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Regioselective Strategies Mediated by Lanthanide Triflates for Efficient Assembly of Oligomannans†

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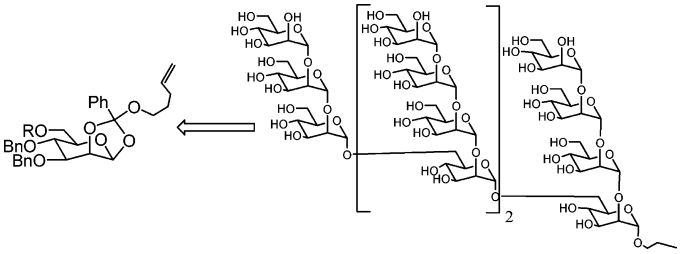

Readily prepared mannosyl *n*-pentenylorthoesters (NPOEs) serve as donors in themselves and as convenient intermediates for other glycosyl donors, such as *n*-pentenyl glycosides (NPGs), thioglycosides, and trichloroacetimidates. These various donors are activated by different reagents, and are therefore amenable to versatile, discriminate use. Scandium and ytterbium triflates respond very differently to these donors, with the result that chemoselective discrimination between NPOEs, NPGs, trichloroacetimidates as well as ethyl and phenyl thioglycosides can be achieved. Appropriate NPOEs are also able to provide 2,6 and 3,6 diol acceptors via rearrangement or glycoside formation, and these can be used for one-pot, sequential glycosidations based on orthogonal donors, and in situ double differential glycosidations. Thus NPOEs activated by iodonium ion, specifically generated from ytterbium triflate/*N*-iodosuccinimide, can be used to monoglycosidate the diols rapidly, with exquisite regio, and sometimes chemo, selectivity. The residual NPOE is converted into disarmed NPG, which is refractory to the reaction conditions, and so poses no threat to the free-OH of the monoglycosidation product. Further glycosidation of the latter can then achieved by direct addition of a trichloroacetimidate or ethyl thioglycoside. This basic strategy has been used to prepare a branched chain pentadecamannan. The success is an example of the efficiency of donor/acceptor MATCH concept for regioselective glycosylation.

Introduction

The fundamental step in oligosaccharide assembly, as illustrated in Scheme 1a, is the coupling of an incipient electrophile, the donor **1**, with an acceptor, **2**.[1] Paulsen's 1982 review of the then fledgling area of oligosaccharide synthesis[2] remains a seminal document, because by summarizing (some of) the early successes and failures, he inadvertently suggested areas that were (are!) in need of future attention. Most activity has focused on the development of novel donors from which the aglycon, LVG**,** can be removed by mild, unique or specific coaxing.[3]

† Portions of this work have been reported in preliminary communications cited in refs 5, 22, 28, and 29.

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(1) Goodman, L. *Adv. Carbohydr. Chem. Biochem.* **1967**, *22*, 109. Toshina, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503. Lindhorst, T. K. *Essentials of carbohydrate chemistry and biochemistry*; Wiley-VCH: New York, 2000. Nitz, M.; Bundle, D. K. In *Glycoscience*: *Chemistry and Chemical Biology*, Fraser-Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, Germany, 2001; Vol. *2*, p 1497. Boons, G.-J. In *Carbohydrate Chemistry*; Boons, G.-J., Ed.; Blackie Academic Professional: London, UK, 1998, Chapter 5. Sinay, P. *Pure Appl. Chem.* **1978**, *50*, 1437.

(2) Paulsen, H. *Angew. Chem., Int. Ed.* **1982**, *21*, 155−177.

(3) See for example: Demchenko, A. V. *Lett. Org. Chem*. **2005**, *2*, 580−589. Osborn, H. M. I.; Khan, T. H. *Oligosaccharides*: *Their synthesis and biological roles*; Oxford University Press: Oxford, UK, 2000. Schmidt, R. R.; Jung, K. H. In *Carbohydrates in Chemistry and Biology*; Ernst, B., Heat, G. W., Sinay, P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 1, p 5. Oscarson, S. In *Carbohydrates in Chemistry and Biology*; Ernst, B., Hart, G. W., Sinay, P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 1, p 93.

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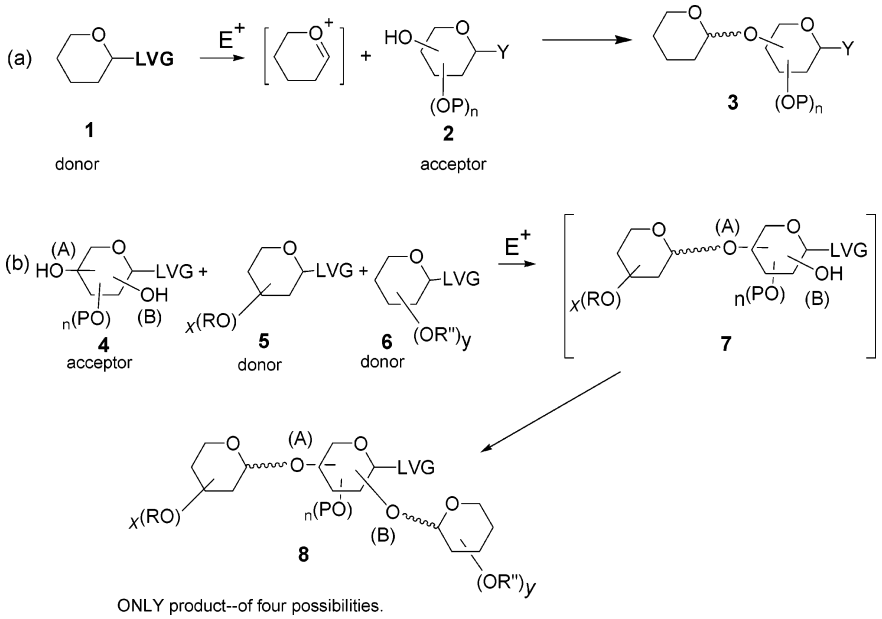
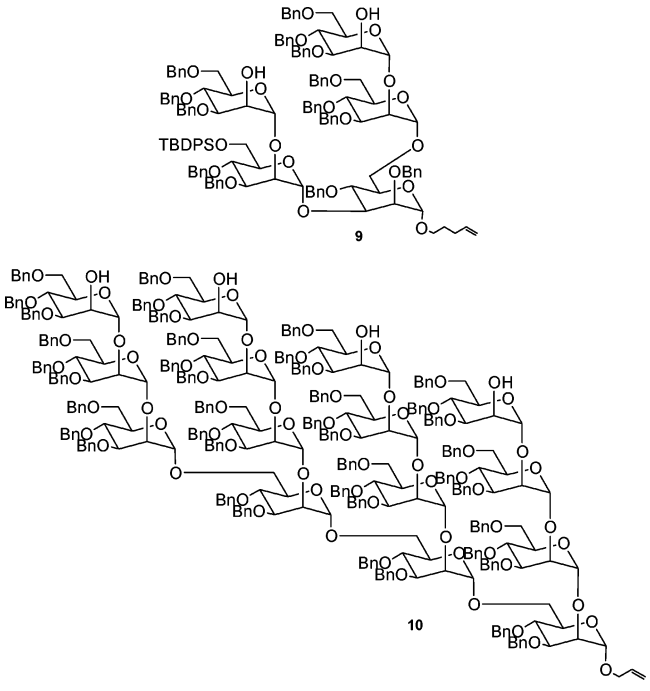
SCHEME 1



With regard to the other partner, the traditional practice is to ensure, as in **2**, that only the targeted OH is free for presentation to the donor during the coupling event. However, Scheme 1b summarizes recent observations in our[4,5] and Lopez'[6] laboratories, in which a diol acceptor, **4**, upon in situ presentation to two donors, **5** and **6**, produced only one double glycosidation product, **8**, of four possibilities.

The MATCH required to produce **7** and thence **8** dispenses with the traditional procedure of extensive protection, as with **2** in Scheme 1a, to ensure that only one free-OH is presented for the coupling event.

In this paper, we further explore the concept of MATCH in context of the α-(3→6) and α-(2→6) mannan arrays **9** and **10**.



The former is an essential component of high-mannose oligosaccharides[7] that currently attracts special attention in view of their implication with HIV therapy.[8] The latter occurs in *Candida albicans* NIH A-204 (serotype A) strain as acid-stable side chains[9] to the β-(1→2) mannan backbone that has attracted so much recent attention.[10]

Results and Discussion

MATCH and Regioselectivity. Our efforts to rationalize the selectivities implicit in Scheme 1b have led us to invoke the phenomenon of MATCH—but because there are (at least) three concepts associated with the word, some clarification is necessary.

Masamune's usage of MATCH[11] exemplified by Scheme 2a reflects the principle of double diastereoselectivity in which one set of chiral reactants, e.g., a (+) and (+) pair, generates more

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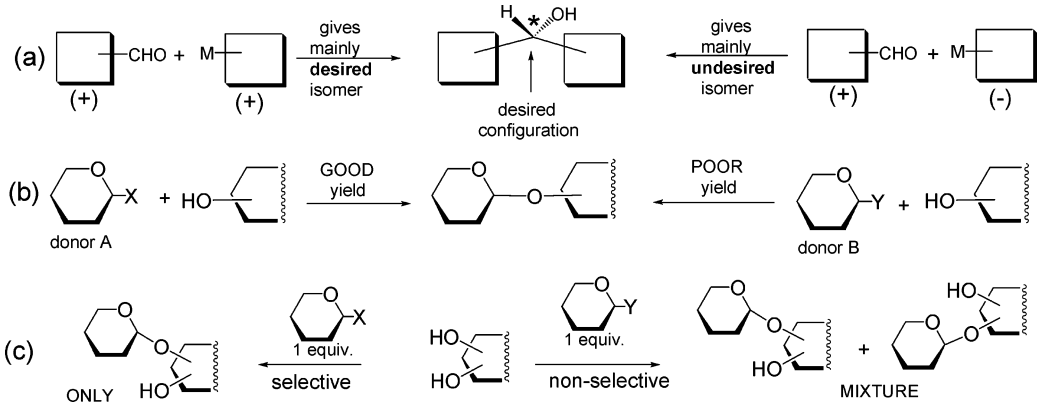
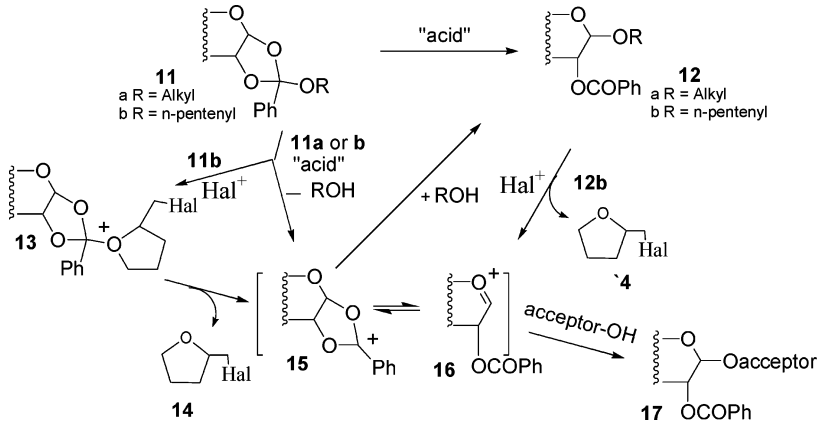
SCHEME 2



SCHEME 3



of the newly created chiral center than does another set, e.g., a (+) and (−) pair. The (+)/(+) pair are therefore a MATCH, and the (+)/(−) pair, a misMATCH.

Paulsen used the term to describe the extensive body of observations in his and other laboratories, which showed that one donor usually reacted more successfully than another, with a given acceptor, success being measured by *yield* (Scheme 2b). The better yielding partners were therefore considered to constitute a MATCH.[12]

The usage of Fraser-Reid and Lopez[13] shown in Scheme 2c implies **regioselectivity**, an issue that was not considered by Paulsen in 1982, nor could it have been, given the narrow range of donors, reagents, and reaction conditions[2,12,14] that were then available for executing glycosidations. Notably, in commenting on the recent synthesis of a dodecasaccharyl lipomannan glycolipid of *Mycobacterium tuberculosis* reported by this laboratory,[15] Paulsen observed that "the study by Fraser-Reid and co-workers demonstrates that this concept can be used to simplify oligosaccharide synthesis using modern reagents...".[16]

Central to our approach to MATCH is the concept of Reciprocal Donor Acceptor Selectivity (RDAS),[17] which is evinced in Scheme 1b. Thus, exclusive formation of **8** requires that monoglycosidation product **7** be the ONLY intermediate. Thus donor, **5**, must select hydroxyl (A), and simultaneously reject hydroxyl (B) of the acceptor diol **7**. Conversely and concomitantly, hydroxyl (A) must select donor **5** rather than donor **6**, whereas hydroxyl (B) must ignore donor **5**. Thus, donor **5** and hydroxyl (A) constitute a MATCH whereas donor **5** and hydroxyl (B) are a misMATCH.

We have examined the competitive double differential glycosidation study depicted in Scheme 1b with three types of donors, LVG = OPentenyl, SEt, and trichloroacetimidate, and found that in all cases, only one of four possible trisaccharides, i.e., **8**, was formed. However, there were substantial differences in the yields, *n*-pentenylorthoesters (NPOEs) giving the best.

Some Aspects of Glycosyl Orthoesters. The functioning of NPOEs as glycosyl donors is relevant to the discussion that follows. Orthoester donors undergo ready acid-catalyzed rearrangement, **11** → **12** (Scheme 3), in which an oxolenium ion, **15**, is the intermediate in transfer of the alkoxy moiety.[18,19] Intermediate **15** could also glycosylate an in situ acceptor-OH to give **17**. However, the re-addition step, **15** → **12**, obviously offers competition. This problem had confronted Kotchetkov and Bachinovsky, the primary exponents of acid-catalyzed

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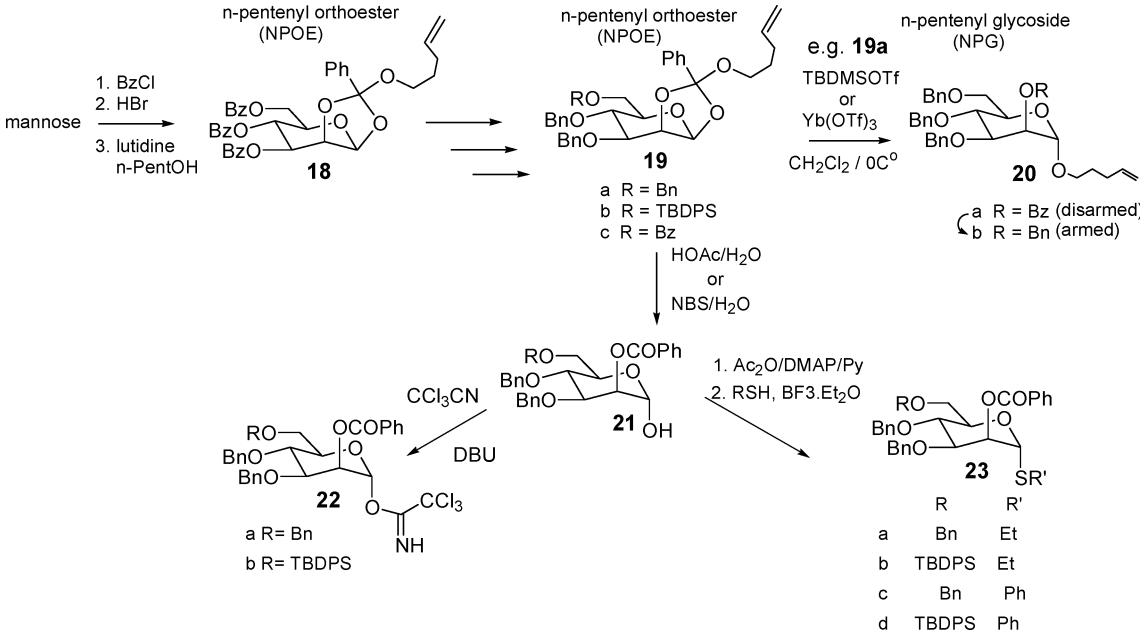
(19) For a recent review see: Kong, F. *Carbohydr. Res.* **2007**, *342*, 345−373.

SCHEME 4



glycosyl orthoester chemistry, and their efforts to overcome it had led to seminal developments.[20]

In this context, the *n*-pentenyl analogues, **11b** (Alk = *n*-pentenyl), offered a way around the re-addition problem, e.g., **15** → **12**, since a halonium ion, e.g., Hal^+, could sequester the *n*-pentenyl moiety as the halomethyltetrahydrofuran, **14**.

The mechanism in Scheme 3 also suggested facile procedures leading to some other types of donors, as well as acceptors, and this versatility prompted us to test for various selectivities in donor/acceptor combinations.

Synthesis of Donors. *n*-Pentenyl orthoesters (NPOEs) can be produced in three easy steps from the corresponding hexose,[21] as exemplified for the case of the mannose derivative **18** (Scheme 4). The three hydroxyls can be readily differentiated as in **19a**, **19b**, or **19c**, thereby providing convenient entry to the NPG family. Thus, an NPOE, e.g., **19a**, can be quantitatively rearranged into disarmed NPG **20a**. The armed counterpart, **20b**, can then be routinely obtained.

Acidic or oxidative hydrolysis converts the NPOE into the corresponding 2-*O*-acylated glycoses[22] (e.g., **19** → **21**), from which trichloroacetimidates **22a/b** or the ethyl and phenyl thioglycosides **23a**−**d** can be obtained by standard procedures.[23,24]

Compounds **18**/**19**, **20**, **22**, and **23** represent a range of donors of different capabilities, each activated by different reagent(s) so that they can be used discriminatingly.

Synthesis of Acceptors. The acceptor diols used in the studies below were obtained from NPOE **18** as the ultimate source, via the differentially protected counterparts **19b** and **19c** as shown in Scheme 5. Diol **25** was obtained by rearrangement of **19b** to **24** followed by uneventful deprotections. Rearrangement of tribenzoate **18** paved the way to tetrol **26b**, which was then converted into the 3,6-diol **27** as described previously.[25] NPOE **19c** was used to glycosylate allyl alcohol, and the resulting 2,6-dibenzoate **28**, upon saponification, gave diol **29.**

MATCH Mediated by Donor/M(OTf)$_3$ Selectivities. Iodonium ion needed to activate *n*-pentenyl donors is usually generated by the action of protic[26] or Lewis[27] acids on *N*-iodosuccinimide (NIS). However, we have recently been investigating the use of lanthanide salts for this purpose,[28] and have found dramatic differences between scandium and ytterbium triflates. When the salt and NIS are mixed in dichloromethane, the formation of I^+ is indicated by an immediately generated purple color. Nevertheless, a substantial amount of acid-catalyzed rearrangement still occurred. Since the latter is an NPG (i.e., **12**, Alk = *n*-pentenyl), it is a potential donor via the oxocarbenium ion **16** raising the possibility of double glycosylation.

However, our experiments have indicated that this potential hazard can be avoided.[28] Thus, as shown in Table 1, entry (i), both salts, in the presence of NIS, promote glycosidation of an alcohol, ROH, with NPOEs. However, entries (ii) and (iii) show that glycosidation by armed or disarmed NPGs is not effected by Yb(OTf)$_3$/NIS.

Entries (i), (ii) ,and (iii) therefore show that lanthanide triflates can be used to discriminate between various *n*-pentenyl donors. Thus, when Sc(OTf)$_3$/NIS is used, all *n*-pentenyl donors can be activated.[5] However, and most significantly, chemospecific

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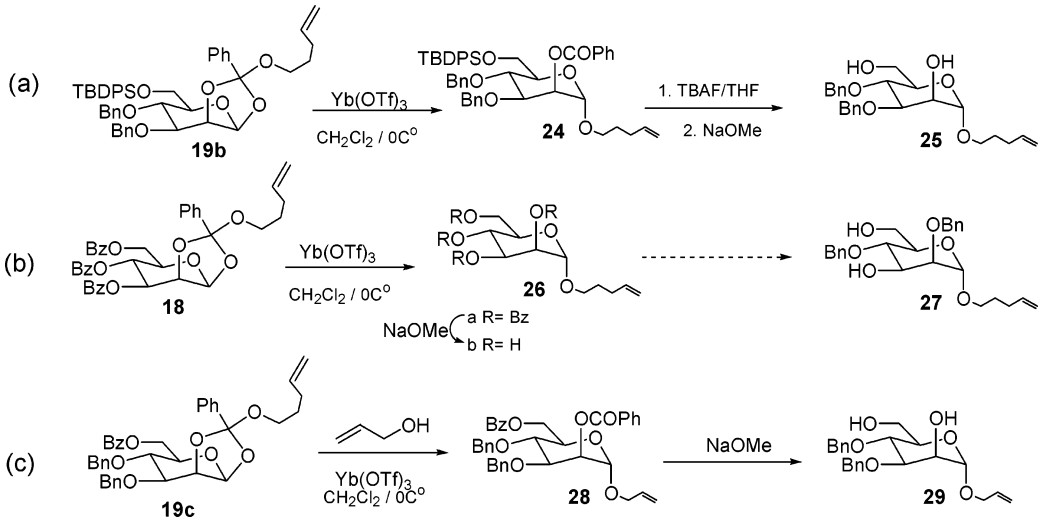
SCHEME 5



SCHEME 6

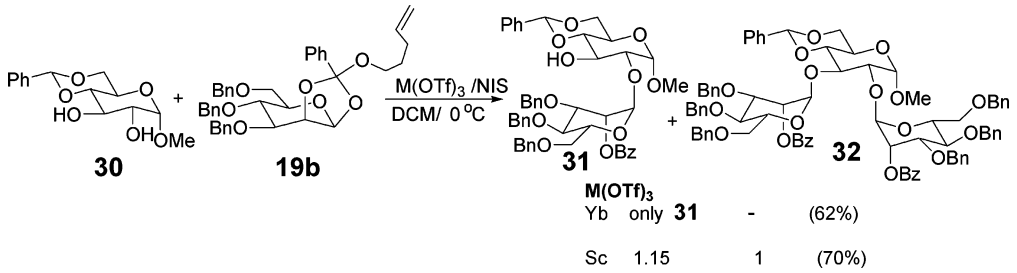


TABLE 1. Glycosidation of an Acceptor with Various Donors Triggered by Scandium and Ytterbium Triflates

		$Sc(OTf)_3$	$Yb(OTf)_3$
(i)	NPOE + (NIS)	+	+
(ii)	NPG_{dis} + (NIS)	+	−
(iii)	NPG_{arm} + (NIS)	+	−
(iv)	ethyl thioglycoside + NIS	+	+
(v)	phenyl thioglycoside + NIS	+	−
(vi)	trichloroacetimidate	+	+

glycosidation with NPOE can be achieved by use of $Yb(OTf)_3$ as the activator for NIS. This possibility is precluded for armed and disarmed NPGs, since these require the use of $Sc(OTf)_3$/NIS, a nondiscriminating medium.

The advantage of the observations in entries (i), (ii), and (iii) is that NPOEs can be used in excess with $Yb(OTf)_3$/NIS to optimize regioselective glycosidation, since any disarmed NPG formed by rearrangement is refractory to these conditions. However, the NPG is activated under $Sc(OTf)_3$/NIS conditions, so double glycosidation would occur. The contrast in using both triflates is exemplified in Scheme 6. Thus, treatment of glucoside **30** with 2 equiv of NPOE **19a**, under the influence of $Yb(OTf)_3$/NIS, afforded the O2 regioisomer **31** exquisitely. Switching to $Sc(OTf)_3$/NIS led to a near equal mixture of **31** and **32**. Interestingly we did not see the O3 regioisomer.[5]

The regioselective glycosidation offered by an NPOE, buttressed by chemoselective activation with $Yb(OTf)_3$/NIS, means that an excess of the donor could be used to optimize MATCH, such as **4** → **7** (Scheme 1b) and **30** → **31** (Scheme 6). One could therefore dispense with the traditional procedure of extensive protection, as with **2** in Scheme 1a, to ensure that only one free-OH is presented for the coupling event.

The effectiveness of lanthanide salts with thioglycosides and trichloroacetimidates was also tested. The results in Table 1, entry (iv), show positive responses for ethyl thioglycosides with both salts; however, phenyl thioglycosides are activated with $Sc(OTf)_3$ but not by $Yb(OTf)_3$, entry (v). Such differences in reactivity between phenyl and ethyl thioglycosides have been noted previously by Garegg and co-workers.[23]

Entry (vi) shows that trichloroacetimidates are activated by both salts. It should be noted that Adinolfi and co-workers have reported the action of lanthanide triflates on trifluoroacetimidate donors.[30]

The data in Table 1 provide a basis for the one-pot use of orthogonal donors[31] suggested in Scheme 7a. Diol **4** can be treated with an NPOE, used in excess, triggered by $Yb(OTf)_3$/NIS, in order to optimize regioselective monoglycosidation leading to **33**. Under the reaction conditions, the excess of the NPOE will undergo acid-catalyzed rearrangement to the disarmed NPG **34**, which being refractory to $Yb(OTf)_3$/NIS, should not glycosidate the free-OH of **33**. However, since this reaction mixture triggers trichloroacetimidates and ethyl thioglycosides, subsequent addition of one of these donors should result in further glycosidation to give **35**.

This hypothesis was reduced to practice in a preliminary experiment involving the 3,6-mannosidyl diol **36**, which upon treatment with NPOE **19a** (2 equiv), $Yb(OTf)_3$ (0.3 equiv), and NIS (2.5 equiv) led to rapid formation of disaccharide **37a**

(29) Jayaprakash, K. N.; Fraser-Reid, B. *Synlett* **2004**, 301−305.

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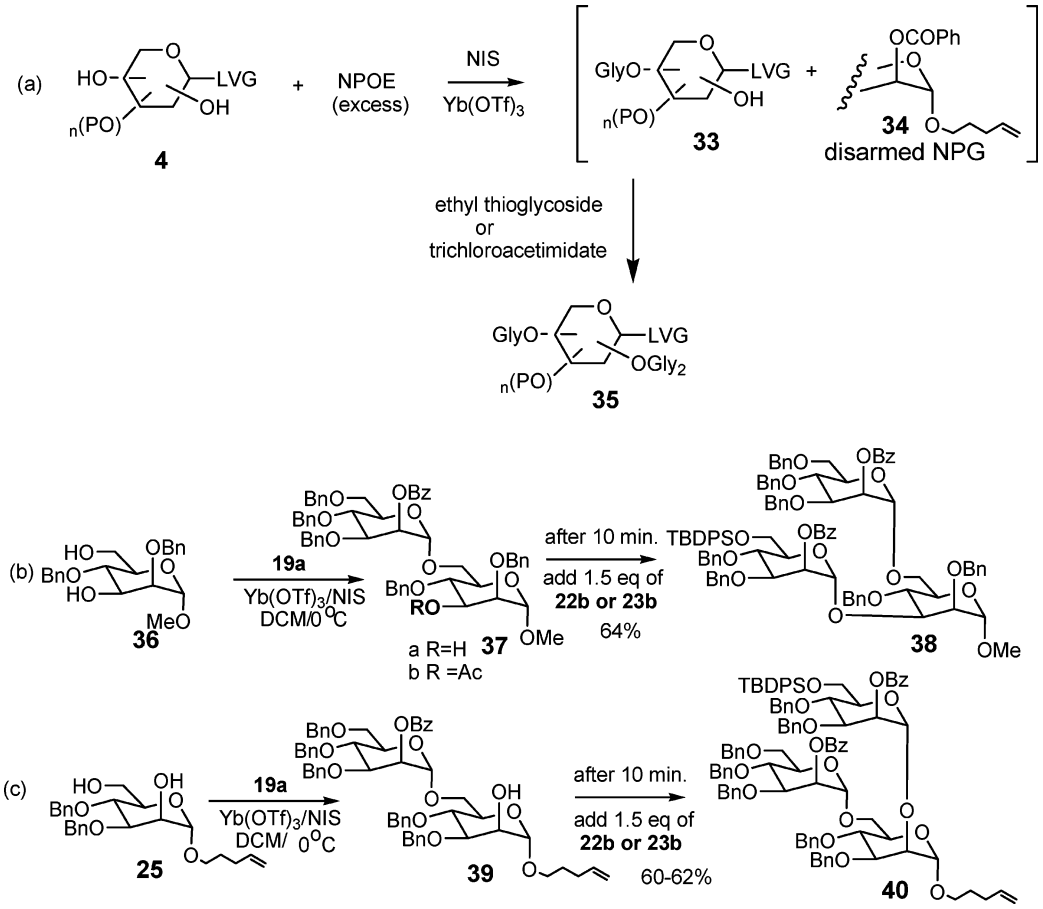
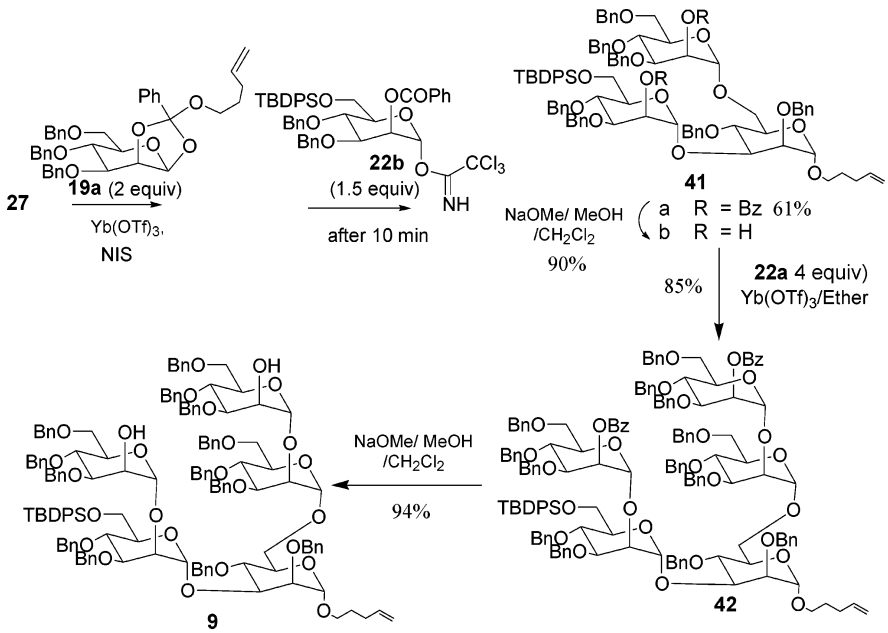
SCHEME 7



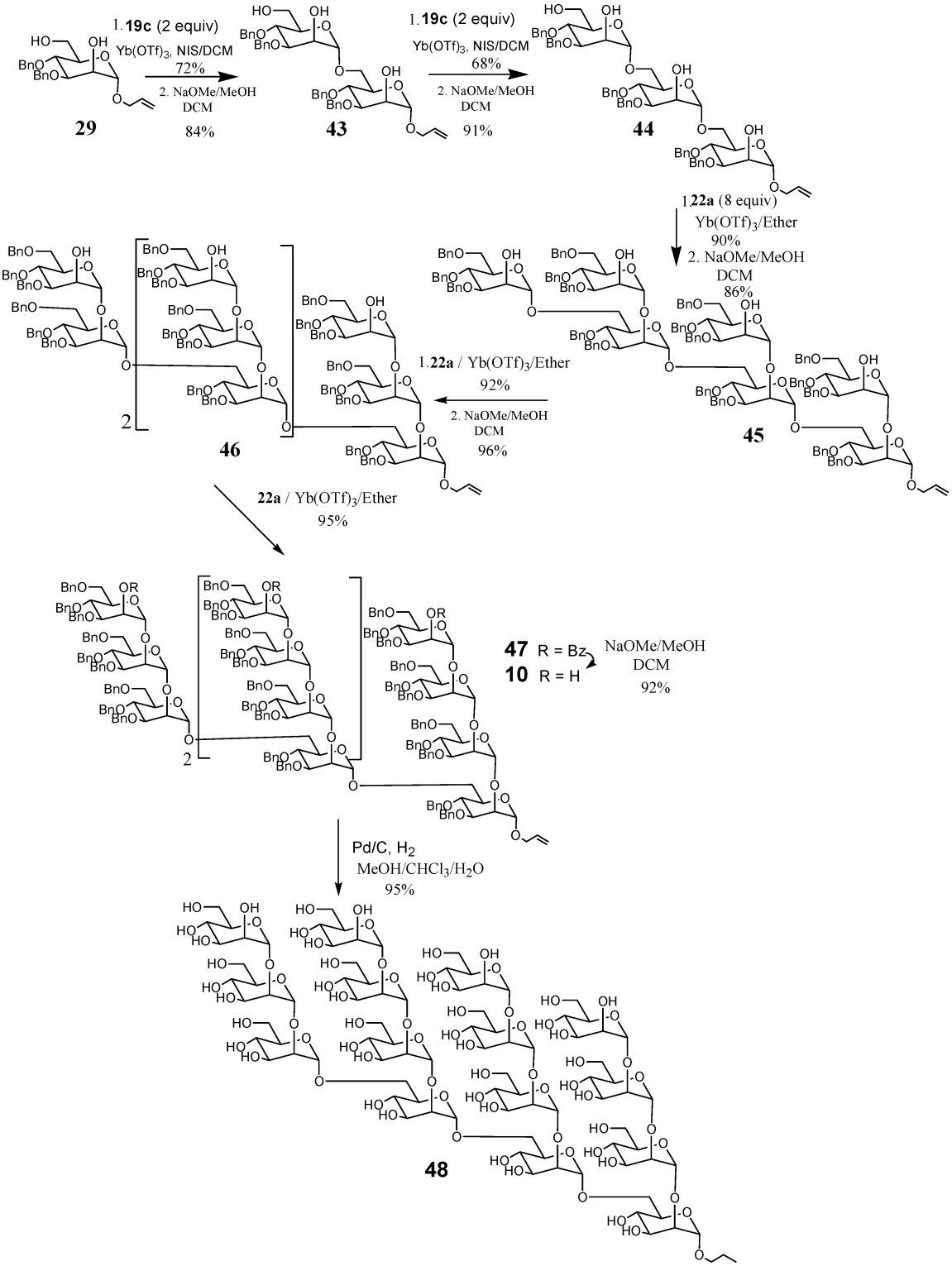
SCHEME 8



(Scheme 7b). This material could be isolated in 76% yield and characterized in the usual way[4,5] by acetylation of **37b** and analysis of the down-shifted proton (5.38 ppm, dd, $J = 1.8$ and 7.2 Hz). However, in a subsequent experiment, trichloroacetimidate **22b** (1.5 equiv) was added after 10 min had elapsed, and stirring was continued for a further 10 min. Trisaccharide **38** was then isolated in 64% overall yield. Alternatively, the ethyl thioglycoside **23b** could be used in the second step to obtain **38**; however, in this case, the amount of NIS used in the first step was increased to 4.0 equiv.

In the experiment in Scheme 7b the NPOE and trichloroacetimidate or ethyl thioglycoside functioned as sequential donors to acceptor **36**. Replacing the latter with the pentenyl glycoside acceptor **25** allowed us to add chemoselectivity to

SCHEME 9



the reaction possibilities (Scheme 7c). Indeed, use of the same sequential methodology as in Scheme 7b led to the *n*-pentenylated disaccharide **39**, which was authenticated by isolation in 71% yield. In the one-pot application, addition of **22b** or **23b** after 10 min afforded the trisaccharide **40** in 60−62% overall yield.

Synthesis of Pentamannan 9. Sequential glycosidations of the 3,6-diol **27** with NPOE **19a** and trichloroacetimidate **22b** (Scheme 8), carried out as in the preliminary tests in Scheme 7, afforded the trisaccharide **41a** in 61% yield. Debenzoylation then afforded diol **41b**. Glycosidation of both hydroxyls of the latter was effected by using the trichloroacetimidate **22a** (4 equiv) with ytterbium triflate as catalyst, to obtain the *n*-pentenyl pentasaccharide **42** in 85% yield. Debenzoylation to the corresponding NPG pentasaccharide diol **9** was routinely carried out in 94% yield.

Synthesis of Pentadecamannan 48. A different approach was taken to pentadecamannan **48** (Scheme 9), which is seen

to have an α-1,6-backbone subtended with α-1,2-branches. The 6-*O*-benzoylated *n*-pentenyl orthoester **19c** was used extensively to provide all units of **48**, the starting allyl glycoside acceptor **29** being most conveniently prepared as indicated in Scheme 5c. Treatment of **29** with 2 equiv of NPOE **19c** in the presence of NIS/$Yb(OTf)_3$ afforded a 72% yield of the disaccharide, which was directly debenzoylated to provide triol **43**. Iteration of the last two steps led to the trisaccharide tetraol **44** in 68% and 91% yields, respectively.

All four hydroxyls of **44** were simultaneously glycosidated by treatment with trichloroacetimidate **22a** (8 equiv) in the presence of $Yb(OTf)_3$ to provide heptasaccharide in 90% yield, which upon debenzoylation led to the heptasaccharyl tetraol **45** in 86% yield. Iteration of exhaustive glycosidation with trichloroacetimidate **22a** (8 equiv) added another four α-mannosidyl residues with extremely high efficiency (92% yield), and after debenzoylation, the corresponding undecasaccharide tetraol **46** was obtained in 96% yield.

Another iteration of exhaustive mannosylation with trichloroacetimidate **22a** was again highly efficient, affording the pentadecasaccharide **47** in 95% yield and its debenzoylated product **10** in 92%.

Exhaustive debenzylation with concomitant saturation of the allylic double bond was achieved by treatment with hydrogen and 5% palladium on carbon for 12 h to give compound **48.**

Conclusion

Mannosyl *n*-pentenylorthoesters (NPOEs) serve as convenient intermediates for other glycosyl donors, *n*-pentenyl glycosides (NPGs), ethyl and phenyl thioglycosides, and trichloroacetimidates, as shown in Scheme 4. These various donors are activated by different reagents, and are therefore amenable to versatile, discriminate use. Thus $Sc(OTf)_3$ and $Yb(OTf)_3$ respond very differently to these donors, with the result that chemoselective distinction between NPOEs and NPGs, as well as ethyl and phenyl thioglycosides, is achieved, as shown in Table 1. The versatility of NPOEs allows them to be used not only as donors, but also as the progenitors to provide 2,6- and 3,6-diol acceptors as shown in Scheme 5. Activation of the NPOEs, used in excess, by iodonium ion, specifically generated from ytterbium triflate/*N*-iodosuccinimide, monoglycosidates the diols rapidly, with exquisite regio, and sometimes chemo, selectivity. The residual NPOE is converted into disarmed NPG, which is refractory to the reaction conditions, and so poses no threat to the free-OH of the monoglycosylated product (Scheme 7). Glycosidation of the latter can then be achieved by direct addition of a trichloroacetimidate or ethyl thioglycoside.

The basic strategy has been used to prepare branched chain mannans **9** and **10**. Particularly in the case of the latter, which is a pentadecasaccharide, glycosidations with both the NPOEs and trichloroacetimidates maintain excellent selectivities and yields, even as the molecule grows larger. The success is an example of the efficiency of the donor/acceptor MATCH concept.

Experimental Section

General Glycosidation Conditions. The acceptor (1 equiv) and NPOE (2.0 equiv) were dissolved together in a small quantity of toluene, azeotroped to dryness, and kept overnight under vacuum. The acceptor was dissolved in dry DCM (7 mL) cooled to 0 °C under argon atmosphere, NIS (2.5 equiv) was added, and after stirring for 5 min, the lanthanide salt (0.3 eq) was added. The reaction was monitored by TLC, and when complete, the reaction was quenched with 10% aqueous sodium thiosulfate and saturated sodium bicarbonate solution, extracted with DCM, and purified by chromatography (gradient elution: hexane/ethyl acetate).

2,3-Di-*O*-benzyl-6-*O*-benzoyl-β-D-mannopyranose 1,2-(Pent-4-enyl orthobenzoate) (19c). The known NPOE[20] **19b** (6 g, 8.07 mmol) was dissolved in THF (30 mL), TBAF (12 mL, 1.00M solution in THF) was added, and the solution was stirred overnight. Solvents were removed and the residue was extracted with DCM, washed with water and brine, and dried under vacuum, and the residue was dissolved in anhydrous pyridine. The mixture was cooled to 0 °C and treated with DMAP (catalytic) and benzoyl chloride (1.20 mL, 1.25 equiv) and stirred overnight. Pyridine was removed by evaporation, and the residue was extracted with DCM, washed with water and $NaHCO_3$ solution, and then evaporated to give a residue that was purified by chromatography (gradient elution 10−30 EtOAc/hexane) to give the desired product, **19c** (4.16 g, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.91(d, J = 8.4 Hz, 2H), 7.69−7.72 (m, 2H), 7.56 (t, J = 8.4 Hz, 1H), 7.28−7.47 (m, 15H), 5.80 (m, 1H), 5.52 (d, J = 2.7 Hz, 1H), 3.46−5.08 (m, 14H), 2.16−2.19 (m, 2H), 1.72−1.77 (m, 2H). MS calcd for $C_{39}H_{40}O_8$ 636.27, found 659.2 (M + Na).

Pent-4-enyl 2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl 3,4-Di-*O*-benzyl-α-D-mannopyranoside (24). Orthoester **19b** (3.00 g, 4.03 mmol) was dissolved in DCM and cooled to 0 °C. TBDMSOTf (0.05 mL) was added and the solution was stirred for 5 min. TLC was checked and the reaction was quenched by adding triethylamine. Solvents were removed and the residue was purified by chromatography to give the desired product (2.6 g, 87%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.19 (d, 8.5 Hz, 2H), 7.79−7.86 (m, 4H), 7.60 (t, J = 8.00 Hz, 1H), 7.23−7.47 (m, 18H), 5.91−5.99 (m, 1H), 5.77 (d, J = 1.8 Hz, 1H), 3.87−5.37 (m, 14H), 1.20 (s, 9H).

Pent-4-enyl 3,4-Di-*O*-benzyl-α-D-mannopyranoside (25). Compound **24** (2.5 g, 3.36 mmol) was dissolved in THF (20 mL) and treated with 5 mL of TBAF solution in THF and the solution was stirred overnight. Solvents were removed and the residue was extracted with DCM and dried, then the residue was dissolved in a mixture of DCM/MeOH (1:1). The mixture was treated with NaOMe (10 mL, 1 M solution in MeOH) and stirred overnight. Solvents were removed and the residue was extracted with DCM, then washed with water and brine. Compound **25** was purified by chromatography, using ethyl acetate/hexane (1.15 g, 79%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.32−7.37 (m, 10), 5.75−5.84 (m, 1H), 5.30 (d, 1.6 Hz, 1H), 3.80 (m, 14H), 2.62 (br s, 2H), 2.06−2.11 (m, 2H), 1.64−1.70 (m, 2H). MS calcd for $C_{25}H_{32}O_6$ 428.22, found 451.3 (M + Na).

Allyl 3,4-Di-*O*-benzyl-α-D-mannopyranoside (29). The orthoester **19c** (5 g, 7.85 mmol), allyl alcohol (0.682 g, 11.7 mmol), and NIS (2.65 g, 11.77 mmol) were made to react under the agency of $Yb(OTf)_3$, using the standard glycosidation procedure, to give the dibenzoylated derivative **28**. The material was purified by chromatography (4.10 g, 86%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.03 (d, 7.5 Hz, 4H), 7.18−7.60 (m, 16H), 5.75−5.84 (m, 1H), 5.63 (d, 1.8 Hz, 1H), 3.44−5.06 (m, 14H). MS calcd for $C_{37}H_{36}O_8$ 608.24, found 631.2 (M + Na). This compound was dissolved in a mixture of DCM/MeOH (1:1) and stirred with an excess of NaOMe overnight. Solvents were removed and product was purified by chromatography to give the desired product **29** (2.41 g, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.24−7.39 (m, 10H), 5.79−5.92 (m, 1H), 5.16−5.28 (m, 2H), 3.66−4.93 (m, 11H), 3.02 (br s, 1H), 2.60 (br s, 1H). MS calcd for $C_{23}H_{28}O_6$ 400.19, found 423.2 (M + Na).

Methyl 2-*O*-(2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-4,6-*O*-benzylidene-α-D-glucopyranoside (31). The acceptor **30** (24 mg, 0.085 mmol) and the donor **19a** (106 mg, 0.170 mmol) were coupled with use of NIS (49 mg, 2.5 equiv) and $Yb(OTf)_3$ (16 mg, 0.3 equiv) in ∼6 mL of CH_2Cl_2, using the general glycosidation procedure to give **31** (44 mg, yield 62%). ^{1}H NMR

($CDCl_3$, 300 MHz) δ 8.05 (d, J = 7.5 Hz, 2H), 7.00−7.6 (m, 23H), 5.78 (dd, J = 1.8, 3.00 Hz, 1H), 5.60 (s, 1H), 5.32 (d, J = 1.8 Hz, 1H), 3.15−4.90 (m, 18H), 2.6 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 138.6, 138.4, 138.2, 137.2, 133.3, 133.2, 130.1, 128.9, 128.5, 128.4, 128.3, 128.1, 128.1, 127.77, 127.74, 127.6, 126.1, 101.1, 100.4, 98.9, 81.5, 78.5, 75.6, 75.3, 74.8, 74.5, 73.7, 71.8, 71.8, 71.7, 69.7, 69.5, 69.3, 69.1, 62.7, 55.7. MS calcd for $C_{48}H_{50}O_{12}$ 818.33, found 841.6 (M + Na).

Methyl 2,3-Di-*O*-(2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-4,6-*O*-benzylidene-α-D-glucopyranoside (32). The acceptor **30** (28 mg, 0.100 mmol) and the donor **19a** (124 mg, 0.200 mmol) were coupled with use of NIS (56 mg, 2.5 equiv) and Sc(OTf)$_3$ (15 mg, 0.3 equiv) in ∼8 mL of CH_2Cl_2, using the general glycosidation procedure to give **32** (43 mg) and **31** (49 mg, yield 70%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.04 (d, J = 7.5 Hz, 2H), 7.93 (d, J = 7.5 Hz, 1H), 7.10−7.53 (m, 41H), 5.80 (dd, J = 1.8, 3.00 Hz, 1H), 5.71 (dd, J = 1.8, 3.00 Hz, 1H), 5.60 (s, 1H), 5.42 (d, J = 1.8 Hz, 1H), 3.53−4.92 (m, 30H), 3.25 (s, 3H). MS calcd for $C_{82}H_{82}O_{18}$ 1354.55, found 1377.7 (M + Na).

Methyl 2,4-Di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl)-α-D-mannopyranoside (37). Diol **36** (0.031 g, 0.084 mmol) was treated with NPOE **19a** (0.105 g, 2 equiv) under glycosidation conditions, using Yb(OTf)$_3$ (0.015 g, 0.3 equiv), to give the title compound **37** (0.056 g, 76%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.09 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.16−7.38 (m, 27H), 5.72 (dd, J = 1.6, 3.2 Hz, 1H), 5.11 (d, J = 1.6 Hz, 1H), 3.57−4.92 (m, 22H), 3.28 (s, 3H), 2.40 (d, J = 10 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7, 138.7, 138.6, 138.1, 137.8, 133.3, 130.2, 129.1, 128.8, 128.58, 128.56, 128.3, 128.2, 128.1, 127.85, 127.80, 127.7, 127.6, 98.2, 97.9, 78.8, 77.8, 75.5, 75.0, 74.5, 73.2, 72.2, 71.9, 71.4, 70.6, 69.7, 69.0, 66.8, 55.1. MS calcd for $C_{55}H_{58}O_{12}$ 910.39, found 933.4 (M + Na).

Methyl 2,4-Di-*O*-benzyl-3-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl)-6-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl)-α-D-mannopyranoside (38): (a) Methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (**36**) (0.043 g, 0.115 mmol) and NPOE **19a** (0.143 g, 2 equiv) were dissolved together in a small amount of toluene, evaporated to dryness, and kept under vacuum overnight. The mixture was then dissolved in ∼10 mL of DCM and cooled to 0 °C. NIS (0.064 g, 2.5 equiv) was added and the solution was stirred for a few minutes, followed by addition of Yb(OTf)$_3$ (0.021 g, 0.3 equiv). The reaction mixture was stirred for 10 min and monitored by TLC to ensure formation of **37**. After 10 min, trichloroacetimidate donor **22b** (0.142 g, 1.5 equiv) was added and the solution was stirred for another 10 min. The reaction mixture was quenched with saturated sodium bicarbonate and 10% sodium thiosulfate solutions, extracted with DCM, and dried over Na_2SO_4. Solvents were removed under reduced pressure and the residue was purified by chromatography to give the desired compound **38** (0.117 g, 64%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.08−8.12 (m, 4H), 7.77 (d, J = 7.7 Hz, 2H), 7.70 (d, J = 7.7 Hz, 2H), 7.53−7.58 (m, 2H), 7.08−7.42 (m, 45H), 5.84 (dd, J = 1.6, 3.00 Hz, 1H), 5.76 (dd, J = 1.5, 3.00 Hz, 1H), 5.37 (d, J = 1.5 Hz, 1H), 5.14 (d, J = 1.6 Hz, 1H), 3.71−5.00 (m, 31H), 3.24 (s, 3H), 1.12 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7, 165.6, 138.9, 138.7, 138.6, 138.1, 138.0, 136.1, 135.8, 133.7, 133.2, 133.10, 129.7, 128.65, 128.60, 128.53, 128.52, 128.49, 128.47, 128.42, 128.2, 128.1, 128.0, 127.9, 127.89, 127.8, 127.7, 127.6, 99.9, 98.4, 78.6, 77.7, 75.4, 79.4, 73.6, 73.5, 72.6, 71.9, 71.3, 69.9, 69.7, 69.2, 69.0, 66.8, 63.2, 55.0, 27.0, 19.1. MS calcd for $C_{98}H_{102}O_{18}Si$ 1594.68, found 1617.7 (M + Na).

(b) The above reaction was repeated with ethyl thioglycoside donor **23b** (instead of **22b**). In this experiment 4 equiv of NIS was used instead of 2.5 equiv. The yield of **38** was also 64%.

Pent-4-enyl 3,4-Di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl)-α-D-mannopyranoside (39). The diol acceptor **25** (39 mg, 0.091 mmol) and the donor **19a** (113 mg, 0.182 mmol) were coupled, using NIS (50 mg, 2.5 equiv) and Yb(OTf)$_3$ (17 mg, 0.3 equiv), in ∼6 mL of DCM, using the general glycosidation procedure, to give **39** (63 mg, yield 71%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.13−7.39 (m, 22H), 5.79 (m, 1H), 5.70 (dd, J = 1.8, 3.00 Hz), 5.12 (d, J = 1.8 Hz, 1H), 3.64−5.04 (m, 24H), 3.35−3.45 (m, 2H), 2.60 (d, J = 2.4 Hz, 1H), 2.06−2.13 (m, 2H), 1.60−1.70 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7, 138.7, 138.6, 138.4, 138.1, 138.1, 133.2, 130.2, 130.1, 128.7, 128.57, 128.5, 128.48, 128.4, 128.2, 128.19, 128.1, 128.0, 127.94, 127.9, 127.8, 127.7, 127.68, 127.6, 115.1, 99.3, 98.3, 80.6, 78.0, 75.4, 75.3, 74.8, 74.5, 74.3, 73.6, 72.1, 71.9, 71.8, 71.5, 71.0, 69.6, 69.2, 68.6, 67.3, 66.8, 30.6, 28.9. MS calcd for $C_{59}H_{64}O_{12}$ 964.44, found 987.8 (M + Na).

Pent-4-enyl 3,4-Di-*O*-benzyl-3-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl)-6-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl)-α-D-mannopyranoside (40): (a) The acceptor diol **25** (27 mg, 0.063 mmol), donor **19a** (78 mg, 0.126 mmol), and donor **22b** (72 mg, 1.5 equiv) were coupled with NIS (36 mg, 2.5 equiv) and Yb(OTf) $_3$ (12 mg, 0.3 equiv) in ∼7 mL of DCM, using the procedure described above for **38**, to give **40** (62 mg, yield 60%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.04−8.08 (m, 4H), 7.71−7.85 (m, 4H) 7.50−7.58 (m, 2H), 7.16−7.40 (m, 45H), 5.81 (dd, J = 1.8, 3.00 Hz, 1H), 5.75 (m, 1H), 5.67 (dd, J = 1.8, 3.00 Hz, 1H), 5.33 (d, J = 1.8 Hz, 1H), 5.06 (d, J = 1.8 Hz, 1H), 3.59−5.01 (m, 37H), 3.25−3.34 (m, 2H), 2.02−2.10 (m, 2H), 1.67−1.65 (m, 2H), 1.14 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 165.5, 138.8, 138.7, 138.6, 138.5, 138.47, 138.4, 138.3, 138.2, 138.18, 138.1, 137.9, 133.3, 133.1, 130.2, 130.1, 129.9, 128.55, 128.5, 128.4, 128.3, 128.29, 128.26, 128.2, 128.09, 128.03, 127.9, 127.79, 127.7, 127.6, 127.6, 115.1, 99.89, 98.8, 97.7, 80.2, 78.4, 75.7, 75.4, 75.2, 75.0, 74.6, 74.4, 74.3, 73.7, 73.6, 72.8, 72.5, 72.3, 72.0, 71.97, 71.9, 71.6, 70.9, 69.5, 69.3, 69.2, 69.1, 69.0, 67.2, 67.0, 30.6, 28.9, 26.9, 19.8. MS calcd for $C_{102}H_{108}O_{18}Si$ 1648.73, found 1671.9 (M + Na).

(b) The acceptor diol **25** (25 mg, 0.058 mmol), donor **19a** (72 mg, 0.116 mmol), and donor **23b** (64 mg, 1.5 equiv) were coupled with NIS (52 mg, 4 equiv) and Yb(OTf) $_3$ (11 mg, 0.3 equiv) in ∼7 mL of DCM, using the above-described procedure, to give **40** (60 mg, yield 62%).

Pent-4-enyl 2,4-Di-*O*-benzyl-3-*O*-(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl)-6-*O*-(3,4,6-tri-*O*-benzyl)-α-D-mannopyranoside (41b). Diol **27** (0.143 g, 0.334 mmol) and the donor **19a** (0.415 g, 2 equiv) were dissolved together in a small amount of toluene, evaporated to dryness, and kept under vacuum overnight. The mixture was then dissolved in ∼20 mL of DCM and cooled to 0 °C. NIS (0.225 g, 3 equiv) was added and the solution was stirred for a few minutes, followed by the addition of Yb(OTf)$_3$ (0.062 g, 0.3 equiv). The reaction mixture was stirred for 10 min and monitored by TLC to check for completion of the first glycosidation. To the above reaction mixture donor **22b** (0.426 g, 1.5 equiv) was added and the solution was stirred for another 10 min. The reaction mixture was quenched with saturated sodium bicarbonate and 10% sodium thiosulfate solutions, extracted with DCM, and dried over Na_2SO_4. Solvents were removed under reduced pressure and the residue was purified by chromatography to give compound **41a** (0.335 g, 61%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.12 (d, J = 8.00 Hz, 2H), 8.05 (d, J = 8.10 Hz, 2H), 7.61−7.77 (m, 4H), 7.03−7.45 (m, 47H), 5.86 (dd, J = 1.5, 3.0 Hz, 1H), 5.79 (s, 1H), 5.56−5.68 (m, 1H), 5.37 (d, J = 1.5 Hz, 1H), 5.14 (d, J = 1.5 Hz, 1H), 3.57−5.01 (m, 39H), 3.22−3.32 (m, 1H), 1.97−2.05 (m, 2H), 1.53−1.60 (m, 2H), 1.11 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 165.7, 139.1, 138.88, 138.8, 138.3, 138.28, 138.2, 136.3, 136.2, 136.1, 135.96, 133.9, 133.4, 133.3, 130.3, 130.2, 129.9, 128.8, 128.78, 128.7, 128.66, 128.6, 128.3, 128.28, 128.2, 128.1, 128.0, 127.97, 127.9, 127.89, 127.8, 115.3, 100.2, 98.6, 97.3, 79.3, 78.8, 78.6, 78.5, 78.1, 77.6, 77.1, 76.0, 75.6, 75.3, 74.6, 74.5, 74.2, 73.8, 73.6, 72.8, 72.6, 72.4, 72.2, 72.1, 72.0, 71.6, 71.5, 70.1, 69.9, 69.4, 69.1, 68.2, 67.5, 67.0, 63.1, 30.8, 29.0, 27.4, 19.9. MS calcd for $C_{102}H_{108}O_{18}Si$ 1648.73, found 1671.8 (M + Na). Trisaccharide **41a** (0.50 g, 0.302 mmol) was dissolved in a DCM/CH_3OH mixture and treated with an excess of NaOMe (0.5 M solution in MeOH). The mixture was stirred for a day at room temperature to complete the debenzoylation. Solvents were removed and the residue was

extracted with CH_2Cl_2 and saturated ammonium chloride solution and dried over Na_2SO_4. Dichloromethane was removed under reduced pressure and residue was purified by chromatography to give the title product **41b** (0.395 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.86 (d, J = 7.5 Hz, 2H), 7.76 (d, J = 7.5 Hz, 2H), 7.23−7.49 (m, 41H), 5.78−5.89 (m, 1H), 5.35 (d, J = 1.5 Hz, 1H), 5.21 (d, J = 1.5 Hz, 1H), 3.65−5.11 (m, 36H), 3.34−3.41 (m, 1H), 2.52 (br s, 2H), 2.08−2.14 (m, 2H), 1.63−1.75 (m, 2H), 1.18 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8, 138.7, 138.5, 138.1, 138.4, 138.3, 138.21, 136.2, 135.93, 133.9, 133.4, 129.85, 128.8, 128.78, 128.7, 128.5, 128.24, 128.21, 128.1, 128.0, 127.96, 127.9, 127.88, 127.84, 127.8, 127.6, 115.2, 101.8, 100.0, 97.2, 80.5, 80.0, 78.3, 75.4, 75.3, 75.1, 74.6, 74.5, 73.7, 73.4, 72.5, 72.4, 71.8, 71.5, 69.2, 69.1, 68.3, 67.5, 66.5, 63.6, 30.7, 28.9, 27.3, 19.8. MS calcd for $C_{88}H_{100}O_{16}Si$ 1440.68, found 1463.7 (M + Na).

Pent-4-enyl 2,4-Di-*O*-benzyl-3-*O*-[(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-mannopyranosyl)-2-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl-α-D-mannopyranosyl)]-6-*O*-[(3,4,6-tri-*O*-benzyl)-2-*O*-(2-*O*-benzoyl-3,4-6-tri-*O*-benzyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (42). Trisaccharide diol **41b** (0.320 g, 0.222 mmol) and mannosyl trichloroacetimidate **22a** (0.610 g, 4 equiv) were dissolved in a small amount of toluene and evaporated to dryness and the mixture was kept under vacuum for 4 h. The reaction mixture was dissolved in ether (∼15 mL), a small amount of molecular sieves was added, and the solution was cooled to 0 °C. Yb(OTf)$_3$, (0.041 g, 0.3 equiv) was added and the solution was stirred for 10 min, TLC was checked and the reaction was quenched with triethylamine. Solvents were removed and the residue was purified by chromatography to give **42** (0.468 g, 85%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.19 (d, J = 7.5 Hz, 4H), 7.84 (d, J = 7.5 Hz, 2H), 7.74 (d, J = 7.5 Hz, 2H), 7.60 (m, 2H), 7.18−7.46 (m, 79H), 5.81−5.87 (m, 3H), 5.39 (d, J = 1.5 Hz, 1H), 5.28 (d, J = 1.5 Hz, 1H), 5.25 (d, J = 1.6 Hz, 1H), 3.35−5.08 (m, 66H), 2.13−2.17 (m, 2H), 1.65−1.70 (m, 2H), 1.15 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 163.6, 138.9, 138.8, 138.7, 138.6, 138.4, 138.3, 138.1, 136.1, 135.8, 133.7, 133.3, 130.2, 129.8, 128.7, 128.6, 128.57, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.5, 127.3, 115.2, 101.6, 99.9, 99.5, 97.0, 80.2, 79.4, 78.5, 75.9, 75.5, 75.4, 75.2, 74.9, 74.8, 74.6, 73.7, 73.6, 73.5, 72.7, 72.5, 72.4, 72.3, 72.1, 72.0, 71.8, 71.6, 69.4, 68.9, 67.5, 66.9, 63.8, 30.7, 28.9, 27.4, 19.7. MS calcd for $C_{156}H_{164}O_{28}Si$ 2513.12, found 2536.2 (M + Na).

Pent-4-enyl 2,4-Di-*O*-benzyl-3-*O*-[(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-mannopyranosyl)-2-*O*-(3,4-6-tri-*O*-benzyl-α-D-mannopyranosyl)]-6-*O*-[(3,4,6-tri-*O*-benzyl)-2-*O*-(3,4-6-tri-*O*-benzyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (9). The pentasaccharide **42** (0.465 g, 0.185 mmol) was debenzoylated with NaOMe to give the title compound **9** (0.401 g (94%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87 (d, J = 7.5 Hz, 2H), 7.79 (d, J = 7.5 Hz, 2H), 7.20−7.49 (m, 75H), 5.76−5.85 (m, 1H), 5.41 (d, J = 1.5 Hz, 1H), 5.32 (d, J = 1.5 Hz, 1H), 5.23 (d, J = 1.5 Hz, 1H), 5.14 (d, J = 1.5 Hz, 1H), 3.40−5.03 (m, 66H), 2.60 (br s, 1H), 2.56 (br s, 1H), 2.09−2.14 (m, 2H), 1.65−1.70 (m, 2H), 1.21 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 138.9, 138.9, 138.8, 138.76, 138.7, 138.5, 138.4, 138.37, 138.3, 138.2, 136.1, 135.8, 133.7, 133.3, 129.8, 128.8, 128.7, 128.69, 128.6, 128.57, 128.5, 128.2, 128.17, 128.1, 128.09, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 115.2, 101.6, 101.5, 99.6, 97.0, 80.4, 80.3, 79.57, 78.54, 75.5, 75.3, 75.2, 74.9, 74.8, 74.7, 79.6, 73.7, 73.5, 72.7, 72.5, 72.4, 72.2, 72.0, 71.9, 71.6, 69.9, 69.3, 69.0, 67.5, 67.0, 63.7, 30.7, 28.9, 27.4, 19.7. MS calcd for $C_{142}H_{156}O_{26}Si$ 2305.07, found 2328.1 (M + Na).

Allyl 3,4-Di-*O*-benzyl-6-*O*-(3,4-di-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (43). Diol **29** (0.415 g, 1.03 mmol) and mannosyl donor **19c** (1.30 g, 2 equiv) were dissolved separately in a small amount of toluene and evaporated to dryness in two different flasks. The acceptor diol was dissolved in ∼20 mL of DCM and cooled to 0 °C. NIS (0.579 g, 2.5 equiv) and Yb(OTf)$_3$ (0.191 g, 0.3 equiv) were added, the solution was stirred for few minutes, and then a DCM solution of donor **19c** was added dropwise to the reaction mixture over a period of 10 min. TLC was checked to ensure complete glycosidation. The reaction was quenched with saturated sodium bicarbonate and 10% sodium thiosulfate solutions, and the extract with DCM, and dried over Na_2SO_4. Solvents were removed under reduced pressure and the residue was purified by chromatography to give the desired disaccharide (0.710 g, 72%—rest of the acceptor was recovered). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.06 (d, J = 7.5 Hz, 4H), 7.55−7.62 (m, 2H), 7.17−7.44 (m, 24H), 5.82−5.95 (m, 1H), 5.76 (dd, J = 2.1,4.8 Hz, 1H), 5.17−5.30 (m, 2H), 5.12 (d, J = 2.1 Hz, 1H), 3.75−4.98 (m, 22H), 2.67 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 165.5, 138.1, 138.0, 137.8, 137.7, 133.5, 133.2, 133.0, 130.5, 129.9, 129.7, 128.6, 128.45, 128.4, 128.3, 128.28, 128.2, 128.1, 128.0, 127.9, 127.7, 127.7, 117.9, 98.2, 98.0, 80.4, 77.9, 75.3, 75.2, 74.2, 73.6, 72.0, 71.4, 70.9, 70.1, 68.9, 68.4, 68.1, 66.7, 63.4. MS calcd for $C_{57}H_{58}O_{13}$ 950.39, found 973.4 (M + Na). The disaccharide (0.700 g, 0.736 mmol) was dissolved in a DCM/CH_3OH mixture and treated with an excess of NaOMe (0.5 M solution in MeOH). The mixture was stirred overnight at room temperature to complete the debenzoylation. Solvents were removed and the residue was extracted with DCM and saturated ammonium chloride solution and dried over Na_2SO_4. Dichloromethane was removed under reduced pressure and residue was purified by chromatography to give the product **43** (0.460 g, 84%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.19−7.40 (m, 20H), 5.78−5.91 (m, 1H), 5.14−5.28 (m, 2H), 5.07 (d, J = 1.5 Hz, 1H), 3.60−4.93 (m, 23H), 2.8 (br s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 138.4, 138.1, 138.0, 133.7, 132.1, 128.7, 128.68, 128.6, 128.5, 128.24, 128.2, 128.16, 128.1, 128.0, 127.9, 127.8, 127.6, 117.8, 99.9, 98.4, 80.4, 79.5, 75.4, 74.3, 74.1, 72.2, 72.0, 71.3, 68.4, 68.2, 66.1, 61.9. MS calcd for $C_{43}H_{50}O_{11}$ 742.34, found 765.4 (M + Na).

Allyl 3,4-Di-*O*-benzyl-6-*O*-bis(3,4-di-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (44). Triol **43** (0.360 g, 0.484 mmol), NPOE **19c** (0.769 g, 2.5 equiv), NIS (0.327 g, 3 equiv), and Yb(OTf)$_3$ (0.090 g, 0.3 equiv) were reacted using the procedure described earlier to give a trisaccharide (0.426 g, 68%—the rest of the triol was recovered). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.01 (d, J = 7.8 Hz, 4H), 7.49−7.56 (m, 2H), 7.13−7.36 (m, 34H), 5.76−5.88 (m, 1H), 5.71 (s, 1H), 3.62−5.25 (m, 36H), 2.76 (br s, 1H), 2.64 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 165.7, 138.6, 138.4, 138.2, 138.0, 133.7, 133.3, 133.1, 130.3, 130.1, 129.9, 128.9, 128.7, 128.0, 128.6, 128.56, 128.5, 128.4, 128.3, 128.2, 128.16, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 118.0, 99.8, 98.4, 98.2, 80.6, 80.1, 78.1, 75.5, 75.4, 75.3, 74.4, 74.3, 73.7, 72.2, 72.1, 71.9, 71.6, 71.1, 70.2, 69.1, 68.5, 68.3, 68.2, 66.7, 66.5, 63.5. MS calcd for $C_{77}H_{80}O_{18}$ 1292.53, found 1315.5 (M + Na). The trisaccharide (0.420 g, 0.330 mmol) was debenzolylated with NaOMe to give tetrol **44** (0.319 g, 91%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.12−7.37 (m, 30H), 5.71−5.89 (m, 1H), 5.03−5.22 (m, 2H), 3.56−4.99 (m, 34H), 3.04 (br s, 1H), 2.95 (br s, 1H), 2.89 (br s, 1H), 2.64 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.2, 138.1, 137.94, 137.9, 137.5, 133.1, 128.36, 128.3, 128.2, 128.13, 128.1, 127.8, 127.75, 127.7, 127.65, 127.6, 127.5, 127.5, 127.4, 127.4, 127.1, 117.9, 98.9, 98.8, 97.5, 80.0, 79.5, 79.3, 75.0, 74.8, 74.2, 74.0, 73.0, 73.9, 72.1, 72.0, 71.8, 71.7, 71.66, 71.6, 70.6, 71.0, 70.6, 69.9, 68.1, 67.9, 67.8, 67.6, 65.9, 65.3, 61.7. MS calcd for $C_{63}H_{72}O_{16}$ 1084.48, found 1107.4 (M + Na).

Allyl 3,4-Di-*O*-benzyl-2-*O*-[(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-{3,4-di-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}]-6-*O*-[{3,4-di-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}-6*O*-3,4-di-*O*-benzyl-α-D-mannopyranosyl]-α-D-mannopyranoside (45). Triisaccharide tetrol **44** (0.210 g, 0.194 mmol) and mannosyl trichloroacetimidate **22a** (1.053 g, 8 equiv) were dissolved in a small amount of toluene, evaporated to dryness, and kept under vacuum for 4 h. The reaction mixture was dissolved in ether (∼15 mL), a small amount of molecular sieves was added, and the solution was cooled to 0 °C. Yb(OTf)$_3$ (0.036 g, 0.3 equiv) was added, the solution was stirred for 10 min, TLC was checked,

and the reaction was quenched with triethylamine. Solvents were removed and the residue was purified by chromatography to give the heptasaccharide.(0.560 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13−8.19 (m, 8H), 7.58−7.65 (m, 4H), 7.13−7.48 (m, 98H), 5.86−5.99 (m, 4H), 5.80 (dd, J = 1.6, 3.00 Hz, 1H), 3.56−5.43 (m, 85H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 165.5, 165.3, 139.0, 138.8, 138.6, 138.4, 138.4, 138.2, 138.1, 137.9, 133.8, 133.3, 130.2, 128.8, 128.7, 128.6, 128.0, 128.5, 128.45, 128.4, 128.3, 128.2, 128.07, 128.0, 127.97, 127.9, 127.83, 127.8, 127.77, 127.7, 127.69, 127.6, 127.5, 127.3, 118.0, 100.1, 99.9, 99.3, 99.0, 98.3, 98.1, 80.3, 79.9, 79.0, 78.8, 78.6, 78.3, 78.1, 75.6, 75.5, 75.4, 75.1, 72.0, 74.8, 74.7, 74.5, 74.3, 74.3, 73.8, 73.7, 73.6, 72.6, 72.5, 72.16, 72.1, 71.9, 71.7, 71.4, 72.2, 70.8, 69.7, 69.6, 69.4, 68.9, 68.1, 67.4, 67.2, 66.3. MS calcd for $C_{199}H_{200}O_{40}$ 3229.36, found 3252.4 (M + Na). The Hepta(OBz)$_4$ (0.558 g, 0.172 mmol) was dissolved in CH_2Cl_2/MeOH and treated with NaOMe for 24 h to give pentaol **45** (0.430 g, 86%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.05−7.30 (m, 90H), 5.72−5.82 (m, 1H), 3.47−5.30 (m, 89H), 2.80 (br s, 1H), 2.60 (br s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.3, 138.2, 138.1, 138.0, 137.9, 137.8, 137.6, 137.5, 137.47, 137.44, 137.4, 133.3, 128.1, 128.07, 128.0, 127.9, 127.85, 127.8, 127.78, 127.7, 127.6, 127.57, 127.5, 127.4, 127.36, 127.3, 127.2, 127.1, 126.9, 126.5, 117.3, 101.5, 101.2, 100.8, 99.7, 96.6, 98.2, 97.7, 80.2, 79.9, 79.6, 79.1, 78.6, 77.1, 75.0, 74.8, 74.6, 74.4, 74.3, 74.1, 73.6, 73.1, 73.05, 73.0, 72.9, 72.0, 71.74, 71.7, 71.4, 71.0, 70.8, 70.6, 70.4, 69.7, 68.6, 68.1, 67.5, 66.6, 66.2, 64.3. MS calcd for $C_{171}H_{184}O_{36}$ 2813.26, found 2836.3 (M + Na).

Allyl 3,4-Di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl] (3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-bis-3,4-di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(3,4,6-tri-*O*-benzyl)-α-D-mannopyranosyl]-[(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)](3,4-di-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-{2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}-α-D-mannopyranoside (46). The heptasaccharide tetraol **45**(0.428 g, 0.152 mmol) and mannosyl trichloroacetimidate **22a** (0.835 g, 8 equiv) were dissolved in a small amount of toluene and evaporated to dryness and mixture was kept under vacuum for 4 h. The reaction mixture was dissolved in ether (∼10 mL), a small amount of molecular sieves was added, and the solution was cooled to 0 °C. Yb(OTf)$_3$ (0.028 g, 0.3 equiv) was added and the solution was stirred for 10 min, TLC was checked, and the reaction was quenched with triethylamine. Solvents were removed and the residue was purified by chromatography to give an undecasaccharide (0.700 g, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.19−8.26 (m, 8H), 7.51−7.67 (m, 4H), 7.10−7.44 (m, 158H), 5.91−5.95 (m, 5H), 3.51−5.46 (m, 137H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.8, 165.6, 165.5, 138.9, 138.9, 138.6, 138.5, 138.4, 138.3, 138.1, 134.0, 133.3, 130.3, 128.8, 128.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.0, 127.7, 127.0, 127.5, 117.9, 101.1, 100.9, 99.8, 99.4, 98.4, 80.3, 78.6, 78.2, 75.5, 74.9, 74.6, 73.8, 73.7, 73.5, 72.6, 72.0, 71.2, 69.8, 69.3, 68.2, 67.7, 64.1. MS calcd for $C_{307}H_{312}O_{60}$ 4958.14, found 4981.2 (M + Na). The above undecasaccharide (0.696 g, 0.140 mmol) was dissolved in DCM/MeOH and treated with NaOMe for 24 h to give undecasaccharyl title tetraol **46** (0.616 g, 96%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.00−7.29 (m, 150H), 5.68−5.80 (m, 1H), 3.20−5.29 (m, 141H), 2.30−2.40 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 138.9, 138.88, 138.8, 138.8, 138.76, 138.7, 138.6, 138.58, 138.5, 138.48, 138.4, 138.34, 138.3, 138.2, 138.1, 138.1, 138.0, 137.9, 133.9, 130.2, 128.77, 128.7, 128.6, 128.5, 128.46, 128.4, 128.39, 128.3, 128.29, 128.2, 128.17, 128.1, 128.09, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1, 117.8, 101.5, 101.38, 101.30, 101.2, 101.1, 101.0, 100.9, 99.4, 99.2, 98.3, 80.3, 80.1, 80.0, 79.8, 79.3, 77.6, 75.4, 75.3, 75.1, 74.9, 74.6, 74.4, 73.6, 73.5, 73.4, 72.7, 72.5, 72.4, 72.3, 72.1, 74.9, 71.8, 71.6, 71.5, 71.2, 71.1, 70.7, 69.6, 69.5, 69.4, 69.3, 69.2, 69.0, 68.9, 68.8, 68.1, 67.8, 67.6, 66.8. MS calcd for $C_{279}H_{296}O_{56}$ 4542.03, found 4565.1 (M + Na).

Allyl 3,4-Di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(2-*O*-{2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-bis-3,4-di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(2-*O*-{2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}-3,4,6-tri-*O*-benzyl)-α-D-mannopyranosyl](3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)]-3,4-di-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-{2-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]}-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}-α-D-mannopyranoside (47). The undecaasaccharide tetraol **46** (0.104 g, 0.023 mmol) and mannosyl trichloroacetimidate **22a** (0.125 g, 8 equiv) were dissolved in a small amount of toluene, evaporated to dryness, and kept under vacuum for 4 h. The reaction mixture was dissolved in ether (∼5 mL), a small amount of molecular sieves was added, and the solution was cooled to 0 °C. Yb(OTf)$_3$ (0.005 g, 0.3 equiv) was added, the solution was stirred for 10 min, TLC was checked, and the reaction was quenched with triethylamine. Solvents were removed and the residue was purified by chromatography to give **47** (0.146 g, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 8.09−8.12 (m, 8H), 7.43−7.62 (m, 4H), 6.89−7.45 (m, 218H), 5.72−5.82 (m, 3H), 5.69 (dd, J = 1.8, 3.2 Hz, 1H), 5.39 (s, 1H), 3.50−5.29 (m, 188H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 165.56, 165.52, 165.5, 138.9, 138.9, 138.8, 138.7, 138.6, 138.5, 138.4, 138.3, 138.2, 138.1, 138.0, 137.8, 135.7, 133.9, 133.5, 133.3, 133.2, 130.3, 130.1, 129.8, 129.2, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.1, 127.0, 126.6, 117.7, 101.8, 101.4, 101.3, 100.9, 100.8, 100.3, 99.7, 99.3, 98.3, 98.1, 80.2, 79.7, 78.5, 78.0, 77.5, 75.8, 75.6, 75.4, 75.4, 75.1, 74.8, 74.6, 74.4, 74.1, 73.7, 73.8, 72.5, 72.5, 72.3, 72.1, 71.9, 71.8, 71.7, 71.4, 71.1, 70.8, 70.6, 70.3, 70.0, 69.8, 69.6, 69.3, 69.1, 68.4, 68.1, 67.6, 65.3. MS calcd for $C_{415}H_{424}O_{80}$ 6686.91, found 6688.3 (M + H).

Allyl 3,4-Di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(2-*O*-{3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl} 3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-bis-3,4-di-*O*-benzyl-2-*O*-{2-*O*-[2-*O*-(2-*O*-{3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}-3,4,6-tri-*O*-benzyl)-α-D-mannopyranosyl](3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)]-3,4-di-*O*-benzyl-α-D-mannopyranosyl)}-6-*O*-{2-*O*-[2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]}-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl}α-D-mannopyranoside (10). The tetrabenzoate **47** (0.145 g, 0.021 mmol) was dissolved in DCM/MeOH and treated with NaOMe for 24 h to give tetraol **10** as a gummy oil (0.125 g, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz,) δ 7.01−7.37 (m, 210H), 5.70−5.84 (m, 1H), 5.25−3.20 (m, 193H), 2.30−2.45 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 141.1, 138.9, 138.8, 138.70, 138.6, 138.5, 138.4, 138.34, 138.3, 138.2, 138.0, 138.0, 137.8, 133.9, 128.65, 128.62, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.15, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 127.1, 127.0, 117.7, 101.8, 101.1, 100.9, 99.6, 99.2, 99.0, 98.3, 80.3, 79.8, 79.6, 77.5, 75.7, 75.6, 75.3, 75.1, 75.0, 74.8, 74.4, 74.0, 73.5, 73.4, 72.6, 72.3, 72.1, 72.0, 71.8, 71.6, 71.0, 70.8, 70.6, 69.5, 69.3, 68.7, 68.1, 67.6, 65.6, 64.7, 60.7. MS calcd for $C_{387}H_{408}O_{76}$ 6270.81, found 6293.9 (M + Na).

***n*-Propyl 2-*O*-{2-*O*-[2-*O*-(2-*O*-α-D-Mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-6-*O*-bis-2-*O*-{2-*O*-[2-*O*-(2-*O*-{α-D-mannopyranosyl}-α-D-mannopyranosyl](α-D-mannopyranosyl)mannopyranosyl)}-6-*O*-{2-*O*-[2-*O*-α-D-mannopyranosyl)α-D-mannopyranosyl]}-α-D-mannopyranosyl}-α-D-mannopyranoside (48).** To a solution of pentadecatetraol **10** (0.032 g, 0.005 mmol) in THF/MeOH/water (3:3:1) was added Pd/C(30 mg, 5%) and the solution was hydrogenated for 12 h. The reaction mixture was filtered through a short celite plug with *i*-PrOH/H_2O as eluent, concentrated, and lyophilized to give **48** as a white solid (0.012 g, 95%). ^{1}H NMR ($CDCl_3$/CD_3OD/D_2O (1:1.5:0.5), 400 MHz) δ 5.32−5.26 (m, 5H), 5.15 (br s, 2H), 5.11−5.00 (br s, 4H), 4.88 (br s, 2H), 4.80 (br s, 2H), 4.40−3.47 (m, 90H), 2.40−2.31 (m, 2H), 1.65−1.55 (m, 2H), 0.93 (t, J = 6.9 Hz, 3H). MS calcd for $C_{93}H_{158}O_{76}$ 2490.85, found 2514.0 (M + Na).

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Supporting Information Available: General experimental methods and ^{1}H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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