggered 5-*exo-trig* cyclization of the terminal OTBDPS group onto the olefin.[35] The related isomeric 6-*exo-trig* cyclization in derivatives **13b** and **13c** was not observed.

Table 2 Synthesis of tetraols based on "chain extended" NPGs **13a–c**



Entry	Olefin (4 equiv.)	Products	Yields (%)
i	 **14a**	 **13a**	*a*) 90 *b*) 95
ii	 **14b**	 **13b**	*a*) 79 *b*) 80
iii	 **14c**	 **13c**	*a*) 60 *b*) 75

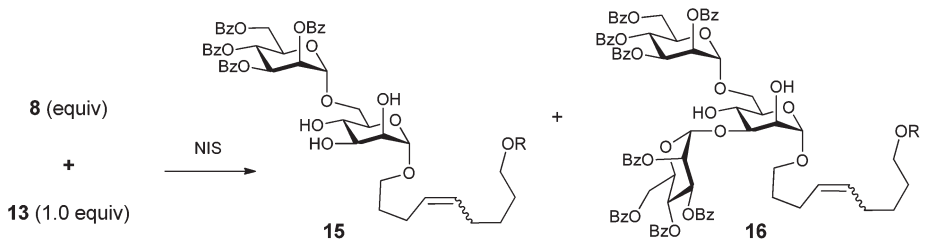
Regioselective synthesis of Man_5 derivative 24

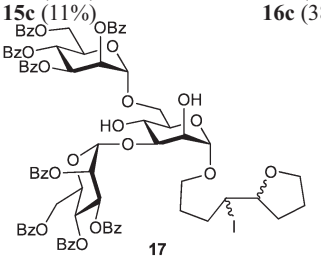
Based on these results, pentasaccharide **21** has been efficiently assembled as shown in Scheme 2. Thus, disaccharide **15c** was glycosylated with NPOE **18**, to give trisaccharide **19** in 63% yield. The latter upon saponification unveiled heptaol **20**, which could be doubly-glycosylated with NPOE **18**, to give pentasaccharide **21** in 44% yield. In this reaction, tetrasaccharide **22** was also isolated in 38% yield. The latter could be transformed into **21** by glycosylation with 2.0 equiv. of **18** (52% yield).

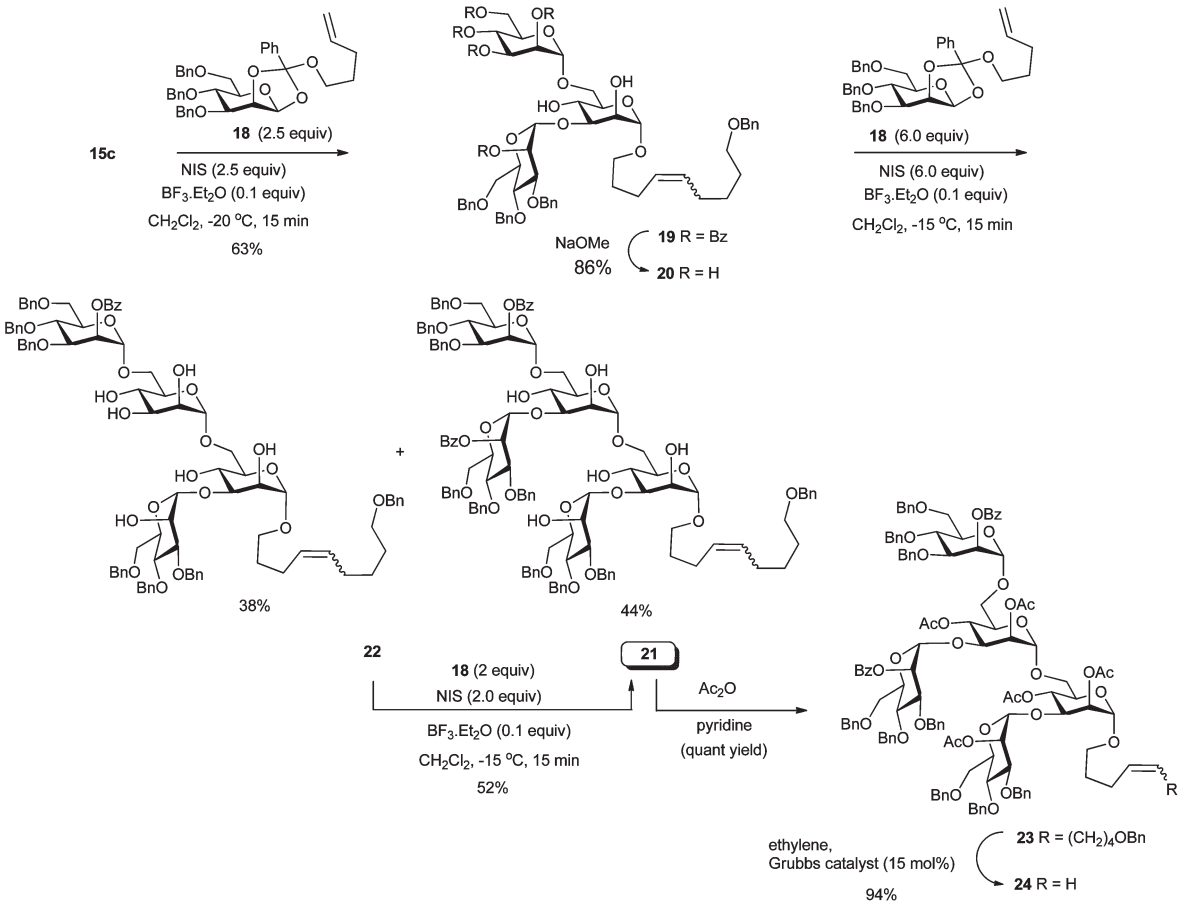
The effectiveness of this approach lies on the regioselectivity displayed in the glycosylation of mannose polyols with NPOEs. Thus, for regioselectivity purposes, heptaol trisaccharide **20** could be viewed as a 2,3,4,6-mannose-tetraol, a 2,4-mannose-diol, and a 2-OH mannoside, and from our previous studies and the results displayed in Table 3, the regioselective glycosylation at positions 3 and 6 of the mannose tetraol residue could have been expected.

The anomeric pentenyl residue in pentasaccharide **23**, obtained by acetylation of **21**, was efficiently transformed into *n*-pentenyl pentasaccharide **24**, by cross-metathesis in the presence of ethylene (94% yield).[36] The *n*-pentenyl moiety in **24** could in principle be: oxidatively hydrolyzed,[37] transformed into a variety of anomeric spacers,[38–43] used as a handle for multivalent presentations,[44–47] or used as a leaving group in further synthetic transformations.[48]

Table 3 Glycosylation of tetraols **13a–c**



Entry	8	Tetraol	Reaction conditions	Disaccharide (yield)	Trisaccharide (yield)
i	(1.2 equiv.)	**13b**	NIS (1.2 equiv.) $Yb(OTf)_3$, 10 °C, 1 h	**15b** (13%)	**16b** (0%)
ii	(3.0 equiv.)	**13b**	NIS (1.2 equiv.) $BF_3{\cdot}OEt_2$, 0 °C, 10 min	**15b** (39%)	**16b** (36%)
iii	(1.2 equiv.)	**13c**	NIS (1.2 equiv.) $BF_3{\cdot}OEt_2$, −5 °C, 10 min	**15c** (46%)	**16c** (10%)
iv	(4.0 equiv.)	**13c**	NIS (4.0 equiv.) $BF_3{\cdot}OEt_2$, 0 °C, 10 min	**15c** (11%)	**16c** (38%)
v	(3.0 equiv.)	**13a**	NIS (4.5 equiv.) $BF_3{\cdot}OEt_2$, −25 °C, 10 min	 **17**	



Scheme 2 Regioselective synthesis of Man_5 derivative **24**.

Conclusions

A regioselective approach based on NPOE-regioselective glycosylations that allows the preparation of a Man_5 saccharide from a starting mannose tetraol has been implemented. Only one deprotection step was required throughout the synthetic sequence. Additionally, the overall process requires only one single NPOE, **8**, as the starting material since NPOE **18** and the starting tetraol **13c** were prepared from **8**. An extended *n*-pentenyl chain was incorporated to the anomeric position of tetraols **13** for solubility purposes, and to facilitate further synthetic transformations.

Experimental section

General methods

^1H NMR and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$ using either a 300, 400 or a 500 MHz spectrometer.

Optical rotations were determined for solutions in chloroform at 25 °C. Column chromatography was performed on silica gel (230–400 mesh). TLC was conducted in precoated Kiesel gel 60 F254 (Merck). Detection was first by UV light (254 nm) then charring with a 1/20/4 solution of sulfuric acid/acetic acid/H_2O. All solvents were purified by distillation over drying agents or by elution through a PURE SOLV purification system. Reactions requiring anhydrous conditions were performed under argon. Anhydrous magnesium sulphate was used for drying solutions. Phenyl 1-thio-α-D-mannopyranoside **9**,[49] 1-*O*-*tert*-butyldiphenylsilyl-4-penten-1-ol **14a**,[50] 1-*O*-*tert*-butyldiphenylsilyl-5-hexen-1-ol **14b**,[51] 1-*O*-benzyl-5-hexen-1-ol **14c**,[52] *n*-pentenyl glycoside **11**[53] and NPOEs **8** and **18**[18] were prepared as previously described.

General procedure for glycosylation with NPOEs. A dry mixture of the corresponding NPOE and the appropriate acceptor in toluene (5 mL) was azeotroped to dryness and subsequently kept overnight under high vacuum. This mixture was then dissolved in the suitable dry solvent (5 mL $mmol^{-1}$), the solution cooled to the appropriate temperature, and NIS was added. After stirring for 5 min, the corresponding acid was added. The mixture was stirred for the indicated time, and the reaction was quenched by addition of aqueous $Na_2S_2O_3$ (10%) and $NaHCO_3$ (satd). The layers were separated, the aqueous phase was extracted with CH_2Cl_2 and the combined organic layers were washed with saturated aqueous NaCl. The resultant organic phase was dried, filtered and concentrated. The residue was purified by flash silica gel column chromatography.

General procedure for the cross-metathesis (CM) reaction. The *n*-pentenyl glycoside **11** (1 mmol) and the appropriate olefin **14a–c** (4 mmol) were dissolved in dry CH_2Cl_2. Argon was bubbled through the solution for 10 min and then 1st generation Grubbs catalyst (5% mol) was added. The reaction mixture was

refluxed for 12 h after which time air was bubbled through the solution. The solvent was evaporated *in vacuo* and the residue was filtered through a FLORISIL pad and then purified by flash silica gel column chromatography.

General procedure for debenzoylation. The corresponding benzoylated glycoside was dissolved in MeOH : THF (1 : 1) (20 mL $mmol^{-1}$) and then treated with a solution of NaOMe (0.1 M) in MeOH. The reaction mixture was stirred until TLC showed complete disappearance of the starting material. The reaction was then neutralized by addition of acidic Amberlite IR-120, filtered off, and concentrated. The residue was purified by flash silica gel column chromatography.

Phenyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-1-thio-α-D-mannopyranoside (10). Following the general procedure for glycosylation, the 1,2-orthoester **8** (number of equivalents shown in Table 1) and the acceptor **9** were dissolved in dry CH_2Cl_2 or dioxane (see Table 1), the solution was cooled to the appropriate temperature, then NIS (number of equivalents shown in Table 1) and $BF_3{\cdot}Et_2O$ (0.3 equiv.) or $Yb(OTf)_3$ (0.3 equiv.) were added. After TLC analysis indicated full disappearance of the starting material, the reaction was quenched and the residue was purified by flash chromatography (EtOAc). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.84 (m, 1H), 3.89 (dd, J = 11.8, 1.6 Hz, 1H), 4.10 (t, J = 9.4 Hz, 1H), 4.23 (dd, J = 11.8, 3.6 Hz, 1H), 4.23–4.28 (m, 1H), 4.30–4.36 (m, 1H), 4.48 (dd, J = 11.7, 4.2 Hz, 1H), 4.52–4.56 (m, 1H), 4.69 (dd, J = 11.7, 2.3 Hz, 1H), 5.27 (d, J = 1.7 Hz, 1H), 5.60 (d, J = 1.3 Hz, 1H), 5.78 (dd, J = 3.3, 1.8 Hz, 1H), 5.91 (dd, J = 10.1, 3.4 Hz, 1H), 6.12 (t, J = 10.0 Hz, 1H), 7.20–8.10 (m, 25H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 63.0, 66.9, 67.2, 67.9, 69.0, 70.7 (×2), 72.6, 72.8 (×2), 88.6, 98.1, 127.7, 128.5 (×2), 128.6 (×2), 128.7 (×3), 128.8 (×2), 129.1, 129.2, 129.3 (×3), 129.4, 130.0 (×3), 130.1 (×3), 131.8 (×3), 133.3, 133.6, 133.7 (×2), 134.2, 165.7, 165.8, 166.1, 166.5. ESI-HRMS: $[M + NH_4]^+$ m/z calcd 868.2639 for $C_{46}H_{46}O_{14}SN$, found 868.2634; $[2M + NH_4]^+$ m/z calcd 1718.4934 for $C_{92}H_{88}O_{28}S_2N$, found 1719.4962; anal. calcd for $C_{46}H_{42}O_{14}S$ (850.88): C, 64.93; H, 4.98; O, 26.32; S, 3.77. Found: C, 64.77; H, 4.75. The structure of the disaccharide **10** was determined by acylation and ^{1}H NMR analysis of the newly downshifted protons. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.00 (s, 3H), 2.06 (s, 3H), 2.12 (s, 3H), 3.64 (dd, J = 11.2, 2.4 Hz, 1H), 3.65–3.74 (m, 1H), 3.94 (dd, J = 11.2, 5.2 Hz, 1H), 4.29–4.35 (m, 1H), 4.37 (dd, J = 12.0, 4.2 Hz, 1H), 4.53 (ddd, J = 9.9, 5.2, 2.2 Hz, 1H), 4.61 (dd, J = 12.0, 2.4 Hz, 1H), 5.06 (d, J = 1.7 Hz, 1H), 5.30 (dd, J = 9.9, 3.2 Hz, 1H, H-3), 5.45 (t, J = 10.1 Hz, 1H, H-4), 5.46 (d, J = 1.7 Hz, 1H), 5.49 (dd, J = 3.2, 1.8 Hz, 1H, H-2), 5.72 (dd, J = 3.3, 1.7 Hz, 1H), 5.85 (dd, J = 10.1, 3.3 Hz, 1H), 6.07 (t, J = 10.0 Hz, 1H), 7.14–8.06 (m, 25H).

8-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-octenyl-2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (12a). *n*-Pentenyl glycoside **11** (1.33 g, 2 mmol), 1-*O*-*tert*-butyldiphenylsilyl-4-penten-1-ol **14a** (2.6 g, 8 mmol) and bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride (82 mg, 0.1 mmol) were reacted according to the general method for the CM reaction. The residue was purified by flash silica gel column chromatography (hexane/EtOAc, 8/2) to give **12a** (1.82 g, 90%) as a colorless gum. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.97 (s, 9H), 1.49–1.61 (m, 2H), 1.62–1.74 (m, 2H), 1.96–2.10 (m, 4H), 4.32–4.44 (m, 2H), 4.61 (dd, J = 11.7, 2.2 Hz, 1H), 5.00 (d, J = 1.9 Hz, 1H), 5.28–5.34 (m, 2H), 5.62 (dd, J = 3.2, 1.9 Hz, 1H), 5.85 (dd, J = 10.1, 3.3 Hz, 1H), 6.03 (dd, J = 10.1, 9.8 Hz, 1H), 7.15–8.03 (m, 30 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 19.4, 27.0 (×3), 28.9, 29.2, 29.3, 32.6, 63.1, 63.4, 67.2, 68.3, 69.0, 70.3, 70.8, 97.8, 127.7 (×4), 128.4 (×2), 128.6 (×4), 128.7 (×2), 129.1, 129.3, 129.4, 129.5, 129.6 (×2), 129.8 (×4), 129.9 (×2), 130.0, 131.0, 133.2, 133.3, 133.5 (×3), 134.2, 135.7 (×4), 165.5, 165.6 (2), 166.3. ESI-HRMS: $[M + H]^+$ m/z calcd 961.3983 for $C_{58}H_{61}O_{11}Si$, found 961.3958; $[M + NH_4]^+$ m/z calcd 978.4248 for $C_{58}H_{64}O_{11}SiN$, found 978.4178; anal. calcd for $C_{58}H_{60}O_{11}Si$ (961,17): C, 72.48; H, 6.29; O, 18.31; Si, 2.92. Found: C, 72.51; H, 6.32.

8-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-octenyl-α-D-manno-pyranoside (13a). This compound was prepared from **12a** (1.36 g, 1.4 mmol) following the general procedure for debenzoylation. The residue was purified by flash chromatography (EtOAc) to give **13a** (720 mg, 95%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.05 (s, 9H), 1.49–1.66 (m, 4H), 1.94–2.11 (m, 4H), 3.26–4.03 (m, 10H), 4.79 (bs, 1H), 5.30–5.42 (m, 2H), 7.30–7.71 (m, 10H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 19.3, 27.0 (×3), 28.9, 29.1, 29.4, 32.5, 61.0, 63.4, 66.2, 67.4, 71.1, 72.3, 100.2, 127.7 (×4), 129.6 (×2), 130.6 (×2), 134.1 (×2), 135.6 (×4). ESI-HRMS: $[M + H]^+$ m/z calcd 545.2934 for $C_{30}H_{45}O_7Si$ 545.2824; $[M + NH_4]^+$ m/z calcd 562.3200 for $C_{30}H_{48}O_7SiN$ 562.3099. Anal. calcd for $C_{30}H_{44}O_7Si$ (544.75): C, 66.14; H, 8.14; O, 20.56; Si, 5.16. Found: C, 66.25; H, 8.30.

[9-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-nonenyl]-2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (12b). *n*-Pentenyl glycoside **11** (664 mg, 1 mmol), 1-*O*-*tert*-butyldiphenylsilyl-5-hexen-1-ol **14b** (1.35 g, 4 mmol) and bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride (41 mg, 0.05 mmol) were reacted according to the general method for the CM reaction. The residue was purified by flash silica gel column chromatography (hexane/EtOAc, 9/1) to give **12b** (770 mg, 79%) as a syrup; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.79–0.92 (m, 1H), 1.04 (s, 9H), 1.22–1.30 (m, 1H), 1.39–1.49 (m, 2H), 1.51–1.61 (m, 2H), 1.72–1.81 (m, 2H), 1.94–2.02 (m, 2H), 2.06–2.18 (m, 2H), 3.53–3.62 (m, 1H), 3.63–3.68 (m, 2H), 3.83 (dt, J = 9.1, 6.5 Hz, 1H), 4.39–4.45 (m, 1H), 4.48 (dd, J = 12.0, 4.5 Hz, 1H), 4.69 (dd, J = 12.0, 2.3 Hz, 1H), 5.08 (d, J = 1.7 Hz, 1H), 5.34–5.51 (m, 2H), 5.69 (dd, J = 3.3, 1.8 Hz, 1H), 5.92 (dd, J = 9.0, 3.3 Hz, 1H), 7.29–8.11 (m, 30H). ESI-HRMS: $[M + NH_4]^+$ m/z calcd 992.4405 for $C_{59}H_{66}O_{11}SiN$, found 992.4676; $[M + H]^+$ m/z calcd 975.4139 for $C_{59}H_{66}O_{11}SiN$, found 975.4436. Anal. calcd for $C_{59}H_{62}O_{11}Si$ (974.40): C, 72.67; H, 6.41; O, 18.05; Si, 2.88. Found: C, 72.72; H, 6.58.

[9-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-nonenyl]-L-α-D-manno-pyranoside (13b). This compound was prepared from **12b** (720 mg, 0.748 mmol) following the general procedure for debenzoylation. After stirring (2 h), the reaction was neutralized, filtered, and concentrated. The residue was purified by flash chromatography (EtOAc) to give **13b** (237 mg, 80%); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 19.3, 25.8, 27.0 (×3), 29.1, 29.4, 32.2, 32.4, 61.0, 63.9, 66.2, 67.4, 71.2, 71.8, 72.3, 100.1, 127.7 (×4),

129.3, 129.6 (×2), 131.1, 134.2 (×2), 135.7 (×4). API-ES positive: 581.9 $[M + Na]^+$. Anal. calcd for $C_{31}H_{46}O_7Si$ (558.7782): C, 66.63; H, 8.30; O, 20.04; Si, 5.03. Found: C, 66.80; H, 8.41.

9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl-2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (12c). *n*-Pentenyl glycoside **11** (2.8 g, 4.2 mmol), 1-*O*-benzyl-5-hexen-1-ol **14c** (1.6 g, 8.4 mmol) and bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride (172 mg, 0.21 mmol) were reacted according to the general method for the CM reaction. The residue was purified by flash silica gel column chromatography (hexane/EtOAc, 9/1) to give **12c** (2.32 g, 67%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.40–1.51 (m, 2H), 1.58–1.68 (m, 2H), 1.75–1.82 (m, 2H), 1.99–2.08 (m, 2H), 2.10–2.23 (m, 2H), 3.45–3.50 (m, 2H), 3.54–3.63 (m, 1H), 3.79–3.89 (m, 1H), 4.40–4.52 (m, 4H), 4.68–4.72 (m, 1H), 5.09 (bs, 1H), 5.36–5.48 (m, 2H), 5.70 (dd, J = 1.8, 3.1 Hz, 1H), 5.93 (dd, J = 3.2, 10.1 Hz, 1H), 6.12 (t, J = 10.1 Hz, 1H);^{13}C-NMR (75 MHz, $CDCl_3$) δ: 26.0, 28.9, 29.0, 29.1, 32.3, 62.8, 66.8, 67.0, 68.7, 70.0, 70.2, 70.5, 72.7, 97.6 (C1), 127.3, 127.5 (×2), 128.1 (×2), 128.2 (×2), 128.3 (×4), 128.5 (×2), 129.2, 129.6 (×3), 129.7 (2), 129.8 (×2), 131.0, 132.9, 133.0, 133.3 (×2), 138.6, 165.3, 165.4 (×2), 166.0. ESI-HRMS: $[M + NH_4]^+$ m/z calcd 844.3696 for $C_{50}H_{55}O_{11}N$, found 844.3601; $[M + H]^+$ m/z calcd 827.3431 for $C_{50}H_{51}O_{11}$, found 827.3279. Anal. calcd for $C_{50}H_{50}O_{11}$ (826.92): C, 72.62; H, 6.09; O, 21.28. Found: C, 72.80; H, 6.22.

[9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl]-α-D-mannopyranoside (13c). This compound was prepared from **12c** (2 g, 2.42 mmol) following the general procedure for debenzoylation. The residue was purified by flash chromatography (AcOEt) to give **13c** (892 mg, 90%) as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.35–1.46 (m, 2H), 1.56–1.67 (m, 4H), 1.95–2.09 (m, 4H), 3.33–3.97 (m, 10H), 4.49 (m, 2H), 4.79 (*b*s, 1H), 5.33–5.40 (m, 2H), 7.23–7.36 (m, 5H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 25.9, 28.9, 29.1 (×2), 32.2, 60.7, 65.9, 67.1, 70.1, 70.9, 71.5, 72.1, 72.7, 99.9, 127.3, 127.5 (×2), 128.2 (×2), 129.3, 130.7, 138.5. ESI-HRMS: $[M + NH_4]^+$ m/z calcd 428.2648 for $C_{22}H_{38}O_7N$, found 428.2576; $[M + H]^+$ m/z calcd 411.2382 for $C_{22}H_{35}O_7$, found 411.2309. Anal. calcd for $C_{22}H_{34}O_7$ (410.50): C, 64.37; H, 8.35; O, 27.28. Found: C, 64.55; H, 8.40.

Glycosylation reaction of tetraol 13a with NPOE 8. According to the general method for glycosylation NPOE **8** (199 mg, 0.3 mmol) and tetraol **13a** (55.5 mg, 0.1 mmol) were dissolved in CH_2Cl_2 (5 mL), and allowed to react for 15 min at −25 °C with NIS (101 mg, 0.45 mmol) and $BF_3{\cdot}Et_2O$ (3.8 μL, 0.03 mmol). Purification by column chromatography (hexane/EtOAc, 7/3) afforded trisaccharide **17** (66 mg, 41%) as a mixture of diastereomers. Selected peaks for **17**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.73 (m, 1 H, C*H*-furanyl), 4.10 (m, 1 H, C*H*-I). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 42.9, 43.0 (*C*H-I), 82.3, 82.4 (*C*H-Ofuranyl). ESI-HRMS: $[M + NH_4]^+$ m/z calcd 1606.4142 for $C_{82}H_{81}O_{25}IN$, found 1606.4237; $[M + H]^+$ m/z calcd 1589.3877 for $C_{82}H_{78}O_{25}I$, found 1589.3831. Anal. calcd for $C_{82}H_{77}IO_{25}$ (1588.37): C, 61.97; H, 4.88; I, 7.98; O, 25.17. Found: C, 61.88; H, 4.92.

Glycosylation reaction of tetraol 13b with NPOE 8

Reaction with Yb(OTf)$_3$. To a stirred solution of tetraol **13b** (56 mg, 0.1 mmol) and NPOE **8** (79 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (4 mL), at 10 °C, were added NIS (26.9 mg, 0.12 mmol) and $Yb(OTf)_3$ (74 mg, 0.12 mmol). Work-up as mentioned in the general procedure of glycosylation was followed by column chromatography ((hexane/EtOAc, 7/3 to 1/1 and finally EtOAc) to give disaccharide **15b** (14 mg, 13%).

Reaction with BF$_3$·Et$_2$O. To a stirred solution of tetraol **13b** (56 mg, 0.1 mmol) and NPOE **8** (79 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (4 mL), at 0 °C, were added NIS (26.9 mg, 0.12 mmol) and $BF_3{\cdot}Et_2O$ (3.8 μL, 0.03 mmol). Work-up as mentioned in the general procedure of glycosylation was followed by column chromatography (hexane:EtOAc 7 : 3 to 1 : 1 and finally AcOEt) to give trisaccharide **16b** (62 mg, 36%) followed by disaccharide **15b** (14 mg, 13%).

[9-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-nonenyl]6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-manno-pyranoside (15b). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.04 (s, 9H), 1.24–1.31 (m, 2H), 1.36–1.43 (m, 2H), 1.51–1.58 (m, 2H), 1.62–1.68 (m, 2H), 1.91–1.98 (m, 2H), 2.00–2.09 (m, 2H), 3.43–3.48 (m, 1H), 3.64 (t, J = 6.4 Hz, 2H), 3.69–3.75 (m, 2H), 3.77–3.81 (m, 1H), 3.82–3.86 (m, 1H), 3.90–3.98 (m, 2H), 4.16 (dd, J = 11.6, 4.2 Hz, 1H), 4.48 (dd, J = 12.1, 4.2 Hz, 1H), 4.57–4.60 (m, 1H), 4.71 (dd, J = 12.1, 2.7 Hz, 1H), 4.86 (*b*s, 1H), 5.32 (*b*s, 1H), 5.33–5.41 (m, 2H), 5.76 (bs, 1H), 5.93 (dd, J = 10.1, 3.4 Hz, 1H), 6.13 (t, J = 10.1 Hz, 1H), 7.23–8.11 (m, 30H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 18.2, 27.0 (×3), 29.3, 29.5, 31.1, 32.2, 32.4, 63.0, 64.0, 66.8, 67.0, 67.6, 68.1, 69.0, 70.2, 70.8, 71.1, 71.4, 72.4, 97.8, 100.0, 127.7 (×4), 128.5 (×2), 128.6 (×3), 128.7 (×2), 129.1 (×2), 129.4, 129.5, 129.6 (×2), 129.9 (×3), 130.0 (×2), 131.1, 133.2, 133.4, 133.6, 133.7, 135.7 (×2), 165.6, 165.7, 165.8, 166.4. ESI-HRMS: $[M + NH_4]^+$ m/z calcd 1154.4933 for $C_{65}H_{76}O_{16}SiN$, found 1155.6382; $[M + H]^+$ m/z calcd 1137.4667 for $C_{65}H_{73}O_{16}Si$, found 1138.2563. Anal. calcd for $C_{65}H_{72}O_{16}Si$ (1137.3431): C, 68.64; H, 6.38; O, 22.51; Si, 2.47. Found: C, 68.89; H, 6.55.

[9-*O*-*tert*-Butyldiphenylsilyl-4-(*Z*,*E*)-nonenyl]3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-manno-pyranoside (16b). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.02 (s, 9H), 1.31–1.43 (m, 2H), 1.48–1.65 (m, 4H), 1.90–2.06 (m, 4H), 3.32–3.40 (m, 2H), 3.62 (t, J = 6.4 Hz, 2H), 3.63–3.72 (m, 2H), 3.80–3.86 (m, 1H), 3.95 (d, J = 11.9 Hz, 1H), 3.99 (dd, J = 9.3, 2.9 Hz, 1H), 4.19 (dd, J = 11.6, 4.1 Hz, 1H), 4.22–4.27 (m, 2H), 4.52 (d, J = 12.0 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 4.56–4.63 (m, 1H), 4.67–4.76 (m, 3H), 4.88–4.94 (m, 1H), 5.29–5.41 (m, 2H), 5.42 (d, J = 1.5 Hz, 1H), 5.80 (dd, J = 3.3, 1.7 Hz, 1H), 5.87 (dd, J = 3.0, 1.7 Hz, 1H), 5.99 (dd, J = 9.7, 3.6 Hz, 1H), 6.02 (dd, J = 10.6, 3.3 Hz, 1H), 6.13 (t, J = 10.6 Hz, 1H), 6.15 (t, J = 9.7 Hz, 1H), 7.22–8.14 (m, 50H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 19.4, 25.9, 32.2, 32.4, 63.1, 63.5, 64.0, 65.6, 66.8, 67.1, 67.2, 67.7, 69.0, 69.6, 70.1, 70.4, 70.5, 70.7, 71.0, 71.7, 83.2, 98.0, 99.9, 100.2, 127.7 (×4), 128.4 (×5), 128.5 (×4), 128.6 (×6), 128.7 (×4), 129.1, 129.2, 129.3, 129.4, 129.5 (×2), 129.6 (×4), 129.9 (×4), 130.0 (×8), 130.1 (×4), 131.1, 133.2 (×2), 133.3, 133.4, 133.5 (×2), 133.6, 133.7, 134.3, 135.7, 165.5, 165.6 (×2), 165.7

(×2), 165.8, 166.4, 166.5. ESI-HRMS: $[M + H]^+$ *m/z* calcd 1715.6244 for $C_{99}H_{99}O_{25}Si$, found 1717.1258. Anal. calcd for $C_{99}H_{98}O_{25}Si$ (1715.9079): C, 69.30; H, 5.76; O, 23.31; Si, 1.64. Found: C, 69.55; H, 5.86. The structure of the disaccharide **16b** was determined by acylation and ^{1}H NMR analysis of the newly downshifted protons: ^{1}H-NMR (300 MHz, $CDCl_3$) ^{1}H-NMR (500 MHz, $CDCl_3$) *δ*: 1.02(s, 9H), 1.33–1.41 (m, 2H), 1.48–1.55 (m, 2H), 1.64–1.72 (m, 2H), 1.91–1.96 (m, 2H), 2.03–2.12 (m, 2H), 2.26 (s, 3H), 2.31 (s, 3H), 3.50 (dt, *J* = 9.6, 6.4 Hz, 1H), 3.61 (t, *J* = 6.5 Hz, 2H), 3.69 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.81 (dt, *J* = 9.6, 6.8 Hz, 1H), 3.98–4.04 (m, 2H), 4.37 (dd, *J* = 9.8, 3.5 Hz, 1H, H-3), 4.49 (dd, *J* = 12.2, 4.4 Hz, 1H), 4.52 (dd, *J* = 12.2, 3.6 Hz, 1H), 4.55–4.61 (m, 2H), 4.67 (dd, *J* = 12.2, 2.6 Hz, 1H), 4.71 (dd, *J* = 12.2, 2.5 Hz, 1H), 4.86 (d, *J* = 1.6 Hz, 1H), 5.15 (d, *J* = 1.8 Hz, 1H), 5.36 (d, *J* = 1.9 Hz, 1H), 5.38–5.41 (m, 2H), 5.43 (dd, *J* = 3.5, 1.6 Hz, 1H, H-2), 5.44 (t, *J* = 9.8 Hz, 1H, H-4), 5.52 (dd, *J* = 3.6, 1.8 Hz, 1H), 5.75 (dd, *J* = 3.3, 1.9 Hz, 1H), 5.81 (dd, *J* = 10.2, 3.2 Hz, 1H), 5.94 (dd, *J* = 10.2, 3.3 Hz, 1H), 6.13 (t, *J* = 10.2 Hz, 1 H), 6.18 (t, *J* = 10.2 Hz, 1 H), 7.23–8.15 (m, 50 H).

Glycosylation reaction of tetraol 13c with NPOE 8. In two different experiments, and following the general procedure for glycosylation, NPOE **8** (80 mg, 0.12 mmol and 265 mg, 0.4 mmol, respectively) and tetraol **13c** (41 mg, 0.12 mmol) in CH_2Cl_2 (3 mL) were reacted with NIS (26.9 mg, 0.12 mmol and 89.6 mg, 0.4 mmol, respectively) and $BF_3{\cdot}Et_2O$ (1.5 μL, 0.012 mmol) at −5 °C. After work-up and column chromatography (hexane/EtOAc, 7/3 to 1/1 and finally EtOAc), trisaccharide **16c** (15 mg, 10% and 60 mg, 38%, respectively) and disaccharide **15c** (46 mg, 46% and 11 mg, 11%, respectively) were obtained.

[9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl]6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (15c). ^{1}H-NMR (300 MHz, $CDCl_3$) *δ*: 1.28–1.36 (m, 2H), 1.48–1.60 (m, 4H), 1.87–1.92 (m, 2H), 1.94–2.01 (m, 2H), 3.33–3.38 (m, 1H), 3.37 (t, *J* = 6.6 Hz, 2H), 3.65 (td, *J* = 6.6, 9.6 Hz, 1H), 3.73 (ddd, *J* = 1.5, 3.9, 9.6 Hz, 1H), 3.80 (dd, *J* = 3.3, 9.6 Hz, 1H), 3.83 (dd, *J* = 1.7, 12.0 Hz, 1H), 3.89 (dd, *J* = 1.4, 3.3 Hz, 1H), 3.94 (t, *J* = 9.6 Hz, 1H), 4.11 (dd, *J* = 4.2, 11.3 Hz, 1H), 4.37–4.43 (m, 3H), 4.52 (m, 1H), 4.65 (dd, *J* = 2.5, 12.2 Hz, 1H), 4.79 (d, *J* = 1.2 Hz, 1H), 5.21 (d, *J* = 1.8 Hz, 1H), 5.29–5.32 (m, 2H), 5.69 (dd, *J* = 1.8, 3.3 Hz, 1H), 5.84 (dd, *J* = 3.2, 10.2 Hz, 1H), 6.07 (t, *J* = 10.2 Hz, 1H), 7.16–7.52 (m, 15H), 7.74–8.04 (m, 8H). ^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 26.0, 29.1, 29.2, 32.3, 62.8, 66.5, 66.7, 67.3, 67.6, 68.7, 70.2, 70.3, 70.5, 70.9, 71.2, 72.3, 72.8, 97.5, 99.9, 127.4, 127.6 (×4), 128.2 (×4), 128.3 (×4), 128.4 (×4), 128.5 (×4), 129.5, 129.7 (×3), 129.8, 130.6, 132.9, 133.2, 133.3, 133.4, 138.5, 165.4, 165.5, 165.7, 166.2. ESI-HRMS: $[M + Na]^+$ *m/z* calcd 1011.3779 for $C_{56}H_{60}O_{16}Na$, found 1011.3785; anal. calcd for $C_{56}H_{60}O_{16}$ (989.0660): C, 68.00; H, 6.11; O, 25.88. Found: C, 68.35; H, 6.25.

[9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl]3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (16c). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.34–1.44 (m, 2H), 1.54–1.66 (m, 4H), 1.92–2.09 (m, 4H), 3.33–3.46 (m, 3H), 3.64–3.75 (m, 1H), 3.81–3.87 (m, 1H), 4.00 (dd, *J* = 9.3, 3.1 Hz, 1H), 3.92–3.97 (m, 1H), 4.20 (dd, *J* = 11.9, 4.4 Hz, 1H), 4.22–4.27 (m, 2H), 4.44–4.47 (m, 2H), 4.52 (dd, *J* = 11.8, 3.9 Hz, 1H), 4.55–4.63 (m, 1H), 4.67–4.76 (m, 2H), 4.88–4.94 (m, 1H), 5.33–5.44 (m, 4H), 5.79 (dd, *J* = 3.2, 1.7 Hz, 1H), 5.86 (dd, *J* = 3.1, 1.8 Hz, 1H), 6.00 (dd, *J* = 9.7, 3.5 Hz, 1H), 6.02 (dd, *J* = 9.6, 3.4 Hz, 1H), 6.10–6.18 (m, 2H), 7.22–8.15 (m, 45H). ^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 26.1, 29.3, 32.4, 63.0, 63.4, 65.8, 66.8, 66.9, 67.0, 67.5, 68.9, 69.5, 70.2, 70.4, 70.5, 70.6 (×2), 70.8, 71.7, 72.9 (×2), 82.9, 97.7, 99.9, 100.0, 127.5 (×3), 127.7 (×3), 128.3 (×3), 128.4 (×7), 128.5 (×3), 128.6 (×3), 128.9, 129.1 (2), 129.2, 129.3, 129.4, 129.6, 129.8 (×6), 129.9 (×9), 130.0 (3), 130.8, 133.1 (×2), 133.2, 133.3, 133.4 (×2), 133.5 (×2), 138.7, 165.4, 165.5, 165.6, 165.7 (×2), 165.9, 166.3, 166.4. ESI-HRMS: $[M + NH_4]^+$ *m/z* calcd 1584.5801 for $C_{90}H_{90}O_{25}N$, found 1584.5727; $[M + H]^+$ *m/z* calcd 1567.5536 for $C_{90}H_{87}O_{25}$, found 1567.5433. Anal. calcd for $C_{90}H_{86}O_{25}$ (1567.6308): C, 68.96; H, 5.53; O, 25.52; found: C, 68.63; H, 5.77.

[9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl]6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (19). Following the general procedure for glycosylation the NPOE **18** (311 mg, 0.5 mmol) and disaccharide **15c** (200 mg, 0.2 mmol) were dissolved in CH_2Cl_2 (10 mL), and treated for 15 min with NIS (112 mg, 0.5 mmol) and $BF_3{\cdot}Et_2O$ (2.5 μL, 0.02 mmol) at −25 °C. After work-up and column chromatography (hexane/EtOAc, 8/2 to EtOAc), trisaccharide **19** (130 mg, 43%, 63% corrected) and recovered disaccharide **15c** (64 mg, 32%) were obtained. For **19**: ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.25–1.37 (m, 2H), 1.46–1.54 (m, 2H), 1.55–1.65 (m, 2H), 1.86–1.93 (m, 2H), 1.94–2.05 (m, 2H), 3.31–3.35 (m, 1H), 3.35 (t, *J* = 6.6 Hz, 2H), 3.56 (dd, *J* = 9.9, 7.4 Hz, 1H), 3.65–3.74 (m, 2H), 3.75–3.83 (m, 3H), 3.86 (dd, *J* = 11.0, 1.7 Hz, 1H), 3.92 (t, *J* = 9.6 Hz, 1H), 4.00 (dd, *J* = 11.0, 8.0 Hz, 1H), 4.09 (m, 2H), 4.24–4.30 (m, 1H), 4.38 (t, *J* = 8.0 Hz, 1H), 4.40–4.45 (m, 2H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.49–4.52 (m, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.57 (d, *J* = 1.5 Hz, 1H), 4.62 (dd, *J* = 12.1, 2.5 Hz, 1H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.79 (d, *J* = 11.1 Hz, 1H), 5.15 (d, *J* = 1.9 Hz, 1H), 5.16 (d, *J* = 2.0 Hz, 1H), 5.28–5.39 (m, 2H), 5.55 (dd, *J* = 3.2, 2.0 Hz, 1H), 5.68 (dd, *J* = 3.2, 1.9 Hz, 1H), 5.88 (dd, *J* = 10.1, 3.2 Hz, 1H), 6.06 (t, *J* = 10.1 Hz, 1H), 7.09–8.07 (m, 45H); ^{13}C-NMR (75 MHz, $CDCl_3$) *δ*: 26.0, 29.1, 29.2, 29.3, 32.3, 62.8, 65.9, 66.9, 67.1, 67.2, 69.2, 69.5, 69.8, 69.9, 70.3, 70.6, 71.2, 71.8, 72.0, 72.8, 73.5, 74.6, 74.8, 78.1, 82.3, 97.5, 99.0, 100.3, 127.4, 127.5 (×2), 127.6, 127.7, 127.8, 127.9 (×3), 128.1 (×3), 128.2, 128.3 (×7), 128.4 (×6), 128.5 (×2), 129.0, 129.1, 129.3, 129.6 (×2), 129.7 (×6), 129.8 (×4), 129.9 (×2), 130.6, 132.9, 133.0, 133.2, 133.8 (×2), 137.4, 137.7, 138.0, 138.6, 165.2, 165.3, 165.7, 166.2. ESI-HRMS: $[M + Na]^+$ *m/z* calcd 1547.5978 for $C_{90}H_{92}O_{22}Na$, found 1548.6020. Anal. calcd for $C_{90}H_{92}O_{22}$ (1525.6803): C, 70.85; H, 6.08; O, 23.07; found: C, 70.45; H, 6.33. The structure of the disaccharide **19** was determined by acylation and ^{1}H NMR analysis of the newly downshifted protons ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.33–1.44 (m, 2H), 1.51–1.61 (m, 2H), 1.62–1.72 (m, 2H), 1.92–2.00 (m, 2H), 2.02–2.09 (m, 2H), 2.10 (s, 3H), 2.20 (s, 3H), 3.41 (t, *J* = 6.6 Hz, 2H), 3.43–3.48 (m, 1H), 3.64–3.69 (m, 1 H), 3.71–3.79 (m, 2H), 3.81–3.84 (m, 1H), 3.87 (dd, *J* = 10.6, 3.0 Hz, 1H), 3.90–3.96 (m, 2H), 4.01 (dd,

J = 9.5, 3.1 Hz, 1H), 4.15 (t, J = 9.6 Hz, 1H), 4.23 (dd, J = 10.0, 3.2 Hz, 1H, H-3), 4.43–4.52 (m, 4H), 4.54 (d, J = 11.3 Hz, 1H), 4.59 (d, J = 11.4 Hz, 1H), 4.67–4.71 (m, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 11.4 Hz, 1H), 4.82 (d, J = 1.8 Hz, 1H), 4.85 (d, J = 11.1 Hz, 1H), 5.13 (d, J = 2.0 Hz, 1H), 5.14 (d, J = 1.7 Hz, 1H), 5.21 (dd, J = 3.3, 1.8 Hz, 1H, H-2), 5.34–5.42 (m, 3H, H-4), 5.44 (dd, J = 2.0, 1.7 Hz, 1H), 5.74 (dd, J = 3.3, 1.8 Hz, 1H), 5.92 (dd, J = 10.1, 3.3 Hz, 1H), 6.12 (t, J = 10.1 Hz, 1H), 7.17–8.13 (m, 45H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 21.0, 21.1, 26.2, 29.3, 29.4 (×2), 32.5, 62.9, 66.8, 66.9, 67.9, 68.0, 68.7, 69.0, 69.3, 69.6, 70.1, 70.4 (×2), 71.7, 71.8, 72.5, 72.9, 73.5, 74.0, 75.0, 76.1, 77.7, 97.2, 97.6, 100.5, 127.5 (×2), 127.6 (×4), 127.7 (×2), 128.0 (×2), 128.1 (×2), 128.3 (×3), 128.4 (×5), 128.5 (×5), 128.6 (×4), 128.7 (×2), 129.1, 129.3, 129.4, 129.6 (×2), 129.8 (×3), 129.9 (×3), 130.0 (×2), 131.0, 133.2 (×2), 133.3, 133.5, 133.6, 138.0, 138.6, 138.7, 138.8, 165.3, 165.4, 165.6, 165.9, 166.3, 170.2, 170.7.

[9-*O*-Benzyl-4-(*Z*,*E*)-nonenyl]-6-*O*-(-α-D-mannopyranosyl)-3-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (20). This compound was prepared from **19** (130 mg, 0.085 mmol) following the general procedure for debenzoylation. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 9/1) to give **20** (73 mg, 86%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.26–1.67 (m, 6H), 1.84–2.06 (m, 4H), 3.10–3.28 (m, 2H), 3.38–3.67 (m, 5H), 3.68–4.08 (m, 8H), 4.22–4.41 (m, 3H), 4.46–4.79 (m, 8H), 4.87 (*bs*, 1H), 5.18–5.25 (m, 2H), 5.26–5.42 (m, 2H), 7.01–7.44 (m, 20H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 26.2, 29.2, 29.4, 32.5, 61.4, 65.4, 66.7, 67.3, 68.7, 69.4, 70.4, 70.6, 71.3, 71.5, 71.7, 72.3, 72.9, 73.0, 73.5, 74.1, 75.0, 77.3, 79.4, 100.0, 100.2, 101.7, 127.6 (×2), 127.7 (×2), 127.8 (×2), 128.0 (×2), 128.1 (×4), 128.4 (×4), 128.5 (×4), 129.7, 130.7, 137.7, 138.0, 138.5, 138.7. ESI-HRMS: $[M + Na]^+$ m/z calcd 1027.4667 for $C_{55}H_{72}O_{17}Na$, found 1027.4663. Anal. calcd for $C_{55}H_{72}O_{17}$ (1005.15): C, 65.72; H, 7.22; O, 27.06. Found: C, 65.55; H, 7.35.

Glycosylation reaction of heptaol trisaccharide 20 with NPOE 18. Following the general procedure for glycosylation, the NPOE **18** (163 mg, 0.26 mmol) and heptaol trisaccharide **20** (44 mg, 0.044 mmol) were dissolved in CH_2Cl_2 (7 mL), and treated with NIS (58 mg, 0.26 mmol) and $BF_3{\cdot}Et_2O$ (0.6 µL, 0.0044 mmol) at −15 °C. After work-up and column chromatography (hexane/EtOAc, 8/2 to EtOAc), pentasaccharide **21** (40 mg, 44%) and tetrasaccharide **22** (26 mg, 38%) were obtained. For **21**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.15–1.22 (m, 2H), 1.29–1.37 (m, 2H), 1.49–1.55 (m, 2H), 1.86–1.98 (m, 4H), 3.22–3.27 (m, 1H), 3.37 (t, J = 6.6 Hz, 2H), 3.44–3.58 (m, 7H), 3.64–3.91 (m, 13H), 3.94–4.09 (m, 5H), 4.15 (m, 1H), 4.18–4.22 (m, 1H), 4.37–4.52 (m, 12H), 4.57 (d, J = 11.4 Hz, 1H), 4.59–4.62 (m, 2H), 4.64 (d, J = 12.1 Hz, 1H), 4.69–4.79 (m, 8H), 4.91 (bs, 1H), 5.02 (bs, 1H), 5.14 (bs, 1H), 5.25–5.35 (m, 2H), 5.54 (bs, 1H), 5.67 (bs, 1H), 7.07–7.99 (60H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 26.2, 29.2, 29.4, 29.5, 32.5, 65.5, 65.8, 66.1, 66.9, 67.2, 68.7, 69.0, 69.1, 69.2, 69.7 (×2), 69.9, 70.4, 70.8, 71.0, 71.6 (×2), 71.7, 72.0 (×2), 72.2, 72.9, 73.0, 73.4, 73.7 (×2), 74.4, 74.7, 74.8, 74.9, 75.0, 75.4, 78.3, 78.4, 80.1, 81.8, 81.9, 97.6, 98.9, 100.3, 100.7, 101.4, 127.6 (×4), 127.7 (×6), 127.8 (×2), 127.9 (×4), 128.0 (×6), 128.1 (×4), 128.2 (×3), 128.3 (×4), 128.4 (×3), 128.5 (×10), 128.6 (×7), 128.7 (×5), 129.7, 130.0, 130.1, 130.8, 133.2, 133.3, 137.6, 137.7, 138.0 (×2), 138.2 (×2), 138.3, 138.4, 138.5, 138.8, 165.8, 166.0. ESI-HRMS: $[M + NH_4]^+$ m/z calcd 2094.9511 for $C_{123}H_{140}O_{29}N$, found 2096.5679. Anal. calcd for $C_{123}H_{136}O_{29}$ (2078.38): C, 69.33; H, 6.80; O, 23.87. Found: C, 69.66; H, 6.95. The structure of the pentasaccharide **21** was confirmed by acylation and ^{1}H NMR analysis of the newly downshifted protons: ^{1}H-NMR (500 MHz, $CDCl_3$, selected signals) δ: 5.11 (dd, J = 3.5, 1.7 Hz, 1H, H-2), 5.13 (dd, J = 3.3, 1.9 Hz, 1H, H-2), 5.21 (dd, J = 3.6, 1.6 Hz, 1H, H-2), 5.22 (t, J = 10.0 Hz, 1H, H-4), 5.38 (t, J = 10.6 Hz, 1H, H-4). For **22**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.39–1.46 (m, 2H), 1.56–1.64 (m, 4H), 1.97–2.07 (m, 4H), 3.26–3.34 (m, 1H), 3.46 (t, J = 6.6 Hz, 2H), 3.47–3.51 (m, 1H), 3.56–3.64 (m, 6H), 3.73–3.89 (m, 7H), 3.90–3.97 (m, 3H), 3.99–4.09 (m, 5H), 4.12 (dd, J = 10.1, 3.2 Hz, 1H), 4.15 (t, J = 10.2 Hz, 1H), 4.45 (d, J = 11.2 Hz, 1H), 4.46 (d, J = 11.8 Hz, 1H), 4.48–4.54 (m, 5H), 4.56 (d, J = 11.5 Hz, 1H), 4.66 (m, 2H), 4.67 (d, J = 12.0 Hz, 1H), 4.76 (d, J = 11.3 Hz, 1H), 4.78 (d, J = 11.2 Hz, 1H), 4.84 (bs, 1H), 4.85 (d, J = 10.6 Hz, 1H), 4.98 (*b*s, 1H), 5.09 (*b*s, 1H), 5.40 (m, 2H), 5.70 (dd, J = 3.0, 1.9 Hz, 1H), 7.10–8.10 (m, 40H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 26.3, 29.3, 29.5, 29.6, 32.6, 65.4, 65.8, 67.0, 67.4, 68.0, 69.0, 69.3, 69.4 (×2), 69.6, 69.9, 70.5 (×2), 70.6, 70.9, 71.2, 71.7 (×2), 71.9, 72.2, 72.5, 73.1, 73.6, 73.8, 74.5, 74.9, 75.0, 75.5, 78.4, 80.1, 82.2, 97.8, 99.7, 100.8, 101.3, 127.7 (×3), 127.8 (×2), 127.9 (×3), 128.0, 128.1 (×4), 128.2 (×2), 128.3 (×5), 128.5 (×5), 128.6 (×6), 128.7 (×4), 129.8, 130.1, 130.2 (×2), 130.9, 133.4, 137.6, 138.0, 138.1, 138.3, 138.4, 138.5, 138.8, 166.2. ESI-HRMS: $[M + Na]^+$ m/z calcd 1563.6866 for $C_{89}H_{104}O_{23}Na$, found 1564.8234. Anal. calcd for $C_{89}H_{104}O_{23}$ (1541.76): C, 69.33; H, 6.80; O, 23.87. Found: C, 69.66; H, 6.95.

Glycosylation reaction of tetrasaccharide 22 with NPOE 18. Following the general procedure for glycosylation, the NPOE **18** (16 mg, 0.026 mmol) and tetrasaccharide **22** (20 mg, 0.0129 mmol) were dissolved in CH_2Cl_2 (3 mL), and treated with NIS (5.8 mg, 0.026 mmol) and $BF_3{\cdot}Et_2O$ (0.3 µL, 0.0026 mmol) at −15 °C. After work-up and column chromatography (hexane/EtOAc, 1/1), pentasaccharide **21** (14 mg, 52%) was obtained.

Acetylation followed by CM with ethylene of pentasaccharide 21. Pentasaccharide **21** (12.5 mg) was acetylated following usual conditions (Ac_2O, pyr) to give acetylated derivative **23**. Argon was then bubbled through a solution of **23** (14 mg, 0.006 mmol) in CH_2Cl_2 (2 mL) and subsequently treated with Grubbs' catalyst (1 mg, 0.0012 mmol). The reaction mixture was purged with ethylene and stirred (rt, 12 h). The residue was filtered through a Florisil pad and purified by flash chromatography (hexane/EtOAc, 7/3) to afford *n*-pentenyl pentasaccharide **24** (12 mg, 94%). Foam. $[\alpha]_D$ = +22.9 (c 1.0, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.55–1.65 (m, 2H), 1.99 (s, 3H), 2.02–2.11 (m, 2H), 2.09 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H), 3.35 (dt, J = 9.7, 6.3 Hz, 1H), 3.46–3.51 (m, 1H), 3.59–3.81 (m, 11H), 3.83 (dd, J = 9.5, 3.3 Hz, 1H), 3.87–3.95 (m, 5H), 4.00 (dd, J = 9.5, 3.0 Hz, 1H), 4.06–4.20 (m, 5H), 4.40–4.48 (m, 3H), 4.50–4.89 (m, 20H), 4.91–4.99 (m, 2H), 4.97 (d,

J = 1.8 Hz, 1H), 5.06 (d, J = 1.9 Hz, 1H), 5.07 (d, J = 2.0 Hz, 1H), 5.11 (dd, J = 3.4, 1.7 Hz, 1H), 5.12 (dd, J = 3.3, 1.6 Hz, 1H), 5.20 (t, J = 10.0 Hz, 1H), 5.21 (dd, J = 3.4, 1.7 Hz, 1H), 5.37 (t, J = 10.0 Hz, 1H), 5.41 (dd, J = 3.0, 2.0 Hz, 1H), 5.66 (dd, J = 3.0, 1.9 Hz, 1H), 5.72 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 7.11–8.07 (m, 55H). ^{13}C-NMR (75 MHz) δ: 20.9, 21.9 (×2), 21.1, 21.2, 28.5, 30.3, 65.8, 66.5, 67.6, 67.7, 68.1, 68.5, 68.7, 69.0, 69.2 (×2), 69.3, 69.6, 69.7, 71.4, 71.7 (×2), 71.9 (×2), 72.0, 72.2, 72.7, 73.5 (×3), 73.9, 74.0, 74.3, 75.0, 75.1, 75.3, 75.8, 76.4, 77.4 (×2), 78.5, 97.1, 97.2, 98.1, 100.4 (×2), 115.2, 127.5 (×4), 127.6 (×5), 127.7 (×4), 127.8 (×4), 127.9 (×4), 128.0 (×3), 128.1 (×5), 128.2 (×3), 128.3 (×5), 128.4 (×6), 128.5 (×10), 130.0, 130.1, 133.2, 133.3, 138.0, 138.1, 138.2, 138.3, 138.6 (×2), 138.7 (×2), 165.7, 165.8, 169.8, 170.0, 170.5, 170.6 (×2). ESI-HRMS: $[M + NH_4]^+$ m/z calcd 2142.8995 for $C_{122}H_{136}O_{33}N$, found 2143.8892. Anal. calcd for $C_{122}H_{132}O_{33}$ (2124.86): C, 68.91; H, 6.26; O, 24.83. Found: C, 68.76; H, 6.63.

Acknowledgements

This research has been supported with funds from the *Ministerio de Ciencia e Innovación* and *Comunidad de Madrid* grants CTQ2009-10343 and S2009/PPQ-1752, respectively. BFR thanks the *National Science Foundation*, grant CHE 0717702. We also thank Ms Marina Rodríguez (IQOG) for skillful technical support.

Notes and references

1 (*a*) *Essentials in Glycobiology*, ed. A. varki, T. Cummings, J. Esko, H. Freeze, G. Hart and J. Marth, Cold Spring Harbor Laboratory Press, Plainview, 1999; (*b*) V. Wittman, in *Glycoscience*, ed. B. Fraser-Reid, K. Tatsuta and J. Thiem, Springer-Verlag, Berlin, Germany, 2008, p. 135.

2 (*a*) S. J. van Vliet, C. Grun and Y. van Kooyk, in *Protein-carbohydrate Interactions in Infectious Diseases*, ed. C. A. Bewly, RSC Publishing, Oxford, UK, 2006, p. 106; (*b*) J. Epstein, Q. Eichbaum, S. Sheriff and R. A. B. Ezekowitz, *Curr. Opin. Immunol.*, 1996, **8**, 29.

3 B. Becker, R. H. Furneaux, F. Reck and O. A. Zubkov, *Carbohydr. Res.*, 1999, **315**, 148–158.

4 E. W. Adams, D. M. Ratner, P. H. Seeberger and N. Hacohen, *ChemBioChem*, 2008, **9**, 294–303.

5 Oligomannose glycans are also recognized as ligands for DC-SIGN a C-type lectin found on the surface of dendritic cells. See: (*a*) H. Feinberg, D. A. Mitchell, K. Drickamer and W. I. Weis, *Science*, 2001, **294**, 2163–2166; (*b*) Y. Guo, H. Feinberg, E. Conroy, D. A. Mitchell, R. Alvarez, O. Blixt, M. E. Taylor, W. I. Weis and K. Drickamer, *Nat. Struct. Mol. Biol.*, 2004, **11**, 591–598; (*c*) D. A. Mitchell, A. J. Fadden and K. Drickamer, *J. Biol. Chem.*, 2001, **276**, 28939–28945.

6 (*a*) R. D. Astronomo and D. R. Burton, *Nat. Rev. Drug Discovery*, 2010, **9**, 308–324; (*b*) L. Morelli, L. Poletti and L. Lay, *Eur. J. Org. Chem.*, 2011, 5723–5777.

7 (*a*) A. Buchacher, R. Predl, K. Strutzenberger, W. Steinfellner, A. Trkola, M. Purtscher, G. Gruber, C. Tauer, F. Steindl, A. Junbauer and H. Katinger, *AIDS Res. Hum. Retroviruses*, 1994, **10**, 359–369; (*b*) A. Trkola, M. Purtscher, T. Muster, C. Ballaun, A. Buchacher, N. Sullivan, K. Srinivasan, J. Sodroski, J. P. Moore and H. Katinger, *J. Virol.*, 1996, **70**, 1100–1108; (*c*) C. N. Scanlan, R. Pantophlet, M. R. Wormald, E. O. Saphire, R. Stanfield, I. A. Wilson, H. Katinger, R. A. Dwek, P. M. Rudd and D. R. Burton, *J. Virol.*, 2002, **76**, 7306–7321.

8 D. A. Calarese, C. N. Scanlan, M. B. Zwick, S. Deechongkit, Y. Mimura, R. Kunert, P. Zhu, M. R. Wormald, R. L. Stanfield, K. H. Roux, J. W. Kelly, P. M. Rudd, R. A. Dwek, H. Katinger, D. R. Burton and I. A. Wilson, *Science*, 2003, **300**, 2065–2071.

9 (*a*) V. Y. Dudkin, M. Orlova, X. Geng, M. Mandal, W. C. Olson and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2004, **126**, 9560–9562; (*b*) I. J. Krauss, J. G. Joyce, A. C. Finnefrock, H. C. Song, V. Y. Dudkin, X. Geng, J. D. Warren, M. Chastain, J. W. Shiver and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2007, **129**, 11042–11044; (*c*) J. G. Joyce, I. J. Krauss, H. C. Song, D. W. Opalka, K. M. Grimm, D. D. Nahas, M. T. Esser, R. Hrin, M. Feng, V. Y. Dudkin, M. Chastain, J. W. Shiver and S. J. Danishefsky, *Proc. Natl. Acad. Sci. U. S. A.*, 2008, **105**, 15684–15689.

10 (*a*) D. A. Calarese, H.-K. Lee, C.-Y. Huang, M. D. Best, R. D. Astronomo, R. L. Stanfield, H. Katinger, D. R. Burton, C.-H. Wong and I. A. Wilson, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 13372–13377; (*b*) S.-K. Wang, P.-H. Liang, R. D. Astronomo, T.-L. Hsu, S.-L. Hsieh, D. R. Burton and C.-H. Wong, *Proc. Natl. Acad. Sci. U. S. A.*, 2008, **105**, 3690–3695.

11 K. J. Doores, Z. Fulton, V. Hong, M. K. Patel, C. N. Scanlan, M. R. Wormald, M. G. Finn, D. R. Burton, I. A. Wilson and B. G. Davis, *Proc. Natl. Acad. Sci. U. S. A.*, 2010, **107**, 17107–17112.

12 (*a*) M. Marradi, P. Di Gianvincenzo, P. M. Enriquez-Navas, O. M. Martinez-Avila, F. Chiodo, E. Yuste, J. Angulo and S. Penades, *J. Mol. Biol.*, 2011, **410**, 798–810; (*b*) P. M. Enriquez-Navas, M. Marradi, D. Padro, J. Angulo and S. Penades, *Chem.–Eur. J.*, 2011, **17**, 1547–1560; (*c*) O. Martinez-Avila, L. M. Bedoya, M. Marradi, C. Clavel, J. Alcami and S. Penades, *Chem. Bio. Chem*, 2009, **10**, 1806–1809.

13 P. Grice, S. V. Ley, J. Pietruszka, H. M. I. Osborn, H. W. M. Priepke and S. L. Warriner, *Chem.–Eur. J.*, 1997, **3**, 431–440.

14 J. R. Merritt, E. Naisang and B. Fraser-Reid, *J. Org. Chem.*, 1994, **59**, 4443–4449.

15 See for example: (*a*) L. Jiang, T. H. Chan and T. K. Nokami, *Can. J. Chem.*, 2005, **83**, 693–701; (*b*) H. Tsuyama, A. Shibuya, T. Nakatsutsumi and J. Yoshida, *Chem. Lett.*, 2008, **37**, 942–943; (*c*) A. Pastore, M. Adinolfi, A. Iadonisi and S. Valerio, *Eur. J. Org. Chem.*, 2010, 711–718; (*d*) M. Takatani and Y. Ito, *Chem.–Asian J.*, 2006, **1–2**, 64–75; (*e*) R. Blattner, R. H. Furneaux and M. Ludewig, *Carbohydr. Res.*, 2006, **341**, 299–321; (*f*) S. N. Lam and J. Gervay-Hague, *J. Org. Chem.*, 2005, **70**, 8772–8779; (*g*) Y. Du, M. Zhang and F. Kong, *Tetrahedron*, 2001, **57**, 1757–1763; (*h*) I. Matsuo, M. Wada, S. Manabe, Y. Yamaguchi, K. Otake, K. Kato and Y. Ito, *J. Am. Chem. Soc.*, 2003, **125**, 3402–3403; (*i*) K. Totani, Y. Ihara, I. Matsuo, H. Koshino and Y. Ito, *Angew. Chem., Int. Ed.*, 2005, **44**, 7950–7954.

16 (*a*) B. Fraser-Reid, J. Lu, K. N. Jayaprakash and J. C. Lopez, *Tetrahedron: Asymmetry*, 2006, **17**, 2449–2463; (*b*) B. Fraser-Reid, J. C. Lopez, K. V. Radhakrishnan, N. Nandakumar, A. M. Gomez and C. Uriel, *Chem. Commun.*, 2002, 2104–2105; (*c*) B. Fraser-Reid, J. C. Lopez, A. M. Gomez and C. Uriel, *Eur. J. Org. Chem.*, 2004, 1387–1395; (*d*) C. Uriel, A. M. Gomez, J. C. López and B. Fraser-Reid, *Eur. J. Org. Chem.*, 2009, 403–411.

17 (*a*) G.-J. Boons, *Tetrahedron*, 1996, **52**, 1095–1121; (*b*) A. V. Demchenko, *Lett. Org. Chem.*, 2005, **2**, 580–589; (*c*) X. Zhu and R. R. Schmidt, *Angew. Chem., Int. Ed.*, 2009, **48**, 1900–1934.

18 P. Cmoch and Z. Pakulski, *Tetrahedron: Asymmetry*, 2008, **19**, 1494–1503.

19 C. Uriel, A. Agocs, A. M. Gomez, J. C. Lopez and B. Fraser-Reid, *Org. Lett.*, 2005, **7**, 4899–4902.

20 J. C. Lopez, A. Agocs, C. Uriel, A. M. Gomez and B. Fraser-Reid, *Chem. Commun.*, 2005, 5088–5090.

21 (*a*) T. W. D. F. Rising, T. D. W. Claridge, N. Davies, D. P. Gamblin, J. W. B. Moir and A. J. Fairbanks, *Carbohydr. Res.*, 2006, **341**, 1574–1596; (*b*) T. W. D. F. Rising, C. D. Heidecke, J. W. B. Moir, Z. Ling and A. J. Fairbanks, *Chem.–Eur. J.*, 2008, **14**, 6444–6464.

22 S. Nakabayashi, C. D. Warren and R. W. Jeanloz, *Carbohydr. Res.*, 1988, **174**, 279–289.

23 Y. Zhu, L. Chen and F. Kong, *Carbohydr. Res.*, 2002, **337**, 207–215.

24 L. V. Backinowsky, P. I. Abronina, A. S. Shashkov, A. A. Grachev, N. K. Kochetkov, S. A. Nepogodiev and J. F. Stoddart, *Chem.–Eur. J.*, 2002, **8**, 4412–4423.

25 D. M. Ratner, O. J. Plante and P. H. Seeberger, *Eur. J. Org. Chem.*, 2002, 826–833.

26 K. N. Jayaprakash, K. V. Radhakrishnan and B. Fraser-Reid, *Tetrahedron Lett.*, 2002, **43**, 6953–6955.

27 C. Uriel, A. M. Gomez, J. C. Lopez and B. Fraser-Reid, *Synlett*, 2003, 2203–2207.

28 J. M. Llera, J. C. Lopez and B. Fraser-Reid, *J. Org. Chem.*, 1990, **55**, 2997–2998.

29 (*a*) R. H. Grubbs, *Handbook of Metathesis*, Wiley-VCH Verlag GmbH & Co. KgaA, Weinheim, Germany, 2003, vol. 1–3; (*b*) R. H. Grubbs, R. R. Schrock and A. Fürstner, *Advanced Synthesis & Catalysis, Olefin Metathesis*, Wiley-VCH Verlag GmbH & Co. KgaA, Weinheim, Germany, 2007, vol. 349, pp. 1–265; (*c*) J. Cossy, S. Arseniyadis and C. Meyer, *Metathesis in Natural Product Synthesis: Strategies, Substrate and Catalysts*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2010.

30 Recent reviews: (*a*) R. Madsen, *Eur. J. Org. Chem.*, 2007, 399–415; (*b*) A. Aljarilla, J. C. Lopez and J. Plumet, *Eur. J. Org. Chem.*, 2010, 6123–6143.

31 Q. Wan, Y. S. Cho, T. H. Lambert and S. J. Danishefsky, *J. Carbohydr. Chem.*, 2005, **24**, 425–440.

32 M. Mach, U. Schlueter, F. Mathew, B. Fraser-Reid and K. C. Hazen, *Tetrahedron*, 2002, **58**, 7345–7354.

33 P. Schwab, M. B. France, J. W. Ziller and R. H. Grubbs, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2039–2041.

34 Glycosides **11** and saccharides obtained therefrom appear as a single spot in thin layer chromatography (hexane/ethyl acetate). In these derivatives, the pyranosidic core does not show duplicate signals in their ^{1}H-NMR spectra.

35 (*a*) S. H. Rang and S. B. Lee, *Tetrahedron Lett.*, 1993, **34**, 7579–7582; (*b*) I. Marek, J.-M. Lefrançois and J.-F. Normant, *Tetrahedron Lett.*, 1992, **33**, 1747–1748.

36 For related cross-metathesis on NPG-derivatives with ethylene, see: R. B. Andrade, O. J. Plante, L. G. Melean and P. H. Seeberger, *Org. Lett.*, 1999, **1**, 1811–1814.

37 D. R. Mootoo, V. Date and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1988, **110**, 2662–2663.

38 T. Buskas, E. Söderberg, P. Konradsson and B. Fraser-Reid, *J. Org. Chem.*, 2000, **65**, 958–963.

39 (*a*) J. R. Allen, C. R. Harris and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2001, **123**, 1890–1897; (*b*) J. R. Allen, J. G. Allen, X.-F. Zhang, L. J. Williams, A. Zatorski, G. Ragupathi, P. O. Livingston and S. J. Danishefsky, *Chem.–Eur. J.*, 2000, **6**, 1366–1375; (*c*) J. R. Allen and S. J. Danishefsky, *J. Am. Chem. Soc.*, 1999, **121**, 10875–10882.

40 NPGs as a source of glycoconjugate polymers: (*a*) A. Miyagawa, H. Kurosawa, T. Watanabe, T. Koyama, D. Terunuma and K. Matsuoka, *Carbohydr. Polym.*, 2004, **57**, 441–450; (*b*) S.-I. Nishimura, K. Matsuoka, T. Furuike, K. Maruyama, K. Nagata, K. Kurita, N. Nishi and S. Tokura, *Macromolecules*, 1994, **27**, 4876–4880; (*c*) S.-I. Nishimura, K. Matsuoka, T. Furuike, S. Ishii, K. Kurita and K. M. Nishimura, *Macromolecules*, 1991, **24**, 4236–4241; (*d*) S.-I. Nishimura, K. Matsuoka and K. Kurita, *Macromolecules*, 1990, **23**, 4182–4184.

41 I. Cumpstey, T. D. Butters, R. J. Tennant-Eyles, A. J. Fairbanks, R. R. France and M. R. Wormald, *Carbohydr. Res.*, 2003, **338**, 1937–1949.

42 M. H. Clausen and R. Madsen, *Carbohydr. Res.*, 2004, **339**, 2159–2169.

43 (*a*) J. L. de Paz, C. Noti and P. H. Seeberger, *J. Am. Chem. Soc.*, 2006, **128**, 2766–2767; (*b*) C. Noti, J. L. de Paz, L. Polito and P. H. Seeberger, *Chem.–Eur. J.*, 2006, **12**, 8664–8686.

44 J. Lu, B. Fraser-Reid and C. Gowda, *Org. Lett.*, 2005, **7**, 3841–3843.

45 (*a*) A. Yamada, K. Hatano, T. Koyama, K. Matsuoka, N. Takahashi, K. I. P. J. Hidari, T. Suzuki, Y. Suzuki and D. Terunuma, *Bioorg. Med. Chem.*, 2007, **15**, 1606–1614; (*b*) A. Yamada, K. Hatano, T. Koyama, K. Matsuoka, Y. Esumi and D. Terunuma, *Carbohydr. Res.*, 2006, **341**, 467–473.

46 (*a*) S. M. Rele, S. S. Iyer, S. Baskaran and E. L. Chaikof, *J. Org. Chem.*, 2004, **69**, 9159–9170; (*b*) S. S. Iyer, S. M. Rele, S. Baskaran and E. L. Chaikof, *Tetrahedron*, 2003, **59**, 631–638.

47 For the use of NPGs as intermediates in the incorporation of oligosaccharides to gold nanoparticles, see: (*a*) O. Martinez-Avila, K. Hijazi, M. Marradi, C. Clavel, C. Campion, C. Kelly and S. Penades, *Chem.–Eur. J.*, 2009, **15**, 9874–9888; (*b*) Y.-Y. Chien, M.-D. Jan, A. K. Adak, H.-C. Tzeng, Y.-P. Lin, Y.-J. Chen, K.-T. Wang, C.-T. Chen, C.-C. Chen and C.-C. Lin, *ChemBioChem*, 2008, **9**, 1100–1109; (*c*) C.-C. Lin, Y.-C. Yeh, C.-Y. Yang, C.-L. Chen, G.-F. Chen, C.-C. Chen and Y.-C. Wu, *J. Am. Chem. Soc.*, 2002, **124**, 3508–3509.

48 A. J. Ratcliffe, P. Konradsson and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1990, **112**, 5665–5667.

49 F. S. Ekholm, M. Poláková, A. J. Pawlowicz and R. Leino, *Synthesis*, 2009, 567–576.

50 D. W. Dias and M. A. Kerr, *Org. Lett.*, 2009, **11**, 3694–3697.

51 C. Cook, X. Guinchard, F. Liron and E. Roulland, *Org. Lett.*, 2010, **12**, 744–747.

52 V. Rawat, P. V. Chouthaiwale, G. Suryavanshi and A. Sudalai, *Tetrahedron: Asymmetry*, 2009, **20**, 2173–2177.

53 K. N. Jayaprakash and B. Fraser-Reid, *Org. Lett.*, 2004, **6**, 4211–4214.

