Synthesis of Divalent 2,2′-Linked Mannose Derivatives by Homodimerization

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Abstract: Several studies have implicated (1→2)-linked mannans as biologically relevant compounds. Recently, there has been a growing interest in the synthesis of multivalent carbohydrate assemblies due to their ability to target multiple receptors simultaneously. In the present work, a protective group strategy, based on the methodology originally developed by Crich, has been utilized for the homodimerization of olefinic carbohydrates, allowing a highly diastereoselective synthesis of some divalent structures. Furthermore, it is shown that divalent donors may undergo coupling reactions without losses in stereoselectivity or efficiency. The strategies described may potentially be applied to the synthesis of diverse neoglycoconjugates and oligosaccharides.

Key words: carbohydrates, divalent molecules, diastereoselective synthesis, homodimerization, (1→2)-linked mannans

In several studies, (1→2)-linked mannans have been found to be of significant importance for the stimulation of biological responses and for functioning as inhibitors of certain diseases and infections (Figure 1).[1,2] Manα(1→2)Man oligomannosides have been shown to bind to specific areas of cyanovirin-N and are considered to be promising structures for the development of anti-HIV vaccines.[3] Manβ(1→2)Man oligosaccharides have been shown to stimulate macrophages to produce TNF-α, and inhibit *Candida albicans* adhesion to endothelial cells.[4–6] In both cases, a polymerization degree of two to seven has been found to be sufficient for obtaining biological activity.[1,3] Recently, several studies have indicated that multivalent assemblies in some cases increase the biological activity of carbohydrates by targeting multiple receptors simultaneously.[7] Divalent molecules can be considered as the simplest model systems for multivalent compounds and to be ideal structures for exploring the minimal structural requirements for such binding.

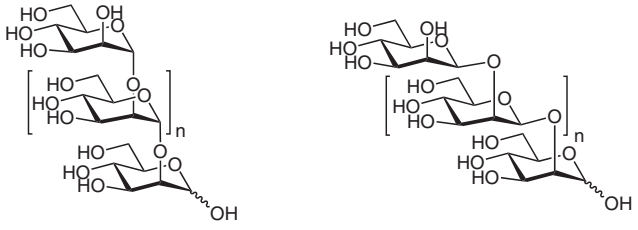

Figure 1 α-Linked mannan (left) and β-linked mannan (right)

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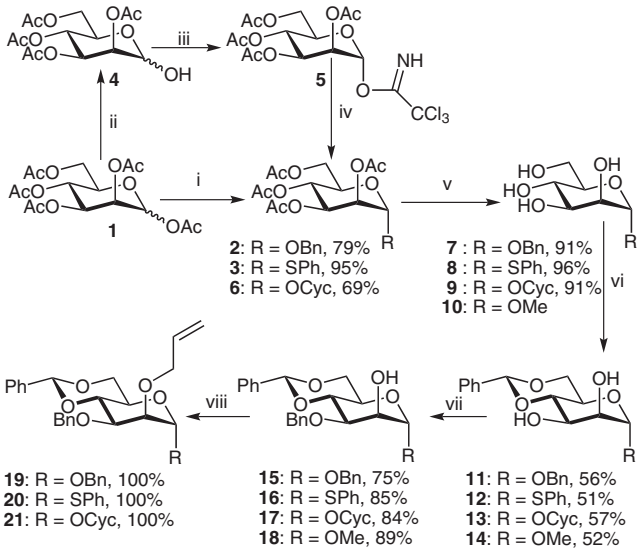
Several methods for the synthesis of divalent molecules have been reported previously.[8–10] One of the most promising routes is based on cross-coupling olefin metathesis. While having great potential in general, several problems have limited the use of cross-coupling metathesis in carbohydrate chemistry. In many cases, the issues are related to the formation of undesired dimers, poor diastereoselectivities and the fact that, in contrast to ring-closing olefin metathesis, the cross-coupling reaction is not driven by an increase in entropy.[11,12]

In the present work, we have specifically targeted the preparation of homodimerization products of mannose monomers and dimers, which could potentially result in biologically relevant oligo/dimeric structures, whilst avoiding many of the problems associated with olefin cross-coupling metathesis mentioned above. Attempts were likewise made to influence the diastereoselectivity of the homodimerization by selecting suitable protecting group strategies. As mentioned, in the mannoside case, (1→2)-linkages between the monosaccharide units have been shown to be of significance in stimulating biological activities.[1,2] Accordingly, as a starting point for the present study, the most reasonable position for the connecting linker to be prepared was between the 2- and the 2′-positions of the mannosides. To our knowledge, such 2,2′-linked divalent sugar moieties have not been reported previously in the literature. Here, we present the preparation of several divalent 2,2′-linked mannoside homodimerization products, which were obtained in good yields and high diastereoselectivities from building blocks containing a terminal olefin. The subsequent deprotection of the metathesis products obtained provided complex divalent carbohydrate structures of potential biological relevance.

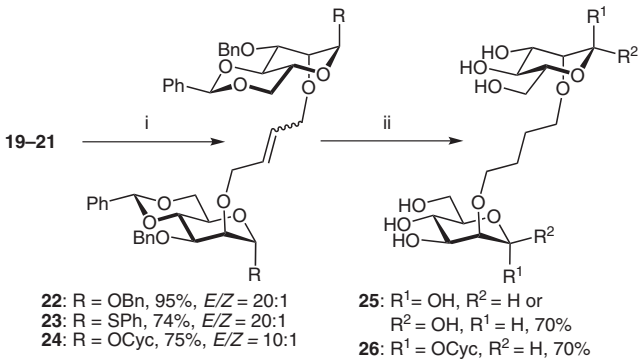
For the preparation of monomeric and olefinic carbohydrate compounds a protective group strategy, developed earlier by Crich et al., was successfully utilized.[13] The essential features of the methodology, relevant in the present work, involves the utilization of 4,6-*O*-benzylidene acetal and 3-*O*-benzyl protection of the mannose starting material, followed by allylation of the 2-position.[14] Accordingly, several 2-*O*-allyl protected mannose building blocks were prepared as illustrated in Scheme 1.

Glycosylation of 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (**1**), using boron trifluoride–diethyl ether complex ($BF_3{\cdot}OEt_2$) as the promoter, with benzyl alcohol and thiophenol, provided the corresponding benzyl (**2**) and



Scheme 1 Synthesis of terminal olefins **19**–**21**. *Reagents and conditions*: (i) $BF_3{\cdot}OEt_2$, corresponding alcohol, CH_2Cl_2, 20–48 h; (ii) hydrazine acetate, DMF, 55 °C, 2 h, 100 %; (iii) DBU, CCl_3CN, CH_2Cl_2, 1.5 h, 72 %; (iv) cyclohexanol, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 22 h; (v) NaOMe, MeOH, 24–48 h; (vi) PTSA, $C_6H_5OCH(OMe)_2$, DMF, 60 °C, 2 h, 200 mbar; (vii) (1) Bu_2SnO, toluene, 120 °C, 3 h; (2) TBABr, CsF, BnBr, 120 °C, 3 h; (viii) NaH, allylbromide, DMF, 1–3 h.

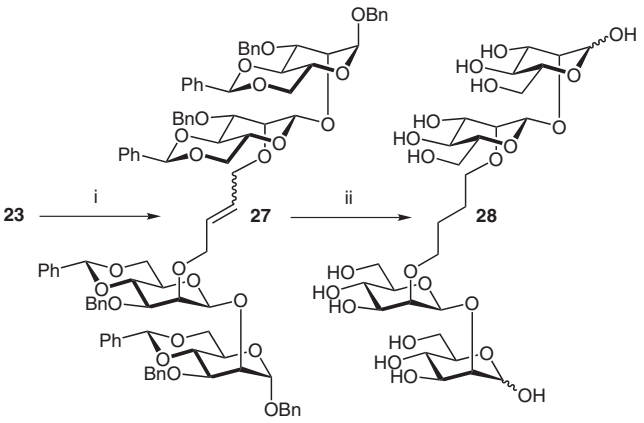
thiophenyl (**3**) 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosides in good to excellent yields. With cyclohexanol, however, only 5% of the glycosylated product was obtained, thus suggesting that an alternative synthetic route should be devised. Accordingly, the cyclohexyl glycoside **6** was prepared by utilizing the corresponding imidate[15] donor **5**, which was prepared by selective deacetylation of the anomeric acetyl group in **1**, followed by reaction with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and trichloroacetonitrile.[16] The coupling reaction between cyclohexanol and **5** was first attempted with trimethylsilyl trifluoromethanesulfonate (TMSOTf) as the promoter, but this resulted in poor yields (22%). Switching to $BF_3{\cdot}OEt_2$, however, led to a significant increase in the yield (69%). Compounds **2**, **3** and **6** were then deacetylated under Zemplén conditions, thereby providing the corresponding benzyl (**7**), thiophenyl (**8**) and cyclohexyl (**9**) α-D-mannopyranosides in excellent yields.[17] Next, the glycosides **7**–**10** were converted into the corresponding 4,6-*O*-benzylidene-protected mannosides by using benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid (PTSA) under reduced pressure in order to remove methanol from the reaction mixture.[13,18] The reaction proceeded in moderate yields with the undesired dibenzylidene-protected substrates formed as side products. Selective benzylation of the 3-position was achieved by refluxing compounds **11**–**14** in toluene with dibutyltin oxide (Bu_2SnO) followed by addition of benzyl bromide. The corresponding acceptors **15**–**18** were obtained in yields ranging from 75–89%, in accordance with the previously reported results by Crich and co-workers.[13] The 2-*O*-allyl derivatives **19**–**21**, required for the cross-coupling metathesis reactions, were then prepared in quantitative yields by reacting the acceptors **15**–**17** with sodium hydride and allylbromide in *N*,*N*-dimethylformamide (DMF), according to procedures reported earlier for similar reactions.[19] The homodimerization reactions of compounds **19**–**21** were carried out according to procedures reported by Das and Roy.[20] In all cases, brownish oils were first obtained, suggesting the presence of ruthenium by-products. The removal of such species has been the focus of several earlier studies; suggested methods include the use of activated carbon followed by flash chromatography on silica gel, triphenylphosphine oxide bound on polymer support and isocyanide.[21–23] For the present work, the method using activated carbon was slightly modified to provide colorless oils or white solids after purification. It should be noted that during the purification procedure, small amounts of the desired products were likely absorbed and hence lost during the process, thus reducing the isolated yields. Nevertheless, good to excellent yields were obtained for the dimerization products **22**–**24** (Scheme 2). In previously described reactions, the presence of sulfur-containing substrates have been reported to decrease the yields by poisoning the catalyst.[10] In the present work, however, such effects were not observed. Generally, *E*/*Z* ratios ranging from 1:1 to 6:1 have been reported for homodimerization reactions.[10,21,24] In the present work, by utilization of the protective group strategy described, highly stereoselective *E*/*Z* ratios of 10:1 to 20:1 were obtained. In the light of literature precedence, these findings can be considered promising and may prove to be useful in future exploration of diastereoselective cross-coupling metathesis reactions in carbohydrate chemistry. In previous examples reporting similar diastereoselectivities, the starting molecules have been tethered prior to the cross-coupling olefin metathesis.[25]



Scheme 2 Synthesis of homodimerization products **25** and **26**. *Reagents and conditions*: (i) Grubbs I catalyst, CH_2Cl_2, 40 °C, 6 h; (ii) H_2 (1.4 bar), Pd/C, MeOH–EtOAc (9:1), 18 h.

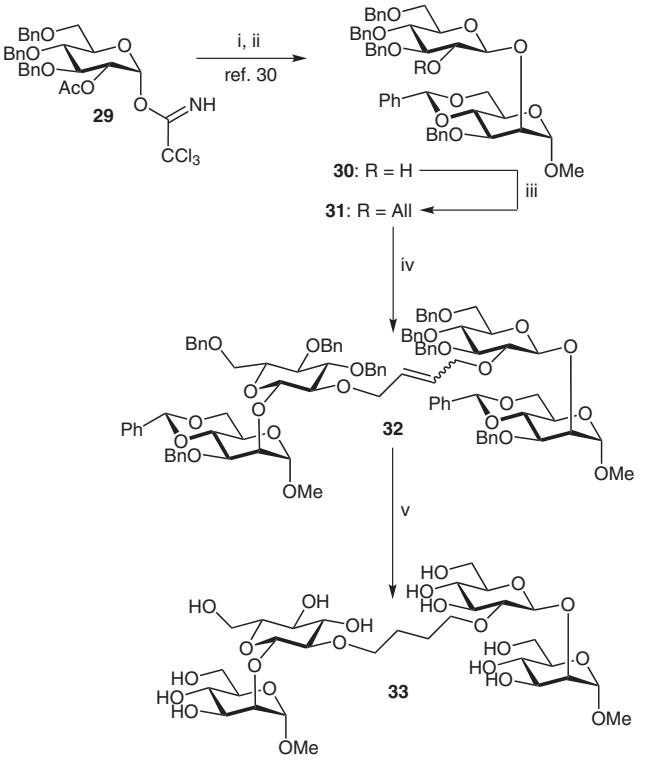
Here, the stereoselectively formed double bond in the metathesis reaction can potentially be subjected to several types of further modifications including hydrolysis and 1,2-*cis*-dihydroxylation. It appears possible that the combination of a 4,6-*O*-benzylidene acetal protecting group, together with sterically congested or electron-rich substituents at the anomeric position, contribute to the high dia-

stereoselectivities observed in the cross-metathesis reaction. The results further suggest that electron-rich groups at the anomeric position may have a larger impact than sterically crowded ones. For the preparation of fully deprotected analogues, the homodimerization products **22** and **24** were subjected to hydrogenolysis. Here, it was observed that high hydrogen pressures (4 bar) resulted in decreased yields, probably due to decomposition of the 2,2′-linker. By lowering the pressure to 1.4 bar, the fully deprotected compounds were obtained in good yields.



Scheme 3 Synthesis of **28**. *Reagents and conditions*: (i) (1) **23**, TTBP, BSP, TF_2O, –60 °C, 0.5 h; (2) **15**, –78 °C, 2 h, 70%; (ii) H_2 (1.4 bar), Pd/C, MeOH–EtOAc (9:1), 50%.

The synthesis of 1,4-bis[2-*O*-β-D-mannopyranosyl-(1→2)-D-mannopyranose]butane (**28**) was accomplished by coupling 2.3 equivalents of benzyl glycoside acceptors with the divalent donor **23** (Scheme 3). For the synthesis of β-linked mannosides, several methods have been reported previously.[13,26,27] The methodology developed by Crich and co-workers has proven to be successful in similar coupling reactions. The key features of this method are the use 4,6-*O*-benzylidene acetal protecting group in combination with a 2-*O*-propargyl group.[13,14,20] In the present case, the olefinic 2-*O*-butenyl linker could be expected to display similar properties to the 2-*O*-propargyl group, thus directing the stereochemical outcome of the glycosidation reaction in a similar fashion. Furthermore, a coupling procedure using 1-benzenesulfinyl piperidine (BSP)/ 2,4,6-tri-*tert*-butylpyrimidine (TTBP) and triflic anhydride (TF_2O) at –78 °C, was reported by Crich to be a powerful tool for creating β-linkages between mannoside units.[28] The aforementioned concepts were successfully utilized in the present work for the synthesis of the divalent β-linked disaccharide **27**. To our knowledge, this is the first example of a synthesis of β-linked mannosides where several leaving groups are simultaneously activated in a coupling reaction. The formation of a β-linkage was confirmed by measuring the $^1J_{C',H'}$ coupling constant by NMR. A value of 155.2 Hz was obtained, thereby indicating that only the β-anomer had been formed ($^1J_{C,H}$ was 168.5 Hz). Furthermore, decreases in yield were not observed, which suggests that similar strategies could also be utilized for the synthesis of larger structures. Hydro-



Scheme 4 Synthesis of **33**. *Reagents and conditions*: (i) **18**, TMSOTf, –10 °C, 0.5 h, 80%; (ii) MeOH–THF (3:1), NaOMe, 18 h, 98% (2 steps)[30]; (iii) NaH, allylbromide, DMF, 3 h, 80%; (iv) Grubbs I catalyst, CH_2Cl_2, 40 °C, 6 h, 61%; (v) H_2 (1.4 bar), Pd/C, MeOH–EtOAc (9:1), 70%.

genolysis of **27** according to earlier procedures resulted in the fully deprotected substrate **28** in moderate yield.

For the preparation of methyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**31**), a strategy utilizing the imidate donor **29**[29] and acceptor **18** was selected (Scheme 4) to provide, after the coupling reaction and deacetylation, the disaccharide **30** with a free 2′-hydroxy group.[30] Employing methods described previously, the disaccharide **30** was converted into the corresponding 2′-*O*-allyl ether derivative in 80% yield. The slightly lower yield, in comparison with the allylation of monosaccharides, may be explained by steric hindrance. Next, the homodimerization of **31** was carried out as described earlier, providing compound **32** in moderate yields and high diastereoselectivity, suggesting that large substituents at the anomeric position have an impact on the diastereoselective outcome of the homodimerization reaction. The slightly lower yield is possibly due to severe steric hindrance in this molecule. Hydrogenolysis of **32** gave 1,4-bis[methyl-α-D-mannopyranosyl-(2→1)-2-*O*-β-D-glucopyranosyl]butane in good yield.

To conclude, a protective group strategy allowing highly diastereoselective homodimerization reactions of carbohydrates has been utilized. The key features of this strategy involve the use of electron-rich substituents at the anomeric position in combination with a 4,6-*O*-benzylidene acetal. Furthermore, it has been shown that sev-

eral leaving groups can be activated and coupled simultaneously without losses in selectivity or yield. Future work in this area may be directed towards expanding the scope of these strategies into the field of oligosaccharide synthesis and cross-coupling olefin metathesis reactions. Modified strategies might prove to be powerful tools for the synthesis of diverse neoglycoconjugates.[31] In the present work, several divalent carbohydrate derivatives were prepared. These compounds may potentially show biological activities and could be screened, for example, against *C. albicans* or cyanovirin-N.

The ^{1}H and ^{13}C NMR spectra as well as the COSY, HSQC and HMBC experiments were recorded at 25 °C with a Bruker AV 600 MHz spectrometer. Chemical shifts (δ) are reported downfield from TMS with residual $CHCl_3$ or MeOH as internal reference. HRMS were recorded using either a Bruker Micro Q-TOF with ESI (electrospray ionization) operated in the positive mode, or a Fison ZabSpecOaTOF with EI (electron impact) ionization operated in the positive mode. Optical rotations were measured with a Perkin–Elmer 241 polarimeter equipped with a Na-lamp (589 nm). TLC was performed on aluminum sheets precoated with silica gel 60 F_{254} (Merck). Spots were visualized by UV followed by charring with 1:10 H_2SO_4/MeOH and burning with a heat gun. Preparative TLC was performed on aluminum sheets precoated with silica gel 60 F_{254} (0.5 cm). Spots were visualized according to the earlier procedure. Flash chromatography was carried out on silica gel 60 (0.040–0.060 mm, Merck) with different solvent systems based on differences in structure. LC-MS analyses were carried out using an Agilent 1100 series LC/MSD Trap SL instrument equipped with an ESI source, operated in the positive mode. HPLC purifications were performed on an Agilent 1100 series liquid chromatographic system. Reaction solvents were dried and distilled under argon before use. All reactions containing sensitive reagents were carried out under an argon atmosphere. Compounds **1** and **10** were obtained from commercial sources. Compounds **3**–**5**, **8**, **11**, **12**, **15** and **16** have previously been reported in the literature, however, to our knowledge, fully characterized NMR data for these compounds are presented here for the first time.[13,32–34]

Benzyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (2)[30]

To a stirred solution of 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (4.5 g, 12.73 mmol) and 4 Å MS (1 g) in CH_2Cl_2 (40 mL), was added BnOH (4 equiv). The reaction mixture was stirred for 20 min, then cooled with an ice bath and $BF_3{\cdot}OEt_2$ (8 equiv) was added dropwise. The resulting mixture was stirred for 15 min, then brought to r.t. and stirring was continued for 48 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and poured into ice-cold H_2O (200 mL) with stirring. The organic phase was separated and washed with sat. $NaHCO_3$ (100 mL), H_2O (100 mL) and brine (100 mL). The organic phase was dried with anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 3:1) to give **2**.

Yield: 4.4 g (79%); colorless oil.

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (3)[13]

To a stirred solution of 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (11.17 g, 28.61 mmol) and 4 Å MS (1 g) in CH_2Cl_2 (200 mL), was added thiophenol (1.5 equiv). The reaction mixture was stirred for 20 min, then cooled with an ice bath and $BF_3{\cdot}OEt_2$ (5 equiv) was added dropwise. The resulting mixture was stirred for 15 min, then brought to r.t. and stirring was continued for 20 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and poured into ice-cold H_2O (150 mL) with stirring. The organic phase was separated and washed with sat. $NaHCO_3$ (100 mL). The organic phase was separated and 1 M NaOH (100 mL) was added. Stirring was continued for 1 h, then the organic phase was separated and washed with sat. $NaHCO_3$ (100 mL) and 1 M NaOH (100 mL). The organic phase was dried with anhydrous $MgSO_4$, filtered and concentrated to give **3**.

Yield: 11.92 g (95%); yellowish oil; R_f = 0.49 (hexane–EtOAc, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50–5.30 (m, 5 H, ArH), 5.50 (dd, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ = 3.2 Hz, 1 H, H-2), 5.50 (d, 1 H, H-1), 5.33 (dd, $J_{4,5}$ = 9.8 Hz, $J_{3,4}$ = 9.9 Hz, 1 H, H-4), 5.32 (dd, 1 H, H-3), 4.55 (ddd, $J_{5,6a}$ = 2.3 Hz, $J_{5,6b}$ = 5.9 Hz, 1 H, H-5), 4.31 (dd, $J_{6a,6b}$ = –12.3 Hz, 1 H, H-6b), 4.11 (dd, 1 H, H-6a), 2.16, 2.08, 2.06, 2.02 (s, 12 H, 4 × $OCCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 169.9, 169.8 (O*C*CH_3), 132.1–129.2 (Ar), 85.7 (C-1), 70.9 (C-2), 69.5 (C-5), 69.4 (C-3), 66.4 (C-4), 62.4 (C-6), 20.9, 20.7 (OC*C*H_3).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{24}O_9SNa$: 463.1033; found: 463.1039.

HRMS: *m*/*z* [M + K]$^+$ calcd for $C_{20}H_{24}O_9SK$: 479.0798; found: 479.0791.

2,3,4,6-Tetra-*O*-acetyl-D-mannopyranose (4)[33]

To a solution of 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (1.87 g, 4.78 mmol) in DMF (28 mL), was added hydrazine acetate (1.12 equiv). The reaction mixture was stirred at 55 °C for 2 h, then cooled to r.t., diluted with EtOAc (80 mL) and extracted with sat. $NaHCO_3$ (60 mL). The resulting mixture was filtered through Celite and the organic layer was separated. The organic layer was washed with brine (50 mL) and H_2O (2 × 50 mL), dried with anhydrous $MgSO_4$, filtered and concentrated to give **4**.

Yield: 1.67 g (100% total; 86% α, 14% β); yellowish oil; R_f = 0.37 (hexane–EtOAc, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ (α-anomer) = 5.43 (dd, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 10.1 Hz, 1 H, H-3), 5.31 (dd, $J_{4,5}$ = 10.1 Hz, 1 H, H-4), 5.29 (dd, $J_{1,2}$ = 1.9 Hz, 1 H, H-2), 5.26 (d, 1 H, H-1), 4.27 (dd, $J_{5,6b}$ = 5.2 Hz, $J_{6a,6b}$ = –12.2 Hz, 1 H, H-6b), 4.24 (ddd, $J_{5,6a}$ = 2.3 Hz, 1 H, H-5), 4.15 (dd, 1 H, H-6a), 2.17, 2.11, 2.06, 2.01 (s, 12 H, 4 × $OCCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ (α-anomer) = 170.7, 170.1, 169.9, 169.8 (O*C*CH_3), 92.3 (C-1), 69.9 (C-2), 68.7 (C-3, C-5), 66.1 (C-4), 62.6 (C-6), 20.9, 20.8, 20.7 (OC*C*H_3).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{20}O_{10}Na$: 371.0949; found: 371.0942.

2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranose Trichloroacetimidate (5)[33]

To a solution of **4** (1.7 g, 4.78 mmol) in CH_2Cl_2 (25 mL), was added DBU (0.13 equiv) and CCl_3CN (1.17 equiv) at 0 °C. The reaction mixture was brought to r.t. and stirring was continued for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with brine (30 mL), dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 2:1 + 0.1% Et_3N) to give **5**.

Yield: 2.0 g (72%); yellowish oil; R_f = 0.58 (hexane–EtOAc, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.79 (s, 1 H, NH), 6.29 (d, $J_{1,2}$ = 2.0 Hz, 1 H, H-1), 5.48 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, H-2), 5.41 (dd, $J_{3,4}$ = 10.1 Hz, 1 H, H-3), 5.40 (dd, $J_{4,5}$ = 10.0 Hz, 1 H, H-4), 4.28 (dd, $J_{5,6b}$ = 5.0 Hz, $J_{6a,6b}$ = –12.4 Hz, 1 H, H-6b), 4.19 (ddd, $J_{5,6a}$ = 2.4 Hz, 1 H, H-5), 4.17 (dd, 1 H, H-6a), 2.20, 2.10, 2.07, 2.01 (s, 12 H, $OCCH_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 169.8, 169.7, 169.6 (O*C*CH_3), 159.8 (*C*NH), 94.5 (C-1), 77.2–76.8 (CCl_3, overlapped

with $CDCl_3$), 71.2 (C-5), 68.8 (C-3), 67.8 (C-2), 65.4 (C-4), 62.0 (C-6), 20.8, 20.7, 20.7, 20.6 (OC*C*H$_3$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{20}Cl_3NO_{10}Na$: 514.0045; found: 514.0029.

Cyclohexyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (6)

To a solution of **5** (0.84 g, 1.70 mmol) in CH_2Cl_2 (10 mL) and 4 Å MS (0.4 g), was added cyclohexanol (5.4 equiv). The reaction mixture was stirred for 30 min, cooled on an ice bath and $BF_3{\cdot}OEt_2$ (10.9 equiv) was added dropwise. The reaction mixture was brought to r.t. and stirring was continued for 21.5 h. The reaction was neutralized with Et_3N, filtered and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 4:1→3:1) to give **6**.

Yield: 0.5 g (69%); colorless oil; R_f = 0.62 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +32.5 (*c* 1, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.38 (dd, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.27 (dd, $J_{4,5}$ = 10.2 Hz, 1 H, H-4), 5.19 (dd, $J_{1,2}$ = 1.8 Hz, 1 H, H-2), 4.96 (d, 1 H, H-1), 4.26 (dd, $J_{5,6b}$ = 5.5 Hz, $J_{6a,6b}$ = –12.2 Hz, 1 H, H-6b), 4.12 (dd, $J_{5,6a}$ = 2.3 Hz, 1 H, H-6a), 4.08 (ddd, 1 H, H-5), 3.64–3.55 (m, 1 H, OC*H*C$_5$H$_{10}$), 2.16, 2.10, 2.05, 1.99 (s, 12 H, OCC*H*$_3$), 1.90–1.71 (m, 4 H, OCHC$_5$*H*$_{10}$), 1.55–1.23 (m, 6 H, OCHC$_5$*H*$_{10}$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.7, 170.2, 170.0, 169.8 (O*C*CH$_3$), 95.9 (C-1), 76.8 (O*C*HC$_5$H$_{10}$), 70.3 (C-2), 69.2 (C-3), 68.4 (C-5), 66.4 (C-4), 62.6 (C-6), 33.2, 31.4, 25.5, 24.1, 23.8 (OCH*C*$_5$H$_{10}$), 21.0, 20.8 (OC*C*H$_3$).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{20}H_{31}O_{10}$: 431.1917; found: 431.1886.

Deacetylation; General Procedure

To a solution of the acetylated compound in MeOH (1 mL/100 mg of acetylated compound), was added 5.4 M NaOMe (0.5 equiv per acetyl group). The reaction mixture was stirred for 24–48 h, neutralized with DOWEX 50 (H$^+$ form), filtered and concentrated. The crude product was purified by flash chromatography (CH_2Cl_2–MeOH, 1:0→5:1) to give the corresponding deacetylated compound.

Benzyl α-D-Mannopyranoside (7)[30,34]

Synthesized from **2** (0.7 g, 1.60 mmol) according to the general procedure for deacetylation, to give **7** with analytical data in agreement with those previously reported.

Yield: 0.39 g (91%); white crystals.

Phenyl 1-Thio-α-D-mannopyranoside (8)[13]

Synthesized from **3** (11.92 g, 27.10 mmol) according to the general procedure for deacetylation.

Yield: 7.10 g (96%); yellowish oil; R_f = 0.29 (MeOH–$CHCl_3$, 1:5).

^{1}H NMR (600 MHz, CD_3OD): δ = 7.53–7.25 (m, 5 H, ArH), 5.42 (dd, $J_{1,2}$ = 1.6 Hz, 1 H, H-1), 4.08 (dd, $J_{2,3}$ = 3.3 Hz, 1 H, H-2), 4.03 (ddd, $J_{5,6a}$ = 2.4 Hz, $J_{5,6b}$ = 5.6 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, H-5), 3.81 (dd, $J_{6a,6b}$ = –12.0 Hz, 1 H, H-6a), 3.76 (dd, 1 H, H-6b), 3.72 (dd, $J_{3,4}$ = 9.5 Hz, 1 H, H-4), 3.68 (dd, 1 H, H-3).

^{13}C NMR (150 MHz, CD_3OD): δ = 136.0–128.6 (Ar), 90.6 (C-1), 75.7 (C-5), 73.8 (C-2), 73.2 (C-3), 68.8 (C-4), 62.7 (C-6).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{16}O_5SNa$: 295.0611; found: 295.0603.

HRMS: *m*/*z* [M + K]$^+$ calcd for $C_{12}H_{16}O_9SK$: 311.0350; found: 311.0348.

Cyclohexyl α-D-Mannopyranoside (9)

Synthesized from **6** (0.41 g, 0.96 mmol) according to the general procedure for deacetylation.

Yield: 0.23 g (91%); white foam; R_f = 0.42 (CH_2Cl_2–MeOH, 4:1); $[\alpha]_D^{23}$ +93.5 (*c* 1, MeOH).

^{1}H NMR (600 MHz, CD_3OD): δ = 4.89 (d, $J_{1,2}$ = 1.8 Hz, 1 H, H-1), 3.80 (dd, $J_{5,6a}$ = 2.2 Hz, $J_{6a,6b}$ = –11.8 Hz, 1 H, H-6a), 3.73 (dd, $J_{2,3}$ = 3.4 Hz, 1 H, H-2), 3.70 (dd, $J_{5,6b}$ = 5.6 Hz, 1 H, H-6b), 3.70 (dd, $J_{3,4}$ = 9.2 Hz, H-3), 3.70–3.62 (m, 1 H, OC*H*C$_5$H$_{10}$), 3.60 (ddd, $J_{4,5}$ = 9.3 Hz, 1 H, H-5), 3.60 (dd, 1 H, H-4), 1.93–1.70 (m, 4 H, OCHC$_5$*H*$_{10}$), 1.58–1.2 (m, 6 H, OCHC$_5$*H*$_{10}$).

^{13}C NMR (150 MHz, CD_3OD): δ = 99.4 (C-1), 75.8 (O*C*HC$_5$H$_{10}$), 74.7 (C-5), 72.8 (C-2), 72.7 (C-3), 68.8 (C-4), 63.0 (C-6), 34.5, 32.4, 26.9, 25.1, 24.9 (OCH*C*$_5$H$_{10}$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{22}O_6Na$: 285.1314; found: 285.1321.

Synthesis of 4,6-*O*-Benzylidene-α-D-mannopyranosides; General Procedure

To a solution of the corresponding deacetylated compound in DMF (1 mL/40 mg deacetylated compound) was added PTSA (10 mol%) and benzaldehyde dimethyl acetal (1 equiv). The reaction mixture was stirred at 60 °C and 200 mbar for 2 h, concentrated and the residue was dissolved in EtOAc (15 mL). The organic phase was washed with sat. $NaHCO_3$ (10 mL) and H_2O (2 × 10 mL) and the combined aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic phase was washed with brine (15 mL), dried with anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (CH_2Cl_2–MeOH, 1:0→5:1) to give the corresponding 4,6-*O*-benzylidene-α-D-mannopyranoside.

Benzyl 4,6-*O*-Benzylidene-α-D-mannopyranoside (11)[32]

Synthesized from **7** (0.37 g, 1.4 mmol) according to the general procedure for the synthesis of 4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.27 g (56%); white solid; R_f = 0.06 ($CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50–7.32 (m, 10 H, ArH), 5.58 (s, 1 H, CHPh), 4.98 (d, $J_{1,2}$ = 1.5 Hz, 1 H, H-1), 4.75 and 4.54 (2 × d, *J* = –11.9 Hz, 2 × 1 H, C*H*$_2$Ph), 4.27 (dd, $J_{5,6a}$ = 5.0 Hz, $J_{6a,6b}$ = –10.4 Hz, 1 H, H-6a), 4.15 (ddd, $J_{3,3\text{-OH}}$ = 0.4 Hz, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 9.6 Hz, 1 H, H-3), 4.11 (ddd, $J_{2,2\text{-OH}}$ = 1.2 Hz, 1 H, H-2), 3.95 (dd, $J_{4,5}$ = 9.5 Hz, 1 H, H-4), 3.90 (ddd, $J_{5,6b}$ = 10.3 Hz, 1 H, H-5), 3.84 (dd, 1 H, H-6b), 2.59 (d, 1 H, 3-OH), 2.56 (d, 1 H, 2-OH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.2–126.2 (Ar), 102.3 (CHPh), 99.3 (C-1), 78.9 (C-4), 71.0 (C-2), 69.5 (CH$_2$Ph), 68.8 (C-6), 68.7 (C-3), 63.2 (C-5).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{22}O_6Na$: 381.1309; found: 381.1316.

Phenyl 4,6-*O*-Benzylidene-1-thio-α-D-mannopyranoside (12)[13]

Synthesized from **8** (7.09 g, 26.1 mmol) according to the general procedure for synthesis of 4,6-*O*-benzylidene-α-D-mannopyranosides, to give compound **12** with analytical data in agreement with those previously reported.

Yield: 4.80 g (51%); white solid.

Cyclohexyl 4,6-*O*-Benzylidene-α-D-mannopyranoside (13)

Synthesized from **9** (0.073 g, 0.28 mmol) according to the general procedure for synthesis of 4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.057 g (57%); colorless oil; R_f = 0.06 ($CHCl_3$); $[\alpha]_D^{23}$ +70.5 (*c* 1, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51–7.36 (m, 5 H, ArH), 5.58 (s, 1 H, CHPh), 5.03 (d, $J_{1,2}$ = 1.5 Hz, 1 H, H-1), 4.27 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.4 Hz, 1 H, H-6a), 4.13 (ddd, $J_{3,3\text{-OH}}$ = 3.4 Hz,

$J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 9.5 Hz, 1 H, H-3), 4.02 (ddd, $J_{2,2\text{-OH}}$ = 2.4 Hz, 1 H, H-2), 3.93 (dd, $J_{4,5}$ = 8.9 Hz, 1 H, H-4), 3.92 (ddd, $J_{5,6b}$ = 10.1 Hz, 1 H, H-5), 3.82 (dd, 1 H, H-6b), 3.67–3.58 (m, 1 H, OC*H*C_5H_{10}), 2.57 (d, 1 H, 2-O*H*), 2.54 (d, 1 H, 3-O*H*), 1.95–1.80 (m, 2 H, OCHC$_5$*H*$_{10}$), 1.78–1.68 (m, 2 H, OCHC$_5$*H*$_{10}$), 1.56–1.18 (m, 6 H, OCHC$_5$*H*$_{10}$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.3–126.2 (Ar), 102.2 (CHPh), 98.0 (C-1), 79.2 (C-4), 75.3 (O*C*HC$_5$H$_{10}$), 71.6 (C-2), 68.9 (C-6), 68.8 (C-3), 63.0 (C-5), 33.4, 31.3, 25.6, 24.0, 23.8 (OCH*C*$_5$H$_{10}$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{26}O_6Na$: 373.1622; found: 373.1632.

Methyl 4,6-*O*-Benzylidene-α-D-mannopyranoside (14)[32]

Synthesized from methyl α-D-mannopyranoside (3.0 g, 15.5 mmol) according to the general procedure for synthesis of 4,6-*O*-benzylidene-α-D-mannopyranosides, to give compound **14** with analytical data in agreement with those previously reported.

Yield: 2.27 g (52%); colorless oil.

Synthesis of 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides; General Procedure

To a solution of the corresponding 4,6-*O*-benzylidene-α-D-mannopyranoside in toluene (4 mL/100 mg starting material), was added Bu_2SnO (1 equiv). The reaction mixture was refluxed for 3 h, cooled to r.t. then TBABr (1.05 equiv), CsF (1.02 equiv) and BnBr (1.04 equiv) were added. The resulting mixture was refluxed for 3 h, cooled to r.t., diluted with EtOAc (40 mL) and sat. $NaHCO_3$ (30 mL) and filtered through Celite. The organic phase was separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phase was washed with H_2O (40 mL), brine (30 mL), dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 4:1) to give the corresponding 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside.

Benzyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (15)[32]

Synthesized from **11** (0.64 g, 1.77 mmol) according to the general procedure for synthesis of 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.65 g (75%); colorless oil; R_f = 0.55 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +55.9 (*c* 1, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51–7.28 (m, 15 H, ArH), 5.63 (s, 1 H, CHPh), 4.97 (d, $J_{1,2}$ = 1.5 Hz, 1 H, H-1), 4.86 and 4.72 (2 × d, *J* = –11.8 Hz, 2 × 1 H, CH_2Ph_a), 4.71 and 4.52 (2 × d, *J* = –11.8 Hz, 2 × 1 H, CH_2Ph_b), 4.27 (dd, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = –10.3 Hz, 1 H, H-6a), 4.12 (dd, $J_{4,5}$ = 9.5 Hz, $J_{3,4}$ = 9.6 Hz, 1 H, H-4), 4.11 (ddd, $J_{2,2\text{-OH}}$ = 1.4 Hz, $J_{2,3}$ = 3.5 Hz, 1 H, H-2), 3.98 (dd, 1 H, H-3), 3.91 (ddd, $J_{5,6b}$ = 10.5 Hz, 1 H, H-5), 3.87 (dd, 1 H, H-6b), 2.65 (d, 1 H, 2-OH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.0–126.0 (Ar), 101.6 (CHPh), 99.2 (C-1), 78.9 (C-4), 75.7 (C-3), 73.1 (CH_2Ph_a), 70.1 (C-2), 69.4 (CH_2Ph_b), 68.9 (C-6), 63.5 (C-5).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{28}O_6Na$: 471.1778; found: 471.1765.

Phenyl 3-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (16)[13]

Synthesized from **12** (2.59 g, 7.20 mmol) according to the general procedure for synthesis of 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 2.90 g (85%); colorless oil; R_f = 0.65 (hexane–EtOAc, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.52–7.28 (m, 15 H, Ph), 5.63 (s, 1 H, CHPh), 5.60 (d, $J_{1,2}$ = 1.2 Hz, 1 H, H-1), 4.90 and 4.75 (2 × d, *J* = –11.8 Hz, 2 × 1 H, CH_2Ph), 4.34 (ddd, $J_{5,6a}$ = 4.9 Hz, $J_{4,5}$ = 9.6 Hz, $J_{5,6b}$ = 10.2 Hz, 1 H, H-5), 4.29 (ddd, $J_{2,2\text{-OH}}$ = 1.4 Hz, $J_{2,3}$ = 3.4 Hz, 1 H, H-2), 4.21 (dd, $J_{6a,6b}$ = –10.4 Hz, 1 H, H-6a), 4.18 (dd, $J_{3,4}$ = 9.6 Hz, 1 H, H-4), 3.97 (dd, 1 H, H-3), 3.86 (dd, 1 H, H-6b), 2.82 (d, 1 H, 2-OH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.7–126.1 (Ar), 101.6 (CHPh), 87.8 (C-1), 79.0 (C-4), 75.7 (C-3), 73.2 (CH_2Ph), 71.4 (C-2), 68.5 (C-6), 64.6 (C-5).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{26}O_5SNa$: 473.1393; found: 473.1403.

Cyclohexyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (17)

Synthesized from **13** (0.13 g, 0.37 mmol) according to the general procedure for synthesis of 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.14 g (84%); colorless oil; R_f = 0.64 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +49.5 (*c* 1, CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.52–7.30 (m, 10 H, ArH), 5.62 (s, 1 H, CHPh), 5.03 (d, $J_{1,2}$ = 1.5 Hz, 1 H, H-1), 4.88 and 4.73 (2 × d, *J* = –11.7 Hz, 2 × 1 H, CH_2Ph), 4.27 (dd, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = –10.4 Hz, 1 H, H-6a), 4.10 (dd, $J_{3,4}$ = 9.6 Hz, $J_{4,5}$ = 9.7 Hz, 1 H, H-4), 4.04 (ddd, $J_{2,2\text{-OH}}$ = 1.4 Hz, $J_{2,3}$ = 3.4 Hz, 1 H, H-2), 3.97 (dd, 1 H, H-3), 3.93 (ddd, $J_{5,6b}$ = 10.4 Hz, 1 H, H-5), 3.85 (dd, 1 H, H-6b), 3.65–3.55 (m, 1 H, OC*H*C$_5$H$_{10}$), 2.63 (d, 1 H, 2-OH), 1.86–1.71 (m, 4 H, OCHC$_5$*H*$_{10}$), 1.58–1.23 (m, 6 H, OCHC$_5$*H*$_{10}$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.1–126.0 (Ar), 101.5 (CHPh), 97.8 (C-1), 79.1 (C-4), 75.8 (C-3), 75.2 (O*C*HC$_5$H$_{10}$), 73.1 (CH_2Ph), 70.6 (C-2), 68.9 (C-6), 63.3 (C-5), 33.4, 31.3, 25.6, 24.1, 23.8 (OCH*C*$_5$H$_{10}$).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{32}O_6$: 440.2198; found: 440.2199.

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (18)[32]

Synthesized from **14** (0.10 g, 0.35 mmol) according to the general procedure for synthesis of 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides, to give **18** with analytical data in agreement with those previously reported.

Yield: 0.12 g (89%); colorless oil.

Synthesis of 2-*O*-Allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides; General Procedure

To a solution of the corresponding 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside in DMF (2 mL/100 mg starting material), was added NaH (1.9 equiv) at 0 °C. The reaction mixture was stirred for 15 min, then brought to r.t., stirred for 10 min then allylbromide (1.5 equiv) was added. The resulting mixture was stirred for 1–3 h, quenched with MeOH (0.4 mL/mmol starting material), diluted with CH_2Cl_2 (30 mL) and washed with sat. $NaHCO_3$ (30 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine (30 mL), dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 8:1) to give the corresponding 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside.

Benzyl 2-*O*-Allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (19)[33]

Synthesized from **15** (0.18 g, 0.39 mmol) according to the general procedure for synthesis of 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.21 g (100%); white crystals; R_f = 0.84 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +66.6 (*c* 1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50–7.27 (m, 15 H, ArH), 5.90 [dddd, $J_{CH2a,CH}$ = 6.0 Hz, $J_{CH2b,CH}$ = 6.2 Hz, $J_{CH,CH2(cis)}$ = 10.3 Hz, $J_{CH,CH2(trans)}$ = 17.2 Hz, 1 H, CH_2CHCH_2], 5.63 (s, 1 H, CHPh), 5.26 [dddd, $J_{CH2a,CH2(trans)}$ = –1.5 Hz, $J_{CH2b,CH2(trans)}$ = –1.5 Hz, $J_{CH2(trans),CH2(cis)}$ = –1.7 Hz, 1 H, $CH_2CHCH_{2(trans)}$], 5.17 [dddd, $J_{CH2a,CH2(cis)}$ = –1.1 Hz, $J_{CH2b,CH2(cis)}$ = –1.2 Hz, 1 H, $CH_2CHCH_{2(cis)}$], 4.90 (d, $J_{1,2}$ = 1.7 Hz, 1 H, H-1), 4.87 and 4.70 (2 × d, J = –12.1 Hz, 2 × 1 H, CH_2Ph_a), 4.72 and 4.49 (2 × d, J = –11.9 Hz, 2 × 1 H, CH_2Ph_b), 4.25 (dddd, $J_{CH2a,CH2b}$ = –12.9 Hz, 1 H, $CH_{2b}CHCH_2$), 4.24 (dd, $J_{5,6a}$ = 4.7 Hz, $J_{6a,6b}$ = –10.2 Hz, 1 H, H-6a), 4.21 (dd, $J_{4,5}$ = 9.2 Hz, $J_{3,4}$ = 10.0 Hz, 1 H, H-4), 4.15 (dddd, 1 H, $CH_{2a}CHCH_2$), 4.01 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, H-3), 3.88 (dd, $J_{5,6b}$ = 10.4 Hz, 1 H, H-6b), 3.85 (ddd, 1 H, H-5), 3.82 (dd, 1 H, H-2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.7–126.0 (Ar), 134.8 (CH_2CHCH_2), 117.8 (CH_2CHCH_2), 101.4 (CHPh), 98.9 (C-1), 79.2 (C-4), 76.6 (C-2), 76.3 (C-3), 73.3 (CH_2Ph_a), 73.1 (CH_2CHCH_2), 69.3 (CH_2Ph_b), 68.8 (C-6), 64.4 (C-5).

HRMS: m/z [M + Na]$^+$ calcd for $C_{30}H_{32}O_6Na$: 511.2091; found: 511.2103.

Phenyl 2-*O*-Allyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (20)[13]

Synthesized from **16** (0.16 g, 0.35 mmol) according to the general procedure for synthesis of 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.18 g (100%); colorless oil; R_f = 0.93 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +145.2 (*c* 1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.52–7.27 (m, 15 H, ArH), 5.92 [dddd, $J_{CH2a,CH}$ = 5.8 Hz, $J_{CH2b,CH}$ = 5.9 Hz, $J_{CH,CH2(cis)}$ = 10.3 Hz, $J_{CH,CH2(trans)}$ = 17.2 Hz, 1 H, CH_2CHCH_2], 5.64 (s, 1 H, CHPh), 5.53 (d, $J_{1,2}$ = 1.5 Hz, 1 H, H-1), 5.29 [dddd, $J_{CH2a,CH2(trans)}$ = –1.5 Hz, $J_{CH2b,CH2(trans)}$ = –1.5 Hz, $J_{CH2(trans),CH2(cis)}$ = –1.7 Hz, 1 H, $CH_2CHCH_{2(trans)}$], 5.20 [dddd, $J_{CH2a,CH2(cis)}$ = –1.2 Hz, $J_{CH2b,CH2(cis)}$ = –1.2 Hz, 1 H, $CH_2CHCH_{2(cis)}$], 4.88 and 4.73 (2 × d, J = –12.2 Hz, 2 × 1 H, CH_2Ph), 4.29 (ddd, $J_{5,6a}$ = 4.8 Hz, $J_{4,5}$ = 9.5 Hz, $J_{5,6b}$ = 10.0 Hz, 1 H, H-5), 4.26 (dd, $J_{3,4}$ = 9.9 Hz, 1 H, H-4), 4.22 (dd, $J_{6a,6b}$ = –10.3 Hz, 1 H, H-6a), 4.20 (dddd, $J_{CH2a,CH2b}$ = –12.2 Hz, 1 H, $CH_{2a}CHCH_2$), 4.18 (dddd, 1 H, $CH_{2b}CHCH_2$), 3.99 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, H-2), 3.96 (dd, 1 H, H-3), 3.88 (dd, 1 H, H-6b).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.4–126.1 (Ar), 134.5 (CH_2CHCH_2), 118.0 (CH_2CHCH_2), 101.5 (CHPh), 87.3 (C-1), 79.1 (C-4), 78.1 (C-2), 76.1 (C-3), 73.2 (CH_2Ph), 72.6 (CH_2CHCH_2), 68.5 (C-6), 65.4 (C-5).

HRMS: m/z [M + Na]$^+$ calcd for $C_{29}H_{30}O_5SNa$: 513.1706; found: 513.1740.

HRMS: m/z [M + K]$^+$ calcd for $C_{29}H_{30}O_5SK$: 529.1446; found: 529.1478.

Cyclohexyl 2-*O*-Allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (21)

Synthesized from **17** (0.02 g, 0.05 mmol) according to the general procedure for synthesis of 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.02 g (100%); colorless oil; R_f = 0.82 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ +48.3 (*c* 0.1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51–7.27 (m, 10 H, ArH), 5.94 [dddd, $J_{CH2a,CH}$ = 5.5 Hz, $J_{CH2b,CH}$ = 6.3 Hz, $J_{CH,CH2(cis)}$ = 10.3 Hz, $J_{CH,CH2(trans)}$ = 17.2 Hz, 1 H, CH_2CHCH_2], 5.63 (s, 1 H, CHPh), 5.29 [dddd, $J_{CH2a,CH2(trans)}$ = –1.6 Hz, $J_{CH2b,CH2(trans)}$ = –1.6 Hz, $J_{CH2(trans),CH2(cis)}$ = –1.7 Hz, 1 H, $CH_2CHCH_{2(trans)}$], 5.20 [dddd, $J_{CH2b,CH2(cis)}$ = –1.1 Hz, $J_{CH2a,CH2(cis)}$ = –1.3 Hz, 1 H, $CH_2CHCH_{2(cis)}$], 4.95 (d, $J_{1,2}$ = 1.7 Hz, 1 H, H-1), 4.88 and 4.71 (2 × d, J = –12.1 Hz, 2 × 1 H, CH_2Ph), 4.30 (dddd, $J_{CH2a,CH2b}$ = –13.0 Hz, 1 H, $CH_{2a}CHCH_2$), 4.24 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.2 Hz, 1 H, H-6a), 4.18 (dd, $J_{4,5}$ = 9.2 Hz, $J_{3,4}$ = 10.0 Hz, 1 H, H-4), 4.17 (dddd, 1 H, $CH_{2b}CH{=}CH_2$), 3.99 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, H-3), 3.87 (ddd, $J_{5,6b}$ = 10.5 Hz, 1 H, H-5), 3.85 (dd, 1 H, H-6b), 3.74 (dd, 1 H, H-2), 3.61–3.53 (m, 1 H, $OCHC_5H_{10}$), 1.89–1.65 (m, 4 H, $OCHC_5H_{10}$), 1.58–1.20 (m, 6 H, $OCHC_5H_{10}$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.8–126.0 (Ar), 135.0 (CH_2CHCH_2), 117.6 (CH_2CHCH_2), 101.3 (CHPh), 97.5 (C-1), 79.4 (C-4), 78.2 (C-2), 76.5 (C-3), 75.1 ($OCHC_5H_{10}$), 73.2 (CH_2Ph), 73.1 (CH_2CHCH_2), 68.9 (C-6), 64.2 (C-5), 33.3, 31.3, 25.6, 24.0, 23.8 ($OCHC_5H_{10}$).

HRMS: m/z [M + H]$^+$ calcd for $C_{29}H_{38}O_6$: 481.2585; found: 481.2574.

HRMS: m/z [M + Na]$^+$ calcd for $C_{29}H_{37}O_6Na$: 503.2404; found: 503.2386.

HRMS: m/z [M + K]$^+$ calcd for $C_{29}H_{37}O_6K$: 519.2143; found: 519.2120.

Homodimerization of Olefins; General Procedure

To a solution of the terminal olefin in CH_2Cl_2 (1 mL/100 mg of olefin), was added Grubbs I catalyst (10 mol%). The reaction mixture was refluxed for 6 h, cooled to r.t. and concentrated. The crude product was purified by flash chromatography (hexane–EtOAc, 8:1→1:1) to give a brownish oil. The resulting product was diluted with CH_2Cl_2 (10 mL) and activated carbon (10 weight%) was added. The resulting mixture was stirred for 19.5 h, filtered through Celite, purified by flash chromatography (hexanes–EtOAc, 3:1→1:1)) and concentrated to give the corresponding divalent compound.

1,4-Bis(benzyl-3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-α-D-mannopyranosyl)but-2-ene (22)

Synthesized from **19** (0.13 g, 0.26 mmol) according to the general procedure for homodimerization of olefins.

Yield: 0.12 g (95%); white foam; R_f = 0.81 (hexane–EtOAc, 1:1); *E*/*Z* = 20:1.

^{1}H NMR (600 MHz, $CDCl_3$): δ (*E*-isomer) = 7.50–7.23 (m, 30 H, ArH), 5.79–5.78 (m, 2 H, $OCH_2CHCHCH_2O$), 5.61 (s, 2 H, CHPh), 4.89 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 4.85 and 4.68 (2 × d, J = –12.1 Hz, 2 × 2 H, CH_2Ph_a), 4.70 and 4.47 (2 × d, J = –11.9 Hz, 2 × 2 H, CH_2Ph_b), 4.26–4.24 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 4.22 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.2 Hz, 2 H, H-6a), 4.19 (dd, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 10.0 Hz, 2 H, H-4), 4.13–4.10 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 4.00 (dd, $J_{2,3}$ = 3.2 Hz, 2 H, H-3), 3.86 (dd, $J_{5,6b}$ = 10.5 Hz, 2 H, H-6b), 3.84 (ddd, 2 H, H-5), 3.78 (dd, 2 H, H-2).

^{13}C NMR (150 MHz, $CDCl_3$): δ (*E*-isomer) = 138.5–126.1 (Ar), 129.8 ($OCH_2CHCHCH_2O$), 101.7 (CHPh), 99.1 (C-1), 79.5 (C-4), 77.0 (C-2), 76.5 (C-3), 73.6 (CH_2Ph_a), 72.5 ($OCH_2CHCHCH_2O$), 69.5 (CH_2Ph_b), 69.0 (C-6), 64.7 (C-5).

HRMS: m/z [M + Na]$^+$ calcd for $C_{58}H_{60}O_{12}Na$: 971.3977; found: 971.3988.

HRMS: m/z [M + K]$^+$ calcd for $C_{58}H_{60}O_{12}K$: 987.3716; found: 987.3726.

1,4-Bis(phenyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-2-*O*-α-D-mannopyranosyl)but-2-ene (23)

Synthesized from **20** (135 mg, 0.28 mmol) according to the general procedure for homodimerization of olefins.

Yield: 98 mg (75%); white foam; R_f = 0.89 (hexane–EtOAc, 1:1); *E*/*Z* = 20:1.

^{1}H NMR (600 MHz, $CDCl_3$): δ (*E*-isomer) = 7.51–7.27 (m, 30 H, ArH), 5.83–5.82 (m, 2 H, $OCH_2CHCHCH_2O$), 5.61 (s, 2 H, CHPh),

5.51 (d, $J_{1,2}$ = 1.3 Hz, 2 H, H-1), 4.87 and 4.70 (2 × d, J = –12.1 Hz, 2 × 2 H, CH_2Ph), 4.28 (ddd, $J_{5,6a}$ = 5.1 Hz, $J_{4,5}$ = 9.4 Hz, $J_{5,6b}$ = 10.2 Hz, 2 H, H-5), 4.24 (dd, $J_{3,4}$ = 9.7 Hz, 2 H, H-4), 4.20 (dd, $J_{6a,6b}$ = –10.4 Hz, 2 H, H-6a), 4.20–4.12 (m, 4 H, $OCH_2CHCHCH_2O$), 3.95 (dd, $J_{2,3}$ = 3.1 Hz, 2 H, H-2), 3.94 (dd, 2 H, H-3), 3.86 (dd, 2 H, H-6b).

^{13}C NMR (150 MHz, $CDCl_3$): δ (*E*-isomer) = 137.6–126.1 (Ar), 129.6 ($OCH_2CHCHCH_2O$), 101.5 (CHPh), 87.3 (C-1), 79.1 (C-4), 78.7 (C-2), 76.2 (C-3), 73.2 (CH_2Ph), 71.6 ($OCH_2CHCHCH_2O$), 68.5 (C-6), 65.3 (C-5).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{56}H_{56}O_{10}S_2Na$: 975.3207; found: 975.3219.

HRMS: *m*/*z* [M + K]$^+$ calcd for $C_{56}H_{56}O_{10}S_2K$: 991.2946; found: 991.2943.

1,4-Bis(cyclohexyl-3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-α-D-mannopyranosyl)but-2-ene (24)

Synthesized from **21** (20 mg, 0.041 mmol) according to the general procedure for homodimerization of olefins.

Yield: 15 mg (75%); white foam; R_f = 0.35 (hexane–EtOAc, 1:1); *E*/*Z* = 10:1.

^{1}H NMR (600 MHz, $CDCl_3$): δ (*E*-isomer) = 7.50–7.23 (m, 20 H, ArH), 5.86–5.84 (m, 2 H, $OCH_2CHCHCH_2O$), 5.62 (s, 2 H, CHPh), 4.94 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 4.87 and 4.70 (2 × d, J = –12.2 Hz, 2 × 2 H, CH_2Ph), 4.33–4.30 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 4.23 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.1 Hz, 2 H, H-6a), 4.17 (dd, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 10.0 Hz, 2 H, H-4), 4.18–4.15 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 3.98 (dd, $J_{2,3}$ = 3.2 Hz, 2 H, H-3), 3.87 (ddd, $J_{5,6b}$ = 10.4 Hz, 2 H, H-5), 3.84 (dd, 2 H, H-6b), 3.72 (dd, 2 H, H-2), 3.60–3.54 (m, 2 H, $OCHC_5H_{10}$), 1.85–1.19 (m, 20 H, $OCHC_5H_{10}$).

^{13}C NMR (150 MHz, $CDCl_3$): δ (*E*-isomer) = 138.8–126.0 (Ar), 129.9 ($OCH_2CHCHCH_2O$), 101.3 (CHPh), 97.5 (C-1), 79.4 (C-4), 77.7 (C-2), 76.6 (C-3), 75.2 ($OCHC_5H_{10}$), 73.3 (CH_2Ph), 72.2 ($OCH_2CHCHCH_2O$), 68.9 (C-6), 64.2 (C-5), 33.3, 31.4, 31.0, 24.1, 23.8 ($OCHC_5H_{10}$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{56}H_{68}O_{12}Na$: 955.4603; found: 955.4607.

HRMS: *m*/*z* [M + K]$^+$ calcd for $C_{56}H_{68}O_{12}K$: 971.4342; found: 971.4340.

Hydrogenolysis; General Procedure

To a solution of the corresponding protected mannoside in MeOH–EtOAc (9:1; 1 mL/10 mg starting material) was added Pd/C (10% Pd, 2.5 equiv by mass). The reaction mixture was stirred in a reactor under H_2 (1.4 bar) overnight, then filtered through Celite and concentrated to give the corresponding fully deprotected mannoside.

1,4-Bis(2-*O*-D-mannopyranose)butane (25)

Synthesized from **22** (16 mg, 0.023 mmol) according to the general procedure for hydrogenolysis and purified by HPLC (Zorbax SB-Aq column; 5 μm, 4.6 × 250 mm; MeCN–H_2O, 1% for 2 min, MeCN–H_2O, 1%→40% over 19 min; 0.5 mL/min).

Yield: 7 mg (70%); colorless oil; αα/αβ/ββ = 5:1:1.

^{1}H NMR (600 MHz, CD_3OD): δ (αα-anomer) = 5.18 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 3.81 (dd, $J_{5,6a}$ = 2.4 Hz, $J_{6a,6b}$ = –11.7 Hz, 2 H, H-6a), 3.79 (dd, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 9.6 Hz, 2 H, H-3), 3.70 (ddd, $J_{5,6b}$ = 5.9 Hz, $J_{4,5}$ = 9.7 Hz, 2 H, H-5), 3.68 (dd, 2 H, H-6b), 3.64–3.59 (m, 4 H, $OCH_2CH_2CH_2CH_2O$), 3.58 (dd, 2 H, H-4), 3.50 (dd, 2 H, H-2), 1.70–1.66 (m, 4 H, $OCH_2CH_2CH_2CH_2O$).

^{13}C NMR (150 MHz, CD_3OD): δ (αα-anomer) = 93.2 (C-1), 81.3 (C-2), 74.2 (C-5), 72.4 ($OCH_2CH_2CH_2CH_2O$, C-3), 69.3 (C-4), 63.2 (C-6), 27.7 ($OCH_2CH_2CH_2CH_2O$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{30}O_{12}Na$: 437.1629; found: 437.1608.

1,4-Bis(cyclohexyl-2-*O*-α-D-mannopyranosyl)butane (26)

Synthesized from **24** (38 mg, 0.04 mmol) according to the general procedure for hydrogenolysis and purified by HPLC (Hypersil BDS-C18 column; 5 μm, 4 × 125 mm; MeCN–H_2O, 10% for 1 min, MeCN–H_2O, 10%→50% over 19 min; 0.5 mL/min).

Yield: 17 mg (70%); colorless oil; $[\alpha]_D^{23}$ +24.3 (*c* 0.3, MeOH).

^{1}H NMR (600 MHz, CD_3OD): δ = 5.01 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 3.81 (dd, $J_{5,6a}$ = 2.3 Hz, $J_{6a,6b}$ = –11.7 Hz, 2 H, H-6a), 3.74 (dd, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 9.4 Hz, 2 H, H-3), 3.70–3.65 (m, 2 H, $OCHC_5H_{10}$), 3.66 (dd, $J_{5,6b}$ = 5.9 Hz, 2 H, H-6b), 3.64–3.58 (m, 4 H, $OCH_2CH_2CH_2CH_2O$), 3.57 (ddd, $J_{4,5}$ = 9.6 Hz, 2 H, H-5), 3.56 (dd, 2 H, H-4), 3.46 (dd, 2 H, H-2), 1.95–1.70 (m, 8 H, $OCHC_5H_{10}$), 1.70–1.60 (m, 4 H, $OCH_2CH_2CH_2CH_2O$), 1.56–1.00 (m, 12 H, $OCHC_5H_{10}$).

^{13}C NMR (150 MHz, CD_3OD): δ = 96.9 (C-1), 81.1 (C-2), 76.1 ($OCHC_5H_{10}$), 74.9 (C-5), 72.6 (C-3), 72.3 ($OCH_2CH_2CH_2CH_2O$), 69.3 (C-4), 63.2 (C-6), 34.5, 32.6 ($OCHC_5H_{10}$), 27.6 ($OCH_2CH_2CH_2CH_2O$), 26.9, 25.2, 25.0 ($OCHC_5H_{10}$).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{50}O_{12}Na$: 601.3194; found: 601.3194.

1,4-Bis[benzyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl-(2→1)-3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-β-D-mannopyranosyl]but-2-ene (27)

To a stirred mixture of **23** (74 mg, 0.8 mmol) and 4 Å MS (0.2 g) in CH_2Cl_2 (2.1 mL), were added BSP (2.4 equiv), TTBP (3 equiv) and Tf_2O (2.6 equiv) at –60 °C (dry ice/acetone). The reaction mixture was stirred for 30 min, cooled to –78 °C and **15** (2.3 equiv) in CH_2Cl_2 (2.0 mL) was added. The resulting mixture was stirred for 2 h, quenched by triethyl phosphite (0.1 mL) and stirred for 1 h. The reaction mixture was brought to r.t. and diluted with CH_2Cl_2 (20 mL) and sat. $NaHCO_3$ (20 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic phase was dried with anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by preparative TLC (EtOAc–hexane, 1:1). The spots containing product were scraped off, diluted with EtOAc (20 mL), stirred for 2 h, filtered and concentrated to give **27**.

Yield: 88 mg (70%); colorless oil; R_f = 0.10 (hexane–EtOAc, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ (*E*-isomer) = 7.50–7.21 (m, 50 H, ArH), 6.02–5.96 (m, 2 H, $OCH_2CHCHCH_2O$), 5.57 (s, 2 H, $CHPh_a$), 5.50 (s, 2 H, $CHPh_b$), 4.89 (d, $J_{1,2}$ = 1.6 Hz, 2 H, H-1), 4.76 and 4.71 (2 × d, J = –10.5 Hz, 2 × 2 H, CH_2Ph_a), 4.72 (s, 4 H, CH_2Ph_b), 4.68 and 4.46 (2 × d, J = –12.0 Hz, 2 × 2 H, CH_2Ph_c), 4.53–4.49 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 4.52 (d, $J_{1',2'}$ = 0.7 Hz, 2 H, H-1′), 4.34–4.30 (m, 2 H, 0.5 × $OCH_2CHCHCH_2O$), 4.20 (dd, $J_{2,3}$ = 3.3 Hz, 2 H, H-2), 4.19 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.1 Hz, 2 H, H-6a), 4.18 (dd, $J_{5',6a'}$ = 4.9 Hz, $J_{6a',6b'}$ = –10.2 Hz, 2 H, H-6a′), 4.15 (dd, $J_{4',5'}$ = 9.3 Hz, $J_{3',4'}$ = 9.9 Hz, 2 H, H-4′), 4.12 (dd, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 10.0 Hz, 2 H, H-4), 3.99 (dd, 2 H, H-3), 3.86 (dd, $J_{2',3'}$ = 3.2 Hz, 2 H, H-2′), 3.84 (ddd, $J_{5,6b}$ = 10.3 Hz, 2 H, H-5), 3.79 (dd, 2 H, H-6b), 3.78 (dd, $J_{5',6b'}$ = 10.1 Hz, 2 H, H-6b′), 3.53 (dd, 2 H, H-3′), 3.21 (ddd, 2 H, H-5′).

^{13}C NMR (150 MHz, $CDCl_3$): δ (*E*-isomer) = 138.8–126.0 (Ar), 130.2 ($OCH_2CHCHCH_2O$), 101.5 ($CHPh_a$), 101.3 ($CHPh_b$), 100.7 ($^1J_{C',H'}$ = 155.2 Hz, C-1′), 97.7 ($^1J_{C,H}$ = 168.5 Hz, C-1), 78.6 (C-4), 78.4 (C-4′), 77.2 (C-3′), 77.1 (C-2′), 75.2 (C-2), 74.3 (C-3), 73.6 ($OCH_2CHCHCH_2O$), 72.2 (CH_2Ph_a), 71.6 (CH_2Ph_b), 69.3 (CH_2Ph_c), 68.8 (C-6, C-6′), 68.5 (C-5′), 67.6 (C-5) .

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{98}H_{100}O_{22}Na$: 1651.6598; found: 1651.6665.

1,4-Bis[2-*O*-β-D-mannopyranosyl-(1→2)-D-mannopyranose]butane (28)

Synthesized from **25** (20 mg, 0.012 mmol) according to the hydrogenolysis general procedure and purified by HPLC (Zorbax SB-Aq column; 5 μm, 4.6 × 250 mm; MeCN–H_2O, 1% for 5 min, then MeCN–H_2O, 1%→40% over 19 min; 0.5 mL/min).

Yield: 5 mg (50%); colorless oil; αα/αβ/ββ = 8:2:1.

^{1}H NMR (600 MHz, CD_3OD): δ (αα-anomer) = 5.18 (d, $J_{1,2}$ = 1.8 Hz, 2 H, H-1), 4.64 (d, $J_{1′,2′}$ = 0.8 Hz, 2 H, H-1′), 3.94 (dd, $J_{2,3}$ = 3.2 Hz, 2 H, H-2), 3.91–3.86 (m, 2 H, 0.5 × OCH_2CH$_2$CH$_2$CH_2O), 3.87 (dd, $J_{5′,6a′}$ = 2.3 Hz, $J_{6a′,6b′}$ = –12.0 Hz, 2 H, H-6a′), 3.82–3.80 (m, 2 H, H-6a), 3.78 (dd, $J_{3,4}$ = 9.6 Hz, 2 H, H-3), 3.77–3.73 (m, 2 H, 0.5 × OCH_2CH$_2$CH$_2$CH_2O), 3.73–3.67 (m, 8 H, H-2′, H-3′, H-6b′, H-6b), 3.65 (dd, $J_{4,5}$ = 10.1 Hz, 2 H, H-4), 3.53 (dd, $J_{4′,5′}$ = 8.8 Hz, $J_{3′,4′}$ = 9.5 Hz, 2 H, H-4′), 3.50–3.45 (m, 2 H, H-5), 3.21 (ddd, J = $J_{5′,6b′}$ = 5.8 Hz, 2 H, H-5′), 1.80–1.60 (m, 4 H, OCH$_2$CH_2CH_2CH$_2$O).

^{13}C NMR (150 MHz, CD_3OD): δ (αα-anomer) = 101.4 (C-1′), 93.7 (C-1), 81.0 (C-2′), 80.6 (C-2), 78.8 (C-5′), 75.3 (C-5), 75.1 (OCH$_2$CH$_2$CH$_2$$CH_2$O), 74.3 (C-3′), 71.6 (C-3), 69.5 (C-4), 68.8 (C-4′), 62.9 (C-6, C-6′), 27.6 (OCH$_2$$CH_2$$CH_2CH_2$O).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{50}O_{22}Na$: 761.2686; found: 761.2688.

Methyl 2-*O*-Allyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (31)

Synthesized from **30**[30] (0.14 g, 0.17 mmol) according to the general procedure for synthesis of 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosides.

Yield: 0.12 g (80%); white foam; R_f = 0.80 (hexane–EtOAc, 1:1); $[\alpha]_D^{23}$ –12.7 (*c* 1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51–7.16 (m, 25 H, ArH), 6.00 [dddd, $J_{CH2a,CH}$ = 6.2 Hz, $J_{CH2b,CH}$ = 6.2 Hz, $J_{CH,CH2(cis)}$ = 10.3 Hz, $J_{CH,CH2(trans)}$ = 17.2 Hz, 1 H, CH$_2$CHCH$_2$], 5.60 (s, 1 H, CHPh), 5.32 [dddd, $J_{CH2b,CH2(trans)}$ = –1.4 Hz, $J_{CH2a,CH2(trans)}$ = –1.5 Hz, $J_{CH2(cis),CH2(trans)}$ = –1.9 Hz, 1 H, CH$_2$CHC$H_{2(trans)}$], 5.19 [dddd, $J_{CH2b,CH2(cis)}$ = –1.0 Hz, $J_{CH2a,CH2(cis)}$ = –1.1 Hz, 1 H, CH$_2$CHC$H_{2(cis)}$], 4.95 and 4.80 (2 × d, J = –10.9 Hz, 2 × 1 H, CH$_2$Ph$_a$), 4.84 and 4.63 (2 × d, J = –12.6 Hz, 2 × 1 H, CH$_2$Ph$_b$), 4.82 and 4.53 (2 × d, J = –10.8 Hz, 2 × 1 H, CH$_2$Ph$_c$), 4.79 (d, $J_{1,2}$ = 1.6 Hz, 1 H, H-1), 4.51 (dddd, $J_{CH2a,CH2b}$ = –11.7 Hz, 1 H, CH_{2a}CH=CH$_2$), 4.47 (s, 2 H, CH$_2$Ph$_d$), 4.40 (d, $J_{1′,2′}$ = 7.8 Hz, 1 H, H-1′), 4.27 (dd, $J_{5,6a}$ = 5.2 Hz, $J_{6a,6b}$ = –10.6 Hz, 1 H, H-6a), 4.21 (dddd, 1 H, CH_{2b}CHCH$_2$), 4.21 (dd, $J_{2,3}$ = 3.5 Hz, 1 H, H-2), 4.10 (dd, $J_{4,5}$ = 9.2 Hz, $J_{3,4}$ = 10.1 Hz, 1 H, H-4), 3.91 (dd, 1 H, H-3), 3.76 (ddd, $J_{5,6b}$ = 10.2 Hz, 1 H, H-5), 3.76 (dd, 1 H, H-6b), 3.72 (dd, $J_{5′,6a′}$ = 1.8 Hz, $J_{6a′,6b′}$ = –10.6 Hz, 1 H, H-6a′), 3.63 (dd, $J_{5′,6b′}$ = 5.4 Hz, 1 H, H-6b′), 3.61 (dd, $J_{3′,4′}$ = 8.5 Hz, $J_{2′,3′}$ = 9.2 Hz, 1 H, H-3′), 3.51 (dd, $J_{4′,5′}$ = 8.8 Hz, 1 H, H-4′), 3.50 (ddd, 1 H, H-5′), 3.47 (dd, 1 H, H-2′), 3.35 (s, 3 H, OCH$_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.6–126.1 (Ar), 135.1 (CH$_2$$CHCH_2$), 117.7 (CH$_2CHCH_2$), 103.0 (C-1′), 101.5 (CHPh), 99.8 (C-1), 84.8 (C-3′), 81.5 (C-2′), 78.3 (C-4), 75.8 (H-4′), 75.6 (CH$_2$Ph$_a$), 75.3 (C-2), 75.1 (CH$_2$Ph$_c$, H-5′), 73.9 (CH_2CHCH$_2$), 73.7 (C-3), 73.5 (CH$_2$Ph$_d$), 70.7 (CH$_2$Ph$_b$), 69.7 (C-6′), 69.1 (C-6), 63.9 (C-5), 54.9 (OCH$_3$).

HRMS: [M + Na]$^+$ calcd for $C_{51}H_{56}O_{11}Na$: 867.3715; found: 867.3696.

HRMS: [M + K]$^+$ calcd for $C_{51}H_{56}O_{11}K$: 883.3454; found: 883.3445.

1,4-Bis[methyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl-(2→1)-3,4,6-tri-*O*-benzyl-2-*O*-β-D-glucopyranosyl]but-2-ene (32)

Synthesized from **31** (0.11 g, 0.13 mmol) according to the general procedure for homodimerization of olefins.

Yield: 66 mg (61%); white foam; R_f = 0.10 (hexane–EtOAc, 1:1); *E*/*Z* = 20:1.

^{1}H NMR (600 MHz, $CDCl_3$): δ (*E*-isomer) = 7.46–7.12 (m, 50 H, ArH), 5.94–5.93 (m, 2 H, OCH$_2$CHCHCH$_2$O), 5.52 (s, 2 H, CHPh), 4.93 and 4.74 (2 × d, J = –11.0 Hz, 2 × 2 H, CH$_2$Ph$_a$), 4.83 and 4.62 (2 × d, J = –12.6 Hz, 2 × 2 H, CH$_2$Ph$_b$), 4.78 and 4.49 (2 × d, J = –10.7 Hz, 2 × 2 H, CH$_2$Ph$_c$), 4.77 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 4.57–4.53 (m, 2 H, 0.5 × OCH_2CHCHCH_2O), 4.47 (s, 4 H, CH$_2$Ph$_d$), 4.37 (d, $J_{1′,2′}$ = 7.8 Hz, 2 H, H-1′), 4.22–4.18 (m, 2 H, 0.5 × OCH_2CHCHCH_2O), 4.20 (dd, $J_{2,3}$ = 3.6 Hz, 2 H, H-2), 4.20 (dd, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = –10.3 Hz, 2 H, H-6a), 4.06 (dd, $J_{4,5}$ = 9.4 Hz, $J_{3,4}$ = 10.1 Hz, 2 H, H-4), 3.89 (dd, 2 H, H-3), 3.72 (ddd, $J_{5,6b}$ = 10.3 Hz, 2 H, H-5), 3.71 (dd, $J_{5′,6a′}$ = 1.5 Hz, $J_{6a′,6b′}$ = –10.5 Hz, 2 H, H-6a′), 3.68 (dd, 2 H, H-6b), 3.62 (dd, $J_{5′,6b′}$ = 5.4 Hz, 2 H, H-6b′), 3.57 (dd, $J_{3′,4′}$ = 8.9 Hz, $J_{2′,3′}$ = 9.2 Hz, 2 H, H-3′), 3.49 (dd, $J_{4′,5′}$ = 9.4 Hz, 2 H, H-4′), 3.48 (ddd, 2 H, H-5′), 3.46 (dd, 2 H, H-2′), 3.30 (s, 6 H, OCH$_3$).

^{13}C NMR (150 MHz, $CDCl_3$): δ (*E*-isomer) = 138.0–126.0 (Ar), 130.3 (OCH$_2$$CHCHCH_2$O), 103.0 (C-1′), 101.4 (CHPh), 99.8 (C-1), 84.6 (C-3′), 81.8 (C-2′), 78.2 (C-4), 77.7 (CH$_2$Ph$_c$, C-4′), 75.1 (CH$_2$Ph$_a$, C-2), 75.0 (C-5′), 73.6 (C-3), 73.5 (CH$_2$Ph$_d$), 73.0 (OCH$_2$CHCHCH$_2$O), 70.8 (CH$_2$Ph$_b$), 69.8 (C-6′), 69.1 (C-6), 64.0 (C-5), 54.9 (OCH$_3$).

HRMS: *m*/*z* [M + H_2O]$^+$ calcd for $C_{100}H_{110}O_{23}$: 1678.7432; found: 1678.7440.

1,4-Bis[methyl-α-D-mannopyranosyl-(2→1)-2-*O*-β-D-glucopyranosyl]butane (33)

Synthesized from **32** (24 mg, 0.014 mmol) according to the general procedure for hydrogenolysis and purified by HPLC (Zorbax SB-Aq column; 5 μm, 4.6 × 250 mm; MeCN–H_2O, 1% for 5 min, then MeCN–H_2O, 1%→40% over 19 min; 0.5 mL/min).

Yield: 8 mg (70%); colorless oil; $[\alpha]_D^{23}$ –1.5 (*c* 0.1, MeOH).

^{1}H NMR (600 MHz, CD_3OD): δ = 4.79 (d, $J_{1,2}$ = 1.7 Hz, 2 H, H-1), 4.40 (d, $J_{1′,2′}$ = 7.8 Hz, 2 H, H-1′), 3.97 (dd, $J_{2,3}$ = 3.5 Hz, 2 H, H-2), 3.97–3.93 (m, 2 H, 0.5 × OCH_2CH$_2$CH$_2$CH_2O), 3.87 (dd, $J_{5,6a}$ = 2.2 Hz, $J_{6a,6b}$ = –11.8 Hz, 2 H, H-6a), 3.84 (dd, $J_{5′,6a′}$ = 2.4 Hz, $J_{6a′,6b′}$ = –12.0 Hz, 2 H, H-6a′), 3.70 (dd, $J_{3,4}$ = 9.5 Hz, 2 H, H-3), 3.68–3.63 (m, 2 H, 0.5 × OCH_2CH$_2$CH$_2$CH_2O), 3.64 (dd, $J_{5,6b}$ = 6.1 Hz, 2 H, H-6b), 3.64 (dd, $J_{5′,6b′}$ = 6.0 Hz, 2 H, H-6b′), 3.50 (ddd, $J_{4,5}$ = 8.9 Hz, 2 H, H-5), 3.50 (dd, 2 H, H-4), 3.41 (s, 6 H, OCH$_3$), 3.37 (dd, $J_{3′,4′}$ = 9.1 Hz, $J_{2′,3′}$ = 9.2 Hz, 2 H, H-3′), 3.30 (dd, $J_{4′,5′}$ = 9.8 Hz, 2 H, H-4′), 3.26 (ddd, 2 H, H-5′), 3.04 (dd, 2 H, H-2′), 1.75–1.62 (m, 4 H, OCH$_2$CH_2CH_2CH$_2$O).

^{13}C NMR (150 MHz, CD_3OD): δ = 103.6 (C-1′), 100.3 (C-1), 82.9 (C-2′), 79.4 (C-2), 77.9 (C-5′), 77.5 (C-3′), 74.9 (C-5), 74.0 (OCH$_2$CH$_2$CH$_2$$CH_2$O), 71.7 (C-3), 71.4 (C-4′), 69.6 (C-4), 63.4 (C-6), 62.6 (C-6′), 55.4 (OCH$_3$), 27.8 (OCH$_2$$CH_2$$CH_2CH_2$O).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{54}O_{22}Na$: 789.2999; found: 789.2996.

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