Exploiting the cross-metathesis reaction in the synthesis of pseudo-oligosaccharides†‡

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An approach to the synthesis of pseudo-oligosaccharides based on the cross-metathesis reaction between distinct sugar-olefins, followed by intramolecular cyclization of the obtained heterodimer, is presented. In particular, the relative efficiency of two alternative approaches, the straightforward cross-metathesis reaction and the two-step procedure (self-metathesis followed by cross- metathesis), was explored and compared for diverse sugar-olefin substrates. Some representative examples of intramolecular cyclization using iodine as an electrophilic promoter, are also reported.

Introduction

Carbohydrates are primarily involved in many biological processes and a wide number of cellular recognition phenomena.[1] Because of their biological importance and unique chemical features, synthetic medicinal chemistry shows a growing interest towards these molecules.[2] Although excellent progress has been made by modern carbohydrate chemistry, the development of saccharide-based drugs using classical carbohydrate synthesis can be still a difficult task.[3] There is therefore a strong demand for general and efficient approaches to sugar mimics endowed with very similar biological properties, but structurally and synthetically simpler than their natural counterparts.

During the last years transition metal catalyzed olefin metathesis has undoubtedly gained a prominent role in modern synthetic organic chemistry.[4] In particular, the recent availability of robust and well-defined ruthenium alkylidene-based pre-catalysts,[5–7] endowed with high reactivity, air-stability and impressive functional-group tolerance has made olefin metathesis an extremely powerful and versatile tool for the construction of carbon–carbon bonds in the most diverse molecular architectures. Most applications of olefin metathesis in synthetic organic chemistry employ the more entropically favoured ring-closing metathesis (RCM), while the intermolecular cross-metathesis (CM) has received much less attention from the scientific community. This holds true in the field of carbohydrate chemistry.[8] Many reports describe the application of the RCM reaction for the synthesis of carbocycles and other carbohydrate derivatives,[9] while there are relatively few examples of CM applied to mono- and oligosaccharide building blocks.[10] The main reason is the poor selectivity often exhibited by CM reactions, due to the formation of undesired self-metathesis products and the difficult control of the configuration at the newly formed double bond (*E*/*Z* ratio). Nonetheless, the advent of the new ruthenium alkylidene complexes mentioned above led to the increasing application of the CM reaction in the total synthesis of natural products.[4] It should be specifically noticed that many applications of the CM reaction in the field of carbohydrates are limited to the homodimerization of O-allyl and C-allyl glycosides.[11] On the other hand, the selective cross coupling of unlike sugar partners is a very attractive process, since the diversity of accessible carbohydrate derivatives would be much higher than that obtained from simple homodimerization. We therefore became interested in exploiting the CM reaction for the synthesis of pseudo-oligosaccharides with potential application as carbohydrate mimics. We were inspired by the paper of Blechert and Schürer[12] who applied a sequence of yne-ene cross metathesis and Diels-Alder reactions for the synthesis of pseudo-trisaccharides.

As outlined in Scheme 1, we reasoned that by using suitable monosaccharide derivatives of type A and B as cross-metathesis partners, the construction of the new ring on type C heterodimer could be achieved through an intramolecular cyclization promoted by electrophilic activation of the C–C double bond, affording tricyclic compounds of type D or E. We report herein our preliminary investigations of this strategy exploring the CM reaction of different substrates of type A and B (Scheme 1), and comparing the efficiency and selectivity of the classical, straightforward cross-metathesis with the two-step procedure (self-metathesis followed by cross-metathesis) developed by Grubbs and co-workers.[13] Moreover the representative synthesis of some tricyclic compounds of type D and E, using iodine as an electrophilic promoter for the intramolecular cyclization, is also described.

Results and discussion

As highlighted in Scheme 1, a type A CM partner equipped with a homoallylic alcohol function (n = 1) should lead to a heterodimer apt to give five-membered ring closure. On the other hand, the introduction of a hydroxyhexenyl appendage (n = 3) will give rise to a dimer that, upon electrophilic activation, should cyclize to form a six-membered ring, strongly preferred to a seven-membered ring.

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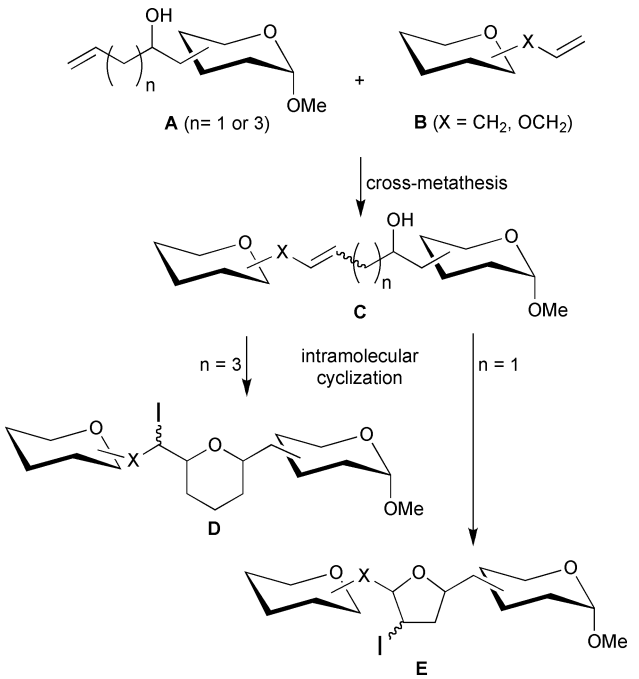
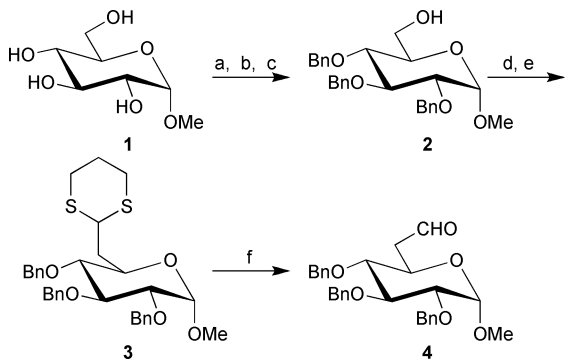
† Dedicated to Prof. Giovanni Russo on the occasion of his 70th birthday.

‡ Electronic supplementary information (ESI) available: Experimental procedures and full characterisation of compounds **3**, **5a**, **6a** and **6b**, and copies of NMR spectra of all new compounds. See DOI: 10.1039/b822989a



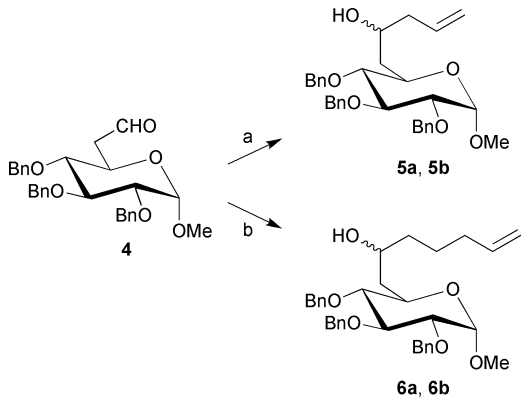
Scheme 1 Synthetic strategy.

Our investigation has been carried out using glucose-based hydroxy olefins **5** and **6** as type A CM partners. Both compounds have been obtained by alkylation of known aldehyde **4**,[14] which in turn was synthesized in 6 steps from commercial methyl α-glucoside **1** as described in Scheme 2.[15]



Scheme 2 Synthesis of aldehyde **4**. (a) $PhCH(OMe)_2$, (+)-β-camphorsulphonic acid, $CHCl_3$ (94%); (b) BnBr, NaH, DMF (96%); (c) $PhBCl_2$, Et_3SiH, MS 4 Å, CH_2Cl_2, –78 °C (95%); (d) I_2, PPh_3, imidazole; (e) 1,3-dithiane, BuLi 1.6 M in hexane, –20 °C, THF; (f) MeI, $NaHCO_3$, H_2O/CH_3CN (73% over 3 steps).

Allylation of **4** (Scheme 3) was carried out by treatment with AllMgBr in Et_2O affording a mixture of alcohol epimers **5a** and **5b** in a 3:2 diastereoisomeric ratio,[16] and in 73% overall yield. The absolute configuration of the newly formed stereogenic center was determined, according to Mosher's method,[17] converting both isomers of **5** into the corresponding esters of (*R*)- and (*S*)-2-methoxy-2-phenyl-2-(trifluoromethyl) acetic acid (MTPA) and analysing their NMR spectra. In this way we assigned the *R* configuration at C-7 of the major isomer **5a** and the *S* configuration at the same carbon of the second isomer **5b**. Remarkably, almost pure **5a** was obtained in a highly stereo-



Scheme 3 Synthesis of type A compounds. (a) Method A: AllMgBr, Et_2O, –78 °C (73%, **5a**:**5b** = 60:40). Method B: AllMgBr, (+)-$MeOB(Ipc)_2$, –78 °C, Et_2O, then 30% v/v H_2O_2, 3 N NaOH, reflux (73%, >95% of **5a**); (b) PentenylMgBr, Et_2O, –78°C (66%, **6a**:**6b** = 58:42).

selective manner using Brown's chemistry.[18] Ligand exchange of (+)-B-methoxydiisopinocampheylborane ((+)-$MeOB(Ipc)_2$) with AllMgBr followed by addition of aldehyde **4** afforded alcohols **5a**/**5b** in 73% overall yield, with a satisfying *d.e.* (>95% of **5a**, as evidenced by NMR spectra). Addition of freshly prepared pentenylMgBr to an ethereal solution of aldehyde **4** (Scheme 3) afforded the hydroxy olefins **6a**, **6b** in moderate yield (66%) with poor diastereoselectivity, that could not be improved even using various Lewis acids as chelating agents. The two diastereoisomers **6a** and **6b** were easily separated by flash chromatography (diastereoisomeric ratio 58:42), and their absolute configurations at C-7 were determined as described above for alcohols **5a** and **5b**, and found to be *R* for **6a** and *S* for **6b**.

The structures of type B CM partners employed in the present study are reported in Fig. 1. Allyl β-glycosides **7**[19] and **8**[20] were synthesised by Zemplén deacetylation (NaOMe, MeOH) and benzylation (NaH, BnBr, DMF) of the corresponding peracetylated

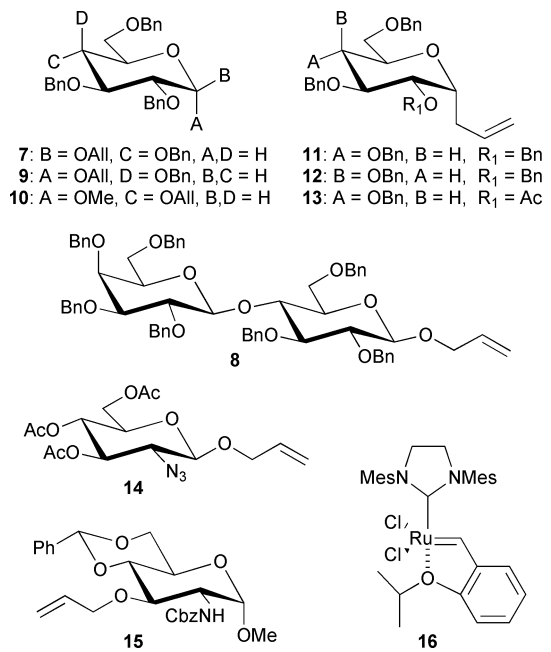


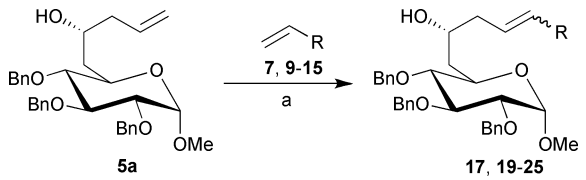
Fig. 1 Structures of type B compounds and Hoveyda's catalyst **16**.

allyl glycosides, while **9** was obtained by standard benzylation of allyl α-D-galactopyranoside.[21]

Allylation (NaH, AllBr, DMF) of known[22] methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside provided 4-*O*-allyl ether **10**. *C*-glucopyranosides **11** and **12** were prepared as reported in the literature,[23] while **13** was derived from chemoselective 2-*O*-debenzylation of **11**[24] followed by standard 2-*O*-acetylation (Ac_2O, pyridine).

Finally, since glycosides of 2-amino-2-deoxy sugars occur in the most important classes of glycoconjugates and biologically relevant oligosaccharides, we explored the behaviour of the glucosamine derivatives **14**[25] and **15**, the latter obtained by allylation (KOH, 18-crown-6, AllBr, THF/H_2O) of known methyl 2-*N*-benzyloxycarbonyl-4,5-*O*-benzylidene-2-deoxy-α-D-glucopyranoside.[26]

After preliminary attempts using first and second generation Grubbs' catalysts, all the CM reactions described in this work have been carried out with the phosphine-free Hoveyda's catalyst **16**[7] (Fig. 1) in CH_2Cl_2. Under these conditions, alcohol **5a** reacted with sugar-olefins **7** and **9–15** to give the corresponding heterodimers **17** and **19–25** (Scheme 4) with excellent stereoselectivities (only *E* isomers were detected in the NMR spectra of the isolated products), but in only moderate yields (25–62%), as summarized in Table 1 (entries 1 and 3–9). In particular, the chemical yields were eroded by the formation of substantial amounts of homodimers derived from self-metatheses of the reaction partners which is, as mentioned above, a typical drawback associated with straightforward CM reactions.

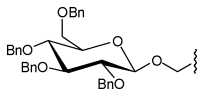
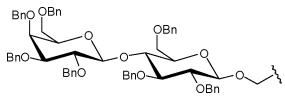
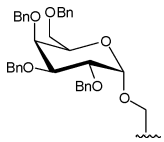
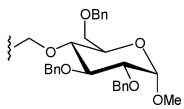
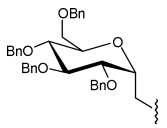
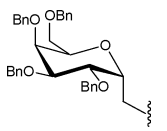
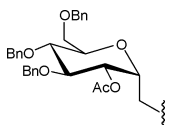
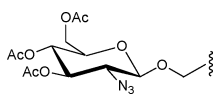
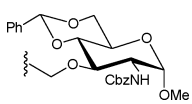


5a **17, 19-25**

Scheme 4 Straightforward CM reactions of alcohol **5a** with sugar-olefins. R are defined in Table 1. (a) 10 mol% of catalyst **16**, CH_2Cl_2, rt.

In order to improve the general efficiency of our CM reactions, we turned our attention to the two-step procedure developed by Grubbs and co-workers.[13] In this approach, a terminal olefin is first homodimerized in a CM reaction (self-metathesis, SM), and the internal olefin product (in excess) is then metathesized with a second terminal olefin (CM step) to give cross-coupled products. Since the homodimerization of **5a** was the predominant side-reaction in our previous experiments, we first carried out the self-metathesis of **5a** in the presence of 5 mol% of **16** in refluxing CH_2Cl_2. The reaction proceeded smoothly providing the dimer **26** as a mixture of *E*,*Z* isomers (*E*/*Z* ratio ≈ 3:1 on the base of NMR spectra) in 85% yield (Scheme 5). Next, an excess (2 eq.) of the symmetrical disubstituted olefin **26** was allowed to react with type B sugar-olefins **7–15** in the presence of the same catalyst (10 mol%), affording the corresponding heterodimers in fair to good yields (34–80% over two steps, Table 1, entries 1–9) and with excellent stereoselectivities (*E*/*Z* >95:5). Notably, the *E*,*Z* mixture of **26** was employed without affecting the efficiency and stereoselectivity of the following CM reaction. Moreover, the unreacted homodimer was easily recovered and re-used in subsequent CM reactions.

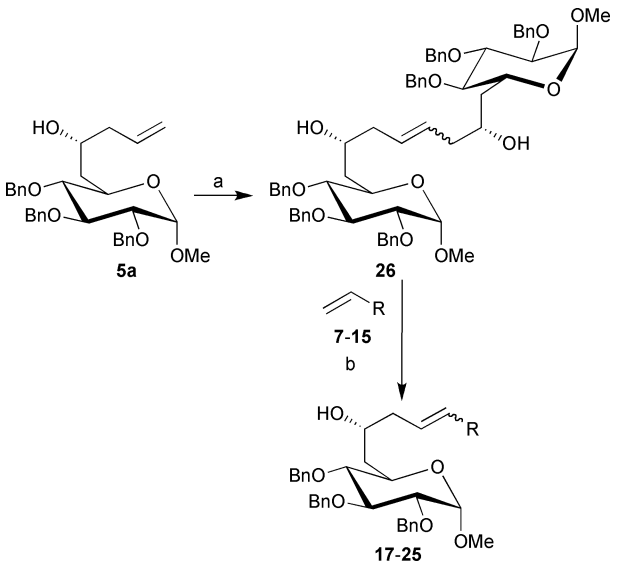
Table 1 Synthesis of sugar heterodimers from alcohol **5a**

Entry	Heterodimer[a]	R	Yield CM	Yield SM-CM
1	**17**		54%	42%
2	**18**		–	40%
3	**19**		45%	40%
4	**20**		37%	80%
5	**21**		25%	55%
6	**22**		34%	64%
7	**23**		40%	68%
8	**24**		62%	45%
9	**25**		41%	34%

[a] In all cases, the *E*/*Z* ratio was higher than 95/5.

These results seem to indicate that the two-step procedure is a favourable approach over the straightforward CM reaction only when the relative homodimerization rates of the reaction partners are markedly different.[27] Sugar-olefins containing non-anomerically linked *O*-allyl groups (**10**) or *C*-glycosides (**11–13**) homodimerize at a much lower rate than **5a**, and therefore they were the best substrates for the SM-CM sequence.

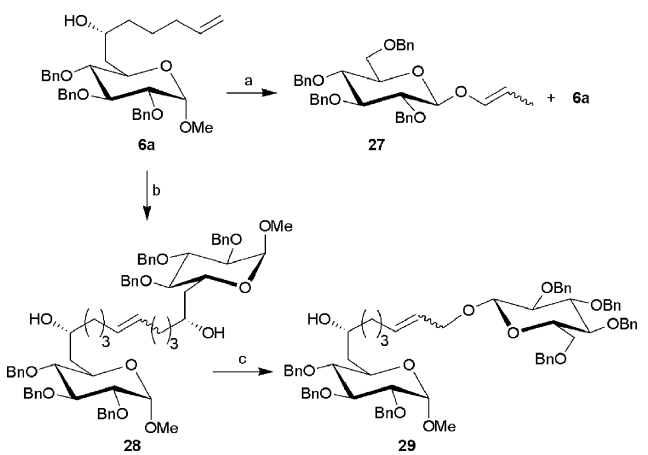
Accordingly, the CM reaction of **26** with sugar-olefins **10–13** led to the corresponding dimers **20–23**, respectively, in much higher yields than compared with the classical CM (Table 1, entries 4–7). On the contrary, allyl glycosides **7–9** and **14**, with a dimerization rate comparable to **5a**, showed poor selectivity in the CM reaction and provided the corresponding heterodimers in statistical yields (Table 1, entries 1–3 and 8), without significant changes on going



Scheme 5 SM-CM sequence of alcohol **5a** with sugar-olefins. R are defined in Table 1. (a) 5 mol% of catalyst **16**, CH_2Cl_2, reflux, (85%); (b) 10 mol% of catalyst **16**, CH_2Cl_2, reflux.

from the classical CM to the SM-CM sequence.[28] Compound **15**, containing a 3-*O*-allyl group, was the only exception to this trend, affording in both cases statistical yields of heterodimer **25** (Table 1, entry 9). We conjectured that this behavior might be due to catalyst trapping caused by unproductive coordination of the Cbz carbonyl oxygen on the ruthenium-alkylidene intermediate.[29]

In a second series of experiments, hexenyl alcohol **6a** was cross metathesized with allyl glucoside **7** to obtain the heterodimer that should lead to six-membered ring closure. However, no cross-metathesis occurred under different reaction conditions (from 5 to 15 mol% of catalyst **16** in CH_2Cl_2, at room temperature or reflux). In all cases, allyl isomerization occurred, leading to propenyl glycoside **27** in almost quantitative yield (Scheme 6). Roy and co-workers reported a similar isomerization of *O*-allyl glycosides under the influence of Grubbs I catalyst.[30] S. Hanessian described the allyl to propenyl isomerization in functionally diverse compounds in the presence of Grubbs II catalyst.[31] Over

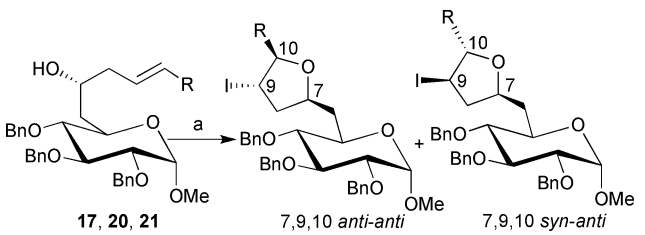


Scheme 6 Cross-metatheses of alcohol **6a**. (a) compound **7**, 5–15 mol% of catalyst **16**, CH_2Cl_2; (b) 5 mol% of catalyst **16**, CH_2Cl_2, reflux; (c) compound **7**, 10 mol% of catalyst **16**, CH_2Cl_2, reflux (43%).

the past few years, various research groups explored the non-metathetic transformations catalysed by ruthenium carbene complexes, presumably promoted by in situ formation of ruthenium hydride species.[32] For example, Snapper[33] and Schmidt[34] reported the preparation of synthetically useful cyclic enol ethers *via* a RCM/double bond isomerization tandem process.

Next, we applied the SM-CM sequence on **6a** (Scheme 6). Homodimerization of the hexenyl alcohol in the presence of 5 mol% of **16** afforded a complex mixture of products (TLC). Besides the desired homodimer **28**, analysis of the mass spectra of the crude mixture suggested the formation of various side-products presumably derived from secondary metathesis events involving constitutional isomers of **6a** generated by one or more shifts of the double bond from its initial terminal position. Moreover, the CM of this mixture with **7** (10 mol% of **16** in refluxing CH_2Cl_2) gave the expected heterodimer **29** in a very low yield (43%, *E*/*Z* ratio ≈ 9:1 on the base of NMR spectra), together with several by-products, whereas no reaction occurred employing **10** as a coupling partner. To test if the configuration at C-7 in the side chain of **6a**/**6b** could affect our results, we repeated the same series of experiments using **6b**, but we did not observe any significant improvement.

At this stage, we faced the intramolecular cyclization of heterodimers **17**, **20** and **21** using iodine to promote the electrophilic activation of the C–C double bond (Scheme 7). The results are summarized in Table 2. As illustrated in Scheme 7, in each case an inseparable mixture of *anti-anti* and *syn-anti* diastereoisomers was obtained.



Scheme 7 Iodocyclization of heterodimers **17**, **20** and **21**. R are defined in Table 1. (a) I_2, THF, base (see text), rt.

The cyclization of dimer **17** with iodine in dry THF at room temperature and in the presence of $NaHCO_3$[35] afforded the expected tricyclic compounds **30**/**31** in 92% overall yield (Table 2, entry 1) and in a 1.5:1 ratio as determined by HPLC, while stereoisomers **34**/**35** (2.9:1 ratio) were obtained in 79% yield from **21** using $CaCO_3$ as acidic scavenger (Table 2, entry 4). The iodocyclization of dimer **20** was carried out in refluxing CH_2Cl_2[36] in the presence of $CaCO_3$ giving the diastereoisomers **32**/**33** in 68% yield (Table 2, entry 2) and in a 1.4:1 ratio. The chemical yield of **32**/**33** was raised to 87% when the iodocyclization of dimer **20** was

Table 2 Iodine promoted cyclization of heterodimers **17**, **20** and **21**

Entry	Heterodimer	Cyclic ether	Yield%
1	**17**	**30**/**31**	92
2[a]	**20**	**32**/**33**	68
3[b]	**20**	**32**/**33**	87
4	**21**	**34**/**35**	79

[a] Reaction carried out in refluxing CH_2Cl_2. [b] Reaction carried out with AgOTf at 0 °C in CH_2Cl_2.

performed in the presence of silver trifluoromethanesulfonate at 0 °C in CH_2Cl_2 (Table 2, entry 3).

The exclusive formation of 9,10-*anti* diastereoisomers is in agreement with the widely accepted mechanism of electrophilic addition to alkenes. The intramolecular nucleophilic attack of the hydroxy group occurs by the back-side at the bridged iodonium ion, giving overall *anti* addition. Since two diastereoisomeric iodonium ions can be formed, the cyclization would lead in principle to a couple of diastereoisomers, where the substituents at C-9 and C-10 are in an *anti* relationship. This was confirmed by NMR analyses of the product mixtures.

Finally, we also tested the iodocyclization reaction on heterodimer **29**. Using iodine and $NaHCO_3$ in THF at room temperature, an inseparable mixture of compounds **36/37** (1.4:1 ratio by HPLC) was obtained in a disappointing 40% yield (Fig. 2), thus confirming the occurrence of the exclusive six-membered ring closure.

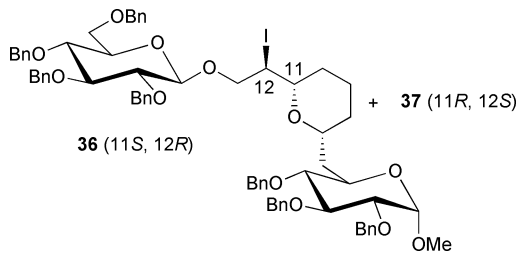


Fig. 2 Structures of tricyclic compounds **36/37** obtained by iodocyclization of **29**.

The iodocyclized compounds **30–35** can be seen as potential precursors of carbohydrate mimics, *via* HI elimination followed by functionalization of the C–C double bond. The low diastereoisomeric ratios obtained in the iodocyclization, however, suggest a poor asymmetric induction from the sugar residues. To overcome this problem, we are currently exploring different electrophilic promoters that could improve the stereoselectivity of the intramolecular cyclization.

Conclusions

In conclusion, we have shown that our approach outlined in Scheme 1 represents a promising methodology for the synthesis of functionally diverse sugar heterodimers which can be employed for the preparation of pseudo-oligosaccharides. These molecules are useful scaffolds for the synthesis of mimics of naturally occurring, biologically relevant carbohydrates. In particular, we have explored and compared the straightforward cross-metathesis reaction with the two-step procedure (self-metathesis followed by cross-metathesis) developed by Grubbs *et al.*[13] on diverse sugar-olefin substrates.

Our results suggest that the relative efficiency of the two approaches seems to depend on the relative homodimerization rates of type A and type B substrates. Furthermore, we found that hexenyl alcohols **6a/6b**, apt to give a heterodimer leading to six-membered ring closure, are poor substrates for both types of cross-metathesis reaction.

Finally, the results of intramolecular cyclizations performed on heterodimers **17**, **20**, **21**, and **29** using iodine as an electrophilic promoter showed that, in all cases, the iodocyclization reaction provided the two expected stereoisomers with poor stereoselectivity, thus implying that the monosaccharide units do not exert a significant asymmetric induction on the reaction course. Further investigations to explore the behavior of different electrophilic promoters for the intramolecular cyclization, and to broaden the scope and applicability of the described reactions are now in progress.

Experimental

General

NMR spectra were recorded on Bruker AC 300, Bruker Avance 400 and Bruker Avance 500 spectrometers at 298 K. In ^{13}C NMR spectra, signals corresponding to aromatic carbons are omitted. Chemical shifts are reported on the δ (ppm) scale and the coupling constants are given in Hz. When possible, peaks assignments were based on the analysis of 2D spectra (H,H-COSY and HSQC or HMQC spectra). HRMS spectra were recorded in positive mode on Bruker Daltonics APEX™ II (FT-ICR). Optical rotations were measured at room temperature with a Perkin-Elmer 241 polarimeter. $[\alpha]_D^{22}$ units are given in 10^{-1} deg cm^2 g^{-1}. HPLC analyses were performed with Varian 9050. Column Lichrocart 125–4 RP-18 5 μm, flow rate 1 mL min^{-1}, UV monitor λ= 210 nm. In all HPLC analyses, acetonitrile-water mixtures were used as eluent. TLC and HPTLC were carried out on Merck Silica-gel 60 F-254 plates (0.25 mm and 0.2 mm thickness, respectively), and spots were visualized by spraying with a solution containing H_2SO_4 (31 mL), ammonium molybdate (21 g) and $Ce(SO_4)_4$ (1 g) in 500 mL water, followed by heating at 110 °C for 5 min. Column chromatography was performed by the flash procedure using Merck Silica-gel 60 (230–400 mesh). Solvents were dried by standard procedures.

Typical procedure for straightforward CM reaction (method A). The proper reaction partners (allyl derivative and sugar hydroxyolefin) were dissolved, under a N_2 atmosphere, in dry CH_2Cl_2 and nitrogen was bubbled through the solution for 15 min. Catalyst **16** (10 mol%) was added in one portion and nitrogen was bubbled through the solution for a further 15 min. The solution was stirred overnight and the reaction was monitored by TLC. The solvent was evaporated under reduced pressure and the crude was purified by flash chromatography.

Typical procedure for SM-CM reaction (method B). Homodimer **26** was dissolved under an argon atmosphere in dry CH_2Cl_2 (0.2 M) and the solution was warmed to 40 °C and argon was bubbled through the solution for 10 min. Catalyst **16** (10 mol%) was added. After 20 min a 0.1 M solution of allyl derivative in dry CH_2Cl_2 was slowly added and the reaction was monitored by TLC. After 6 h DMSO (20 μL) was added and stirring was continued overnight. The solvent was removed under reduced pressure and the crude was purified by flash chromatography.

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2,3,4,6-tetra-*O*-benzyl-β-D-1-*O*-glucopyranosyl]-5-hexen-2-ol (17).

Method A. The allyl derivative **7** (202 mg, 0.348 mmol) and alcohol **5a** (150 mg, 0.289 mmol) were dissolved in CH_2Cl_2 (10 mL) and were cross-metathesized as described above. After work-up,

flash chromatography (hexane-AcOEt 7:3) afforded **17** (167 mg, 54% yield) as a white foam.

Method B. Homodimer **26** (200 mg, 0.198 mmol) was cross-metathesized with **7** (57 mg, 0.098 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **17** (52 mg, 42% over two step) as a white foam. $[\alpha]_D^{22} = +15.6$ (c 0.5 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.41–7.25 (m, 35H, H(Ar)), 5.76–5.71 (2H, m, 10-H, 9-H), 5.02–4.55 (15H, m, 14 × C*H*HPh, 1-H), 4.46 (1H, d, *J* 7.8, 1a-H), 4.40 (1H, dd, *J* 12.3, *J* 7.0, 11-H), 4.17 (1H, dd, *J* 12.3, *J* 7.0, 11′-H), 3.97 (t, 1H, *J* 9.2, 3-H), 3.81–3.69 (4H, m, 7-H, 5-H, 6a-H, 6a′-H), 3.62–3.67 (2H, m, 4a-H, 3a-H), 3.54–3.51 (3H, m, 2-H, 2a-H, 5a-H), 3.40 (3H, s, OC*H*$_3$), 3.24 (2H, m, 4-H, O*H*), 2.24–2.17 (2H, m, 8-H, 8′-H), 2.13–1.96 (m, 1H, 6-H), 1.34–1.45 (m, 1H, 6′-H); δ_C (100 MHz, $CDCl_3$) 130.47 (CH, C-9), 128.70 (CH, C-10), 102.65 (CH, C-1a), 98.07 (CH, C-1) 84.73 (CH, C-4a), 82.32 (CH, C-2a), 81.85 (CH, C-4), 81.69 (CH, C-3), 79.47 (CH, C-2) 77.87 (CH, C-2a) 75.87, 75.74, 75.38, 75.04, 75.88, 74.82, 73.50 (*C*H$_2$Ph), 74.82 (CH, C-5a), 71.36(CH, C-5 or C-7), 71.21 (CH, C-5 or C-7), 70.06 (CH$_2$, C-11), 68.96 (CH$_2$, C-6a), 55.47 (O*C*H$_3$), 40.43 (CH$_2$, C-8), 37.73 (CH$_2$, C-6); HRESIMS m/z 1093.5074 ($C_{67}H_{74}O_{12}Na$ [M + Na]$^+$ requires 1093.5072).

(2*R*)-1-[Methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2,3,4,6-tetra-*O*-benzyl-β-D-galactopyransyl(1–4)-2,3,6-tetra-*O*-benzyl-β-D-glucopyranosyl]-5-hexen-2-ol (18).

Method B. Homodimer **26** (80 mg, 0.079 mmol) was cross-metathesized with **8** (42 mg, 0.042 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 75:25) afforded **18** (29 mg, 40% yield over two step) as a white foam. $[\alpha]_D^{22} = +11.0$ (c 0.4 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.37–7.25 (50H, H(Ar)), 5.75–5.66 (2H, m, 10-H 9-H), 5.04–4.53 (18 H, m, 17 × C*H*HPh H-1), 4.58–4.26 (5H, m, 3 × C*H*HPh 11-H 1a-H 1b-H), 4.07 (1H, dd, *J* 12.4 *J* 5.8, 11′-H), 3.94–3.91 (3H, m, 3-H 3a-H 4b-H), 3.78–3.73 (5H, m, 2b-H 7-H 5-H 6b′-H 6b-H), 3.58–3.52 (m, 3H, 4a-H 2-H 6a-H), 3.41–3.35 (8H, m, 5b-H 5a-H 2a-H 6a′-H OC*H*$_3$ 3b-H), 3.20 (1H, t, *J* 9.0, 4-H), 2.18–2.05 (2H, m, 8-H, 8′-H), 1.98–1.95 (1H, m, 6-H), 1.40–1.36 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$): δ (ppm) : 130.89–129.50 (2 × CH, C-9 C-10), 103.46–103.35 (2 × CH, C-1a C-1b), 98.75 (CH, C-1), 83.69, 83.26, 82.56, 82.49, 82.37, 80.66, 80.50, 78.00, 75.85, 74.32, 73.66 (11 × CH, C-2a C-3a C-4a C-5a C-2b C-3b C-4b C-5b C-2 C-3 C-4), 76.46, 76.00, 75.65, 75.38, 74.07, 73.66, 73.26 (CH$_2$Ph), 71.96 (CH, C-5 or C-7), 71.79 (CH, C-5 or C-7), 70.60 (CH$_2$, C-11), 69.05 (CH$_2$, C-6b), 68.78 (CH$_2$, C-6a), 56.20 (O*C*H$_3$) 41.10 (CH$_2$, C-8), 38.47 (CH$_2$, C-6); HRESIMS *m/z* 1525.7008 (100) ($C_{94}H_{102}O_{17}Na$ [M + Na]$^+$ requires 1525.7009).

(2*R*)-1-[Methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2,3,4,6-tetra-*O*-benzyl-α-D-1-*O*-galactopyranosyl]-5-hexen-2-ol (19).

Method A. Allyl derivative **9** (28 mg, 0.048 mmol) and alcohol **5a** (20 mg, 0.039 mmol) were dissolved in CH_2Cl_2 (1 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded compound **19** (19 mg, 45%) as a white foam.

Method B. Homodimer **26** (138 mg, 0.137 mmol) was cross-metathesized with **9** (40 mg, 0.069 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **19** (35 mg, 40% yield over two steps) as a white foam. $[\alpha]_D^{22} = +79.5$ (c 0.6, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.40–7.25 (35H, m, H(Ar)), 5.71–5.66 (2H, m, 10-H, 9-H), 5.00–4.40 (16H, m, 14 × C*H*HPh, 1-H, 1a-H), 4.10–3.94 (7H, m, 11-H, 11′-H, 4a-H, 2a-H, 3a-H, 5a-H, 3-H), 3.83–3.79 (2H, m, 5-H, 7-H), 3.58–3.51 (3H, m, 2-H, 6a-H, 6a′-H), 3.38 (3H, s, OC*H*$_3$), 3.21 (1H, t, *J* 9.1, 4-H), 2.26–2.13 (2H, m, 8-H, 8′-H), 2.01–1.97 (1H, m, 6-H), 1.45–1.35 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$) 131.12 (2 × CH, C-9 C-10), 98.10 (CH, C-1), 96.18 (CH, C-1a) 81.93 (CH, C4), 81.71 (CH, C-3), 76.89 (CH, C-2), 79.20 (CH, C-3a or C-4a), 76.55 (C-2a), 75.28 (CH, C-3a or C-4a), 75.80, 75.34, 74.36, 73.47, 73.28 (*C*H$_2$Ph), 71.33 (CH, C-7 or C-5), 71.12 (CH, C-7 or C-5), 63.38 (CH, C-5a), 69.09 (CH$_2$, C-6a), 67.98 (CH$_2$, C-11), 55.45 (O*C*H$_3$), 40.48 (CH$_2$, C-8), 37.83 (CH$_2$, C-6); HRESIMS *m/z* 1093.5078 (100) ($C_{67}H_{74}O_{12}Na$ [M + Na]$^+$ requires 1093.5075).

(2*R*)-1-[methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[methyl-2,3,6-tri-*O*-benzyl-α-D-4-*O*-glucopyranosyl]-5-hexen-2-ol (20).

Method A. allyl derivative **10** (177 mg, 0.351 mmol) and alcohol **5a** (152 mg, 0.293 mmol) were dissolved in CH_2Cl_2 (10 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 75:25) afforded **20** (107 mg, 37% yield) as a colourless oil.

Method B. Homodimer **26** (181 mg, 0.179 mmol) was cross-metathesized with **10** (45 mg, 0.089 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **20** (98 mg, 80% over two step) as a colourless oil. $[\alpha]_D^{22} = +7.7$ (c 0.5 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.37–7.26 (30H, m, H(Ar)), 5.56 (1H, dt, *J* 15.4 *J* 7.0, 9-H), 5.51 (1H, dt, *J* 15.4 *J* 5.7, 10-H), 5.00 (1H, d, *J* 10.9, C*H*HPh), 4.94 (1H, d, *J* 10.9, C*H*HPh), 4.90 (1H, d, *J* 11.0, C*H*HPh), 4.84–4.78 (4H, m, 4 × C*H*HPh), 4.69–4.60 (4H, m, 3 × C*H*HPh, 1-H), 4.61–4.49 (3H, m, 2 × C*H*HPh, 1a-H), 4.24 (1H, dd, *J* 5.5 *J* 11.2, 11-H), 3.97 (2H, m, *J* 9.4, 3-H, 11′-H), 3.91 (1H, t, *J* 9.4, 3a-H), 3.83–3.76 (2H, m, 5-H, 7-H), 3.71–3.62 (3H, m, 6a-H, 6a′-H, 5a-H), 3.53 (2H, dd, *J* 5.5 *J* 11.2, 2a-H 2-H), 3.47 (1H, t, *J* 9.1, 4a-H), 3.41 (3H, s, OC*H*$_3$), 3.40 (3H, s, OC*H*$_3$), 3.21 (1H, t, *J* 9.3, 4-H), 3.13 (1H, bs, O*H*), 2.19–2.07 (2H, m, 8-H, 8′-H), 1.96 (1H, dd, *J* 12.2, 6′-H), 1.43–1.31 (1H, m, 6-H); δ_C (100 MHz, $CDCl_3$) 130.75–130.11 (2 × CH, C-10, C-9), 98.89, 98.77 (2 × CH, C-1 C-1a), 82.71, 82.59, 82.38 (3 × CH, C-4 C-3a C-3), 80.47 (2 × CH, C-2 C-2a), 78.26 (CH, C-4a), 76.46, 76.33, 76.00 (*C*H$_2$Ph), 74.17 (CH$_2$, C-11 or *C*H$_2$Ph), 74.06 (CH$_2$, C-11 or *C*H$_2$Ph), 71.93 (CH, C-5 or C-7), 71.94 (CH, C-5 or C-7), 70.83 (CH, C-5a), 69.29 (CH$_2$, C-6a), 56.11 (O*C*H$_3$), 55.81 (O*C*H$_3$), 41.10 (CH$_2$, C-8), 38.58 (CH$_2$, C-6); HRESIMS *m/z* 1017.4757 (100) ($C_{61}H_{70}0_{12}Na_1$ [M + Na]$^+$ requires 1017.4759).

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2,3,4,6-tetra-*O*-benzyl-1-deoxy-β-D-1-*C*-glucopyranosyl]-5-hexen-2-ol (21).

Method A. Allyl derivative **11** (298 mg, 0.528 mmol) and alcohol **5a** (232 mg, 0.447 mmol) were dissolved in CH_2Cl_2 (10 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded compound **21** (117 mg, 25%) as a colourless oil.

Method B. Homodimer **26** (150 mg, 0.149 mmol) was cross-metathesized with **11** (42 mg, 0.074 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded

21 (49 mg, 55% over two steps) as a colourless oil. $[\alpha]_D^{22} = +37.5$ (c 1.7 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.37–7.26 (35H, m, H(Ar)), 5.52–5.48 (2H, m, 9-H, 10-H), 5.00 (1H, d, *J* 10.8, C*H*HPh), 4.95 (1H, d, *J* 10.9, C*H*HPh), 4.90 (1H, d, *J* 10.9, C*H*HPh), 4.84–4.79 (5H, m, 5 × C*H*HPh), 4.70–4.59 (4H, m, 4 × C*H*HPh), 4.55 (1H, d, *J* 3.5, 1-H), 4.48 (1H, d, *J* 12.1, C*H*HPh), 4.47 (1H, d, *J* 10.6, C*H*HPh), 4.10–4.07 (1H, m, 1a-H), 3.96 (t, 1H, *J* 9.3, 3-H), 3.83–3.73 (4H, m, 2a-H, 3a-H, 5-H, 7-H), 3.63–3.58 (4H, m, 6a-H, 6a′-H, 5a-H, 4a-H), 3.52 (1H, dd, *J* 3.6 *J* 9.7, 2-H), 3.40 (3H, s, OC*H*$_3$), 3.25 (1H, t, *J* 9.3, 4-H), 3.18 (1H, bs, O*H*), 2.48–2.44 (2H, m, 11-H, 11′-H), 2.16–2.13 (2H, m, 8-H, 8′-H), 2.00 (dt, 1H, *J* 11.4, *J* 2.7, 6-H), 1.49–1.45 (m, 1H, 6′-H). δ_C (100 MHz, $CDCl_3$) 129.38 (CH, C-10), 129.00(CH, C-9), 98.05 (CH, C-1), 82.39 (CH, C-3a), 82.05 (CH, C-4), 81.80 (CH, C-3), 80.12 (CH, C-2a), 79.90 (CH, C-2), 78.28 (CH, C-4a), 75.81, 75.47, 75.37, 75.11 (CH_2Ph), 73.72 (CH, C-1a), 73.46, 73.20, 73.04 (*C*H_2Ph), 71.07 (CH, C-5a), 70.75 (CH, C-7 C-5), 70.53 (CH, C-7 C-5), 69.04 (CH_2, C-6a), 55.40 (O*C*H_3), 40.89 (CH_2, C-8), 32.83 (CH_2, C-6), 28.73 (CH_2, C-11). HRESIMS *m/z* 1077.5126 (100) ($C_{67}H_{74}O_{11}Na$ [M + Na]$^+$: requires 1077.5123).

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2,3,4,6-tetra-*O*-benzyl-1-deoxy-β-D-1-*C*-galactopyranosyl]-5-hexen-2-ol (22).

Method A. Allyl derivative **12** (71 mg, 0.126 mmol) and alcohol **5a** (54 mg, 0.104 mmol) were dissolved in CH_2Cl_2 (5.2 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 75:25) afforded compound **22** (37 mg, 34%) as a colourless oil.

Method B. Homodimer **26** (100 mg, 0.0990 mmol) was cross-metathesized with **12** (28 mg, 0.050 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **22** (40 mg, 64% over two steps) as a colourless oil. $[\alpha]_D^{22} = +46.3$ (c 0.1 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.38–7.25 (35H, m, H(Ar)), 5.46–5.44 (2H, m, 9-H 10-H), 4.99 (1H, d, *J* 10.8, C*H*HPh), 4.89 (1H, d, *J* 10.8, C*H*HPh), 4.82 (1H, d, *J* 10.8, C*H*HPh), 4.80 (1H, d, *J* 12.4, C*H*HPh), 4.75–4.51 (11H, m, 10 × C*H*HPh, 1-H), 4.03–3.93 (4H, m, 5a-H, 3-H, 1a-H, 4a-H), 3.85–3.71 (5H, m, 6a-H, 3a-H, 2a-H, 5-H, 7-H), 3.63 (1H, dd, *J* 4.8 *J* 10.4, 6a′-H), 3.51 (1H, dd, *J* 3.6 *J* 9.6, 2-H), 3.38 (3H, s, OC*H*$_3$), 3.22 (1H, t, *J* 9.2, 4-H), 2.42–2.30 (2H, m, 11-H, 11′-H), 2.11–2.07 (2H, m, 8-H, 8′-H), 1.99 (1H, bd, *J* 12.0, 6-H), 1.46–1.37 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$) 131.85 (CH, C-9 or C-10), 127.48 (CH, C-9 or C-10), 98.10 (CH, C-1), 82.03 (CH, C-4), 81.76 (CH, C-3), 79.88 (CH, C-2), 76.48 (2 × CH, C2a C3a), 75.80, 75.37 (CH_2Ph), 74.41 (CH, C-4a or C-1a), 73.45, 73.19, 73.03 (CH_2Ph), 72.31 (CH, C-5a), 71.39 (C1a or C4a), 70.97 (CH, C-5 or C-7), 70.86 (CH, C-5 or C-7), 67.49 (CH_2, C-6a), 55.39 (O*C*H_3), 40.83 (CH, C-8), 37.81 (CH_2, C-6), 23.56 (CH_2, C-11); HRESIMS *m/z* 1077.5127 (100) ($C_{67}H_{74}O_{12}Na$ [M + Na]$^+$ requires 1077.5123).

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-deoxy-β-D-1-*C*-glucopyranosyl]-5-hexen-2-ol (23).

Method A. Allyl derivative **13** (176 mg, 0.341 mmol) and alcohol **5a** (152 mg, 0.293 mmol) were dissolved in CH_2Cl_2 (10 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 8:2) afforded **23** (118 mg, 40% yield) as a white foam.

Method B. Homodimer **26** (52 mg, 0.052 mmol) was cross-metathesized with **13** (13 mg, 0.025 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **23** (20 mg, 68% over two steps) as a white foam. $[\alpha]_D^{22} = +52.7$ (c 1, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.41–7.26 (m, 30H, C*H*(Ar)), 5.57–5.45 (2H, m, 10-H, 9-H), 5.01 (1H, dd, *J* 2.5 *J* 8.2, 2a-H), 4.99–4.51 (13H, m, 12 × C*H*HPh, 1-H), 4.20–4.15 (1H, m, 1a-H), 3.98 (1H, t, 3-H), 3.87–3.81 (3H, m, 3a-H, 5-H, 7-H), 3.76–3.64 (4H, m, 5a-H, 6a-H, 6a′-H, 4a-H), 3.54 (1H, dd, *J* 3.5 *J* 9.3, 2-H), 3.41 (3H, s, OC*H*$_3$), 3.26 (1H, t, *J* 9.3, 4-H), 2.51–2.44 (1H, m, 11-H), 2.36–2.15 (3H, m, 8′-H, 8-H, 11′-H), 2.06 (3H, s, COC*H*$_3$), 1.96 (1H, m, 6-H), 1.52–1.44 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$) 170.01 (−*C*OCH3), 129.70 (CH, C-9), 128.72 (CH, C-10), 98.08 (CH, C-1), 82.05 (CH, C-4), 81.78 (CH, C-3), 79.86 (2 × CH, C-2 C-3a), 77.54 (CH, C-4a), 75.82, 75.37, 75.02, 74.67, 74.47, 73.40 (*C*H_2Ph), 72.63 (CH, C-2a), 71.91 (CH, C-1a or C-5a), 71.84 (CH, C-1a or C-5a), 70.90 (CH, C-5 or C-7), 70.95 (CH, C-5 or C-7), 68.85 (CH_2, C-6a), 55.42 (O*C*H_3), 40.82 (CH_2, C-8), 37.87 (CH_2, C-6), 30.05 (CH_2, C-11), 20.98 (*C*H_3CO); HRESIMS *m/z* 1029.4752 (100) ($C_{62}H_{70}0_{12}Na_1$ [M + Na]$^+$ requires 1029.4759).

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-β-D-glucopyranosyl]-5-hexen-2-ol (24).

Method A. Allyl derivative **14** (34 mg, 0.092 mmol) and alcohol **5a** (40 mg, 0.077 mmol) were dissolved in CH_2Cl_2 (5.2 mL) and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded compound **24** (41 mg, 62%) as a colourless oil.

Method B. Homodimer **26** (103 mg, 0.102 mmol) was cross-metathesized with **14** (18 mg, 0.051 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **26** (23 mg, 45% over two steps) as a colourless oil. $[\alpha]_D^{22} = +7.7$ (c 1.8 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.38–7.27 (15H, m, H(Ar)), 5.80 (1H, dt, *J* 15.6 *J* 7.2, H-9), 5.70 (1H, dt, *J* 15.6 *J* 6.0, H-10), 5.04–4.97 (m, 3H, 3a-H, 4a-H, C*H*HPh), 4.95 (1H, d, *J* 11.2, C*H*HPh), 4.83 (1H, d, *J* 10.8, C*H*HPh), 4.82 (1H, d, *J* 12.4, C*H*HPh), 4.68 (1H, d, *J* 12.0, C*H*HPh), 4.57 (1H, d, *J* 3.6, 1-H), 4.44 (1H, d, *J* 8, 1a-H), 4.37 (1H, dd, *J* 12.0 *J* 5.6, 11-H), 4.30 (1H, dd, *J* 12.4 *J* 5.2, 6a-H), 4.15–4.12 (2H, m, 6a′-H, 11′-H), 3.97 (1H, t, *J* 9.2, 3-H), 3.88–3.80 (2H, m, 5-H, 7-H), 3.69–3.63 (1H, m, 5a-H), 3.58–3.51 (2H, m, 2a-H, 2-H), 3.41 (3H, s, OC*H*$_3$), 3.22 (1H, t, *J* 9.2, 4-H), 2.19–2.25 (2H, m, 8-H, 8′-H), 2.10 (3H, s, COC*H*$_3$), 2.09 (3H, s, COC*H*$_3$), 2.03 (3H, s, COC*H*$_3$), 2.01–1.98 (1H, m, 6-H), 1.46–1.37 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$) 170.65–170.01–169.62 (3 × *C*OCH$_3$), 131.85 (CH, C-9), 127.48 (CH, C10), 100.87 (CH, C-1a), 98.10 (CH, C-1), 81.87, 81.68 (2 × CH, C-3 C-4), 79.80 (CH, C-2), 75.84, 75.32, 73.48 (*C*H_2Ph), 72.57 (CH, C-3a or C-4a), 71.75 (CH, C-5a), 71.75 (2 × CH, C-5 C-7), 70.41 (CH_2, C-6a), 68.43 (C-3a or C-4a), 61.93 (C-11); 55.48 (O*C*H_3), 40.30 (CH_2, C-8), 37.81 (CH_2, C-6), 20.75–20.71–20.60 (3 × CH_3CO); HRESIMS *m/z* 884.3573 (100) ($C_{45}H_{55}O_{14}N_3Na$ [M + Na]$^+$ requires 884.3576).

(2*R*)-1-[Methyl-2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-6-[methyl-2-amino-*N*-benzyloxycarbonyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside]-5-hexen-2-ol (25).

Method A. Allyl derivative **15** (38.5 mg, 0.088 mmol) and alcohol **5a** (40 mg, 0.078 mmol) were dissolved in CH_2Cl_2 (1.7 mL)

and were cross-metathesized as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded compound **25** (29 mg, 41%) as a colourless oil.

Method B. Homodimer **26** (118 mg, 0.117 mmol) was cross-metathesized with **15** (24 mg, 0.054 mmol) as described above. After work-up, flash chromatography (hexane-AcOEt 7:3) afforded **25** (20 mg, 34% over two steps) as a colourless oil. $[\alpha]_D^{22} = +5.5$ (c 0.5 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.40–7.26 (20H, m, H(Ar)), 5.63–5.49 (3H, m, 9-H, 10-H, PhC*H*(O-)$_2$), 5.18 (1H, d, *J* 12.0, C*H*HPh), 5.10 (1H, d, *J* 12.0, C*H*HPh), 4.98 (1H, d, *J* 10.8, C*H*HPh), 4.91 (1H, d, *J* 11.2, C*H*HPh), 4.83 (1H, d, *J* 10.8, C*H*HPh), 4.82 (1H, d, *J* 12.4, C*H*HPh), 4.73 (1H, d, *J* 3.2, 1a-H), 4.67 (1H, d, *J* 12.0, C*H*HPh), 4.60 (1H, d, *J* 11.2, C*H*HPh), 4.52 (1H, d, *J* 3.6, 1-H), 4.32–4.28 (2H, m, 6a-H, 11-H), 4.02–3.91 (3H, m, 2a-H, 3-H, 11′-H), 3.83–3.78 (4H, m, 6a′-H, 5-H, 7-H, 5a-H), 3.66–3.62 (2H, m, 3a-H, 4a-H), 3.52 (1H, dd, *J* 9.6 *J* 3.2, H-2), 3.39 (3H, s, OC*H*$_3$), 3.35 (3H, s, OC*H*$_3$), 3.21 (1H, t, *J* 9.2, 4-H), 2.12–2.09 (2H, m, 8-H, 8′-H), 1.95 (1H, bd, *J* 3.6, 6-H), 1.40–1.37 (1H, m, 6′-H); δ_C (100 MHz, $CDCl_3$) 159.25 (–NH*C*OOCH$_2$Ph), 130.89 (CH, C-9), 129.70 (CH, C-10), 101.25 (CH, PhC*H*(O-)$_2$), 99.59 (CH, C-1a), 98.08 (CH, C-1), 82.43 (CH, C-3a or C-4a), 81.96 (CH, C-4), 81.69 (CH, C-3), 79.85 (CH, C-2), 75.83 (*C*H$_2$Ph), 75.43 (CH, C-3a or C-4a), 75.35 (CH$_2$Ph), 71.28 (CH, C-5 or C-7), 71.06 (CH, C-5 or C-7), 69.09 (CH$_2$, C-6a), 69.79 (CH$_2$Ph), 62.73 (CH, C-5a), 55.39 (O*C*H$_3$), 55.23 (O*C*H$_3$), 54.71 (CH, C-2a), 40.57 (CH$_2$, C-8), 38.16 (CH$_2$, C-6); HRESIMS *m/z* 968.4189 (100) ($C_{55}H_{63}O_{13}NNa$ [M + Na]$^+$ requires 968.4191).

(2*R*,7*R*) 1,8-bis-[Methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-4-octen-2,7-diol (26). Compound **5a** (370mg, 0.713 mmol) was dissolved in dry CH_2Cl_2 (15 mL) and solution was warmed to 40 °C and argon was bubbled through the solution for 10 min. Then catalyst **16** (20mg, 0.033 mmol) was added. The reaction was monitored by TLC (hexane-AcOEt 4:6). After 3 h DMSO (20 μL) was added and stirring was continued overnight at room temperature. The solvent was removed under reduced pressure and the crude compound was purified by flash chromatography (hexane-AcOEt 1:1) affording compound **26** (306 mg, 85% yield, *E*/*Z* ratio ≈ 3:1 on the base of NMR spectra) as a white foam. Major isomer (E): δ_H (400 MHz, $CDCl_3$) 7.38–7.25 (30H, m, H(Ar)), 5.49–5.45 (2H, m, 2 × 9-H), 5.00 (2H, d, *J* 10.9, *2* × C*H*HPh), 4.90 (2H, d, *J* 11.0, 2 × C*H*HPh), 4.83 (2 H, d, *J* 10.8, 2 × C*H*HPh), 4.81 (2H, d, *J* 12.0, 2 × C*H*HPh), 4.67 (2H, d, *J* 10.9, 2 × C*H*HPh), 4.60–4.58 (2H, m, 2 × C*H*HPh), 4.55 (2H, d, *J* 3.5, 2 × 1-H), 3.96 (bt, 2H, *J* 9.3 *J* 9.2, 2 × 3-H); 3.83–3.77 (4H, m, 2 × 5-H, 2 × 7-H); 3.52 (2H, d, *J* 9.6 *J* 3.5, 2 × 2-H), 3.39 (6H, s, 2 × OC*H*$_3$), 3.20 (2H, bt, *J* 9.3, 2 × 4-H), 3.17 (2H, bs, O*H*), 2.14–2.09 (4H, m, 2 × 8-H, 2 × 8′-H), 2.02–1.98 (2H, bd, *J* 14.3, 2 × 6-H), 1.42–1.38 (2H, m, *J* 14.3, 2 × 6′-H); δ_C (100 MHz, $CDCl_3$) 138.08 (CH, C-9), 98.09 (CH, C-1), 82.09 (CH, C-4), 81.71 (CH, C-3), 79.89 (CH, C-2), 75.79, 75.34, 73.46 (*C*H$_2$Ph), 71.25 (CH, C-5 or C-7), 71.13 (CH, C-5 or C-7), 55.42 (O*C*H$_3$), 40.81 (CH$_2$, C-8), 37.83 (CH$_2$, C-6); HRESIMS *m/z* 1031.4916 (100) ($C_{62}H_{72}0_{12}Na_1$ [M + Na]$^+$ requires 1031.4916).

(2*R*,11*R*)-1,12-bis-[Methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-5-dodecen-2,11-diol (28). Compound **6a** (126 mg, 0.230 mmol) was dissolved under argon atmosphere in dry CH_2Cl_2 (2.3 mL) and the solution was warmed to 40 °C and bubbled with argon for 10 min. Then Hoveyda catalyst (7 mg, 0.012 mmol) was added. The reaction was monitored by TLC (dichloromethane-AcOEt 9:1). After 3 h DMSO (20 μL) was added and stirring was continued overnight at room temperature. The solvent was removed under reduced pressure and the crude was filtered over a silica gel column affording a complex mixture of isomers (106 mg), containing compound **28** as the major component. A pure analytical sample of **28** was isolated during chromatography and characterised by NMR. δ_H (400 MHz, $CDCl_3$): 7.36–7.26 (30H, m, H(Ar)), 5.44 (2H, m, 2 × 11-H), 4.99 (2H, m, *J* 10.8, 2 × C*H*HPh), 4.91 (2H, d, *J* 11.0, 2 × C*H*HPh), 4.82 (2H, d, *J* 10.8, 2 × C*H*HPh), 4.80 (2H, d, *J* 10.8, 2 × C*H*HPh), 4.66 (2H, d, *J* 10.8, 2 × C*H*HPh), 4.68–4.50 (4H, m, 2 × C*H*HPh 2 × 1-H), 3.98 (2H, bt, *J* 9.3, 2 × 3-H), 3.81 (2H, bt, *J* 9.7, 2 × 5-H), 3.75 (2H, m, 2 × 7-H), 3.51 (2H, dd, *J* 3.5 *J* 11.0, 2 × 2-H), 3.40 (6H, s, 2 × OC*H*$_3$), 3.20 (4H, m, *J* 9.1, 2 × 4-H 2 × O*H*), 1.99 (H, m, 2 × 10-H 2 × 10′-H, 2 × 6-H), 1.43–1.27 (5H, m, 2 × 6′-H, 2 × 8′-H, 2 × 8-H, 2 × 9-H, 2 × 9′-H); δ_C (100 MHz, $CDCl_3$) 130.94 (CH, C-11), 98.78 (CH, C-1), 82.74 (CH, C-4), 82.37 (CH, C-3), 80.52 (CH, C-2), 76.48, 76.04, 74.13 (*C*H$_2$Ph), 72.45 (2 × CH, C-7 C-5), 56.10 (O*C*H$_3$), 41.38 (CH$_2$, C-6), 33.21 (CH$_2$, C-10), 37.73 (CH$_2$, C-8 or C-9), 26.02 (CH$_2$, C-8 or C-9); HRESIMS *m/z* 1087.5544 ($C_{66}H_{80}N_60_{12}Na_1$ [M + Na]$^+$ requires 1087.5542).

The compound mixture containing **28** was directly employed in the following cross-metathesis reaction.

(2*R*)-1-[Methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]-8-[2,3,4,6-tetra-*O*-benzyl-β-D-1-*O*-glucopyranosyl]-6-octen-2-ol (29). The compound mixture described above (**28**) (106 mg) was dissolved under an argon atmosphere in dry CH_2Cl_2 (2 mL) and the solution was warmed to 40 °C and bubbled with argon for 10 min then catalyst **16** (6 mg, 9.6 μmol) was added. After 20 min a solution of compound **7** (56 mg, 0.096 mmol) in 1 mL CH_2Cl_2 was added dropwise and the reaction was monitored by TLC hexane:AcOEt 6:4). After 6 h DMSO (20 μL) was added and stirring was continued overnight. The solvent was removed under reduced pressure and the crude was purified by flash chromatography (hexane-AcOEt 7:3) affording compound **29** (45 mg, 43%) as a colourless oil. $[\alpha]_D^{22} = +26.9$ (c 0.5, $CHCl_3$); major diastereoisomer (E): δ_H (400 MHz, $CDCl_3$) 7.40–7.31 (35H, m, H(Ar)), 5.76 (1H, m, 11-H), 5.65 (1H, m, 12-H), 5.02–4.45 (15H, m, 14 × C*H*HPh 1-H), 4.46 (1H, d, *J* 7.8, 1a-H), 4.40 (1H, d, *J* 12.2, 13-H), 4.12 (1H, d, *J* 12.2, 13′-H), 3.98 (1H, bt, *J* 9.3, 3-H), 3.85–3.59 (6H, m, 5-H, 7-H, 6a-H, 6a′-H, 4a-H, 3a-H), 3.55–3.47 (m, 3H, 2-H, 5a-H, 2a-H), 3.42 (s, 3H, OC*H*$_3$), 3.21 (2H, m, 4-H, O*H*), 2.13–2.08 (2H, m, 10-H, 10′-H), 1.96 (1H, bt, *J* 14.3, 6-H), 1.72–1.29 (5H, m, 6′-H, 8-H, 8′-H, 9-H, 9′-H); δ_C (100 MHz, $CDCl_3$) 134.71 (CH, C-11), 125.92 (CH, C-12), 102.57 (CH, C-1a), 98.08 (CH, C-1), 84.77 (CH, C-4a or C-3a), 82.33 (CH, C-2a), 82.04 (CH, C-4), 81.70 (CH, C-3), 79.82 (CH, C-2), 77.95 (CH, C-4a or C-3a), 75.84, 75.71, 75.38, 75.01 (CH$_2$Ph), 74.89 (CH, C-5a), 74.82 (CH$_2$Ph), 71.67 (2 × CH, C-5 C-7), 70.26 (CH$_2$, C-13), 69.06 (CH$_2$, C-6a), 38.36 (CH$_2$, C-6), 37.11 (CH$_2$, C-8 or C-9), 32.31 (CH$_2$, C-10), 24.85 (CH$_2$, C-9 or C-8); HRESIMS *m/z* 1121.5385 ($C_{69}H_{78}0_{12}Na_1$ [M + Na]$^+$ requires 1121.5386).

2-{Methyl-[2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl]}-5-{methyl-[methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]}-3-iodo-tetrahydrofuran (30/31). Compound **17** (20 mg, 0.018 mmol) was dissolved in dry THF (1 mL) under an N_2 atmosphere, then $NaHCO_3$ (3 mg, 0.04 mmol) and I_2 (23 mg, 0.09 mmol) were added and the solution was stirred at rt. The reaction progress was monitored by TLC (hexane-AcOEt 7:3). After 3 h the reaction mixture was diluted with CH_2Cl_2 (8 mL) and the solution was washed with $Na_2S_2O_3$ satd. sol. in water (3 × 4 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 5 mL). The organic layers were collected, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (hexane-AcOEt 9:1) afforded **30/31** (20 mg, 92% yield) as an inseparable mixture of diastereoisomers. A diastereomeric ratio of 1:1.5 was determined by HPLC analysis (CH_3CN:H_2O 85:15). Major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 7.40–7.18 (m, 35H, H(Ar)), 5.00–4.58 (14H, m, 14 × C*H*HPh), 4.54 (1H, bs, 1-H), 4.48 (d, 1H, *J* 7.2, 1a-H), 4.25–4.20 (3H, m, 10-H, 9-H, 7-H), 4.20–4.12 (1H, m, 11-H), 4.04 (1H, dd, *J* 10.8 *J* 2.0, 11′-H), 3.94 (1H, t, *J* 9.2, 3-H), 3.77–3.72 (2H, m, 6a-H, 6a′-H), 3.65–3.62 (3H, m, 3a-H, 4a-H, 5-H), 3.49–3.42 (3H, m, 2-H, 2a-H, 5a-H), 3.32 (3H, s, OC*H*$_3$), 3.25 (1H, t, *J* 9.3, 4-H), 2.56–2.53 (1H, m, 8-H), 2.10–2.03 (1H, m, 8′-H), 1.97–1.88 (1H, m, 6-H, 6′-H); δ_C (100 MHz, $CDCl_3$) 103.67 (CH, C-1a); 97.93 (CH, C-1), 85.67 (CH, C-10), 84.72 (CH, C-4a), 82.20 (CH, C-2a), 81.99 (CH, C-4), 81.77 (CH, C-3), 80.05 (CH, C-2), 77.80 (CH, C-3a), 76.50 (CH, C-7), 75.74, 75.65, 75.22, 74.83 (CH_2Ph), 73.80 (CH, C-5a), 73.56, 73.35 (CH_2Ph), 68.80 (CH_2, C-6a), 68.05 (CH, C-5), 67.04 (CH_2, C-11), 55.33 (OCH_3), 45.04 (CH_2, C-8), 37.44 (CH_2, C-6), 17.24 (CH, C-9). Maldi-Tof *m/z* 1220.4 (100)($C_{67}H_{73}IO_{12}Na$ [M + Na]$^+$: requires 1220.2).

2-{Methyl-[2,3,6-tri-*O*-benzyl-α-D-4-*O*-glucopyranosyl]}-5-{methyl-[methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]}-3-iodo-tetrahydrofuran (32/33).

Method C. Compound **20** (118 mg, 0.119 mmol) was dissolved in dry CH_2Cl_2 (5 mL) under an N_2 atmosphere. $CaCO_3$ (12 mg, 0.12 mmol) and I_2 (180 mg, 0.71 mmol) were subsequently added and the reaction heated at 40 °C. The reaction was monitored by TLC (hexane-AcOEt 7:3). After 3 h, the reaction was diluted with CH_2Cl_2 (12 mL) and the solution was washed with $Na_2S_2O_3$ satd. sol. in water (3 × 10 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were collected, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (hexane-AcOEt 9:1) afforded **32/33** (91 mg, 68% yield) as a mixture of diastereoisomers. A diastereomeric ratio of 1:1.4 was determined by HPLC analysis (CH_3CN:H_2O 85:15).

Method D. Compound **20** (118 mg, 0.119 mmol) was dissolved in dry CH_2Cl_2 (3 mL) under an inert atmosphere and $CaCO_3$ (6 mg, 0.06 mmol) and AgOTf (6 mg, 0.023 mmol) were successively added. The mixture was cooled to 0 °C, stirred for 10 min and I_2 (55 mg, 0.217 mmol) was added. The reaction was stirred at 0 °C for 3 h, then warmed at rt and stirred for 1 h. The reaction was diluted with CH_2Cl_2 (10 mL) and the solution was washed with $Na_2S_2O_3$ satd. sol. in water (3 × 5 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 5mL). The organic layers were collected, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (hexane-AcOEt 9:1) afforded **32/33** (115 mg, 87% yield) as a mixture of diastereoisomers. A pure analytical sample of a single diastereoisomer was isolated during column chromatography. Major diastereoisomer: δ_H (400 MHz, $CDCl_3$) : 7.32–7.15 (30H, m, H(Ar)), 4.95 (1H, d, *J* 10.8, C*H*HPh), 4.88–4.82 (3H, m, 3 × C*H*HPh), 4.79–4.72 (2H, m, 2 × C*H*HPh), 4.63 (1H, d, *J* 4.6, 1-H), 4.64–4.49 (6H, m, 6 × C*H*HPh), 4.45 (1H, d, *J* 3.6, 1a-H), 4.12–4.07 (2H, m, 7-H, 11-H), 4.02 (1H, dd, *J* 2.0 *J* 9.9, 11′-H), 3.94 (3H, m, 3-H, 3a-H, 9-H), 3.74 (1H, dd, *J* 2.0 *J* 9.9, 6a-H), 3.67–3.59 (1H, dd, H-6a′), 3.60–3.54 (2H, m, 5-H, 5a-H), 3.52–3.42 (m, 3H, 2-H, 2a-H), 3.34 (3H, s, OC*H*$_3$), 3.30 (3H, s, OC*H*$_3$), 3.22 (1H, t, *J* 9.4, 4-H), 2.60–2.47 (1H, m, 8-H), 2.05–1.95 (1H, m, 8′-H), 1.92–1.85 (2H, m, 6-H, 6′-H). Maldi-Tof *m/z* 1143.48 (100) ($C_{67}H_{73}I0_{12}Na$ [M + Na]$^+$ requires 1143.36).

2-{Methyl-[2,3,4,6-tetra-*O*-benzy l-1-deoxy-β-D-1-*C*-glucopyranosil]}-5-{methyl[methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]}-3-iodo-tetrahydrofuran (34/35). Compound 21 (30 mg, 0.028 mmol) was dissolved, under a N_2 atmosphere, in dry THF (1.5 mL) and iodocyclized at rt with I_2 (35 mg, 0.14 mmol) in the presence of $CaCO_3$ (4 mg, 0.028 mmol). After 3 h the reaction mixture was diluted with CH_2Cl_2 (8 mL) and the solution was washed with $Na_2S_2O_3$ satd. sol. in water (3 × 4 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 5 mL). The organic layers were collected, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (hexane-AcOEt 9:1) afforded **34/35** (26 mg, 79% yield) as an inseparable mixture of diastereoisomers. A diastereomeric ratio of 1:2.9 was determined by HPLC analysis (CH_3CN:H_2O 85:15). Major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 7.34–7.27 (35H, m, H(Ar)), 4.99 (1H, d, *J* 10.9, C*H*HPh), 4.95 (1H, d, *J* 10.6, C*H*HPh), 4.92 (1H, d, *J* 10.4, C*H*HPh), 4.85–4.77 (4H, m, 4 × C*H*HPh), 4.69–4.59 (5H, m, 5 × C*H*HPh), 4.54 (1H, d, *J* 3.5, 1-H), 4.51–4.39 (3H, m, 2 × C*H*HPh, 10-H), 4.31–4.21 (3H, m, 1a-H, 7-H, 9-H), 3.96 (1H, t, *J* 9.4, 3-H), 3.83–3.64 (6H, m, 2a-H, 3a-H, 4a-H, 5a-H, 6a-H, 6a′-H), 3.51 (1H, dd, *J* 3.5 *J* 9.7, 2-H), 3.36 (3H, s, OC*H*$_3$), 3.30 (1H, t, *J* 9.3, H-4), 2.64–2.58 (1H, m, H-8), 2.12–2.10 (2H, m, 11-H, 11′-H), 2.06–1.98 (1H, m, 8′-H), 1.97–1.90 (2H, m, 6-H, 6′-H); δ_C (100 MHz, $CDCl_3$) 98.01 (C-1), 84.64 (CH, C-7), 82.03 (CH, C-3), 82.03 (CH, C-4), 80.10 (CH, C-2); 82,36, 79.54, 77.88, 71.62, 67.99 (5 × CH, C-2a C-4a C-3a C-5a C-5), 75.97 (CH, C-1a), 75.74, 75.44, 75.19, 75.09, 73.55, 73.35, 72.51 (Ch_2Ph), 70.50 (CH, C-10), 68.88 (CH_2, C-6a), 55.29 (O*C*H$_3$), 45.01 (CH_2, C-8), 38.00 (CH_2, C-6), 23.99 (CH, C-11), 21.86 (CH, C-9). Maldi-Tof *m/z* 1220.40 ($C_{67}H_{73}I0_{12}Na$ [M + Na]$^+$ requires 1220.22).

2-{1-Iodo-2-[2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl] ethyl}-6-{methyl-[methyl 2,3,4-tri-*O*-benzyl-α-D-xilopyranosidyl]}-tetra-hydro-2H-pyran (36/37). Compound **29** (10 mg, 0.0091 mmol) was dissolved in dry THF (1 mL) under an N_2 atmosphere, then $NaHCO_3$ (2 mg, 0.024 mmol) and I_2 (11 mg, 0.043 mmol) were added and the solution stirred at rt. The reaction was monitored by TLC (hexane-AcOEt 7:3). After 3 h the reaction was diluted with CH_2Cl_2 (4 mL) and the solution was washed with $Na_2S_2O_3$ satd. sol. in water (3 × 2 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 3 mL). The organic layers were collected, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (hexane-AcOEt 9:1) afforded **36/37** (4 mg, 40% yield) as an inseparable mixture of

diastereoisomers. A diastereomeric ratio of 1:1.4 was determined by HPLC analysis (CH_3CN:H_2O 93:7). Major diastereoisomer: δ_H (500 MHz, $CDCl_3$) 7.46–7.16 (35H, m, H(Ar)), 4.90–4.86 (2H, m, 2 × C*H*HPh), 4.81–4.76 (3H, m, 3 × C*H*HPh), 4.70–4.60 (7H, m, 7 × C*H*HPh), 4.54–4.49 (m, 3H, 2 × C*H*HPh, 1-H), 4.43 (1H, d, *J* 8.2, 1a-H), 4.31–4.26 (m, 1H, 12-H), 4.25–4.20 (1H, m, 13-H), 3.99–3.96 (1H, m, 3-H), 3.92–3.86 (2H, m, 13′-H, 5-H), 3.73–3.60 (m, 4H, 6a-H, 6a′-H, 4a-H, 3a-H), 3.56–3.53 (1H, m, 7-H), 3.48 (1H, dd, *J* 3.6, *J* 9.5, 2a-H), 3.44–3.40 (2H, m, 2-H, 5a-H), 3.33 (3H, s, OCH_3), 3.17–3.09 (2H, m, 11-H, 4-H), 2.03–2.01 (1H, m, 6-H), 1.84–1.81 (1H, m, 10-H), 1.32–1.27 (1H, m, 6′-H), 1.27–1.16 (5H, m, 10′-H, 8-H, 8′-H, 9-H, 9′-H); δ_C (100 MHz, $CDCl_3$) 103.10 (CH, C-1a), 98.07 (CH, C-1), 84.52 (CH, C-4a), 82.57 (CH, C-4), 81.90 (CH, C-2a), 81.76 (CH, C-3), 80.54 (CH, C-2), 77.9 (CH, C-3a), 77.13 (CH, C-11), 77.00 (CH, C-5a), 75.67, 75.62 (CH_2Ph), 75.00 (CH, C-5), 74.80, 74.90, 74.76 (CH_2Ph), 74.23 (CH, C-7), 73.19, 73.40 (CH_2Ph), 72.00 (CH_2, C-13), 69.12 (CH_2, C-6a), 55.34 (OCH_3), 38.98 (CH_2, C-6), 29.97 (CH_2, C-10), 34.12 (CH_2, C-8 or C-9), 28.63 (CH_2, C-8 or C-9), 19.53 (CH, C-12). HRESIMS *m/z* 1247.4355 (100) ($C_{69}H_{77}0_{12}INa_1$ $[M + Na]^+$ requires 1247.4352).

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