Organic & Biomolecular Chemistry

RSC Publishing

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2013, **11**, 3903

One-pot synthesis of branched oligosaccharides by use of galacto- and mannopyranosyl thioglycoside diols as key glycosylating agents†

Xing-Yong Liang, Qiang-Wei Liu, Hua-Chao Bin and Jin-Song Yang*

Received 28th February 2013,
Accepted 5th April 2013

DOI: 10.1039/c3ob40421h

www.rsc.org/obc

We describe in this paper the efficient four-component one-pot synthesis of three fully protected oligosaccharides **22**, **36**, and **50** with di-branched structures by employing D-galacto- and mannopyranosyl thioglycoside diols as central glycosylating agents. After global deprotection, they were converted respectively into the 3-aminopropyl linker-containing free oligosaccharide fragments **14**, **24**, and **38** structurally related to cell wall oligosaccharides from *Atractylodes lancea DC*, the marine fungus *Lineolata rhizophorae* and pathogenic *Mycobacterium tuberculosis*. The 3-aminopropyl linker at the anomeric carbon can enable conjugation of these synthetic oligomers to a suitable protein carrier.

Introduction

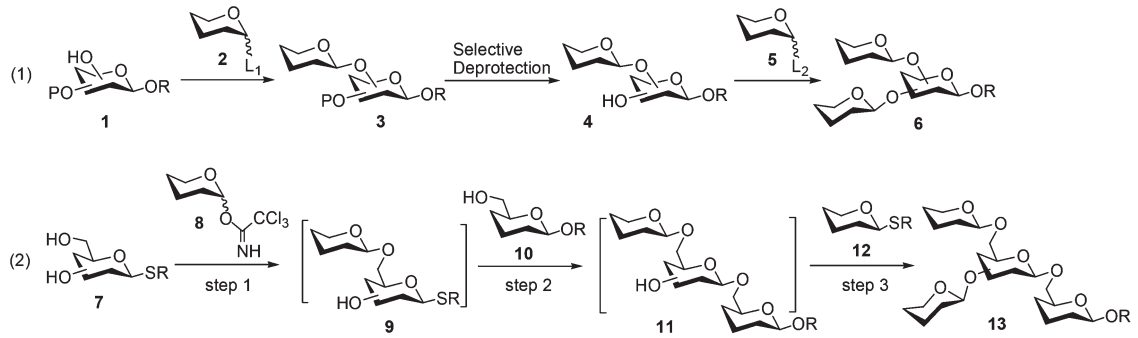
The oligosaccharide chains, typically conjugated to proteins and lipids, play a significant role in cell recognition and signal transduction in numerous biological processes.[1] Among these oligosaccharides, many have been found to have branched-chain structures. For example, branched oligomannose residues are a structural feature common to all asparagine-linked glycans (*N*-glycans) widely distributed on mammalian cell surface, and are crucial constituents of the HIV-associated envelope glycoprotein gp120.[2] While 2,6- and 3,6-branched arabinogalactopyranosyl units are common structural components of arabinogalactans (AGs) present on the cell surface of plants including some traditional herbal medicines.[3] Moreover, 3,6-di-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl structure is the characteristic of phytoalexin elicitor-active β-glucoheptasaccharide isolated from mycelial walls of *Phytophthora megasperma* f. sp. *glycinea*.[4] Due to their occurrence in biological structures and their challenging branched framework, a number of efforts have been made towards the synthesis of this type of oligosaccharides.[5] Much of the work published so far normally relied upon fragment couplings at the branching sites and required multiple protection/deprotection steps for elongation of the sugar chain, namely, glycosylation of a sugar alcohol **1** with a glycosyl donor **2**, then selective deprotection of the resulting **3** (→**4**), and a second glycosylation of **4** with another glycosyl donor **5**. These three steps together work out the branched sugar **6** (Scheme 1, eqn (1)).

The solution-phase one-pot multi-step glycosylation method wherein several glycosylation steps are sequentially completed in a single reaction vessel shows particular efficiency in the rapid preparation of oligosaccharides.[6] But most of the one-pot glycosylation methods are based on sequential activation of glycosyl donors to provide linear oligosaccharides. Few approaches involve the one-pot synthesis of branched sugars.[7] In this respect, Takahashi and co-workers have focused on the branched-type one-pot approach based on the regioselective glycosylation of a diol glycoside acceptor.[7b–d] The reactivity differences between the two hydroxy (OH) groups toward a proper glycosyl donor are exploited to control the one-pot glycosylation. The synthetic utility of this methodology was exemplified by the one-pot assembly of a range of branched galacto- and mannoside trisaccharides[7b–d] as well as glycosyl amino acid derivatives.[7f,g] Furthermore, on the synthesis of the Lewis family of oligosaccharides, Huang and Ye *et al.* have reported the construction of branched oligosaccharides by a combination of preactivation and reactivity-based chemoselective one-pot glycosylations. The efficiency of this strategy was further demonstrated in the synthesis of two branched oligosaccharides, *i.e.*, Lewis^x pentasaccharide and dimeric Lewis^x octasaccharide.[7h]

Very recently, we described the development of a novel regioselective furanosylation methodology[8] using partially protected arabino- and galactofuranosyl thioglycosides as central glycosylating building blocks. This method has proven to be very useful in one-pot preparation of a series of linear and branched-type arabino- and galactofuranoses of bacterial and plant origins. Here, the aim of our work is to apply this viable

Key Laboratory of Drug Targeting, Ministry of Education, and Department of Chemistry of Medicinal Natural Products, West China School of Pharmacy, Sichuan University, Chengdu 610041, P. R. China. E-mail: yjs@scu.edu.cn, yjscd@163.com

†Electronic supplementary information (ESI) available. See DOI: 10.1039/c3ob40421h



Scheme 1 Strategies for synthesis of branched oligosaccharides.

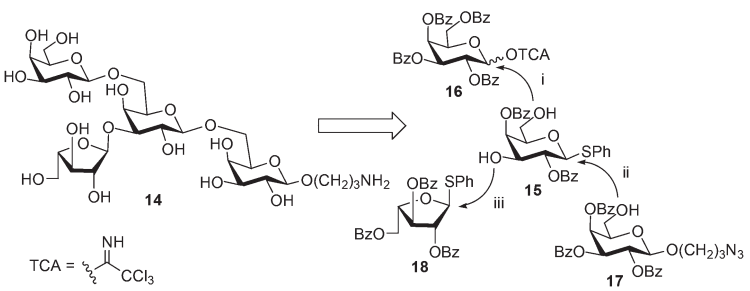
synthetic method to the one-pot synthesis of pyranose counterparts. As outlined in Scheme 1, eqn (2), the principal of the strategy is built on the following considerations. Regio- and chemoselective glycosylation of the primary alcohol on position 6 of the thioglycoside diol **7** with glycosyl trichloroacetimidate donor **8** gives disaccharide **9** that is then coupled *in situ* with the primary OH group of a glycosyl acceptor to form a trisaccharide intermediate **11**, which upon activation and coupling with the second thioglycosyl donor (the fourth component) will provide the corresponding branched tetrasaccharide **13**. Compound **7** functions as an acceptor for the first glycosylation, a donor for the second glycosylation and again an acceptor for the third glycosylation. In this way, three glycosidic linkages are sequentially constructed in a one-pot three-step reaction.

In this paper, we report the facile one-pot assembly of three branched oligosaccharides, *i.e.*, 3,6-branched D-galacto- and mannosides (**22** and **35**, respectively), and 2,6-branched D-mannoside (**49**) by application of the proposed regioselective glycosylation approach. Global deprotection followed by transformation of the azido group into an amino group created successfully 3-aminopropyl spacer-containing free sugars **14**, **24**, and **38**, whose structures are related to cell-surface polysaccharides from *Atractylodes lancea DC*, the marine fungus *Lineolata rhizophorae* and *Mycobacterium tuberculosis*, respectively. The amine spacer can ensure future conjugation of these synthetic oligomers to a microarray or suitable protein carrier for biological studies.

Results and discussion

Arabinogalactans (AGs) are a class of polysaccharides mainly consisting of a (1→4)- or (1→6)-β-D-galactopyranose backbone with α-linked L-arabinofuranose side chains at position 2 or 3.[3c] They are often found in higher plants and in some situations they occur in covalent association with protein as proteoglycans (arabinogalactan proteins, AGPs). Although the most popular AGs have been used for food additives, other AG-containing polysaccharides have been evaluated for their pharmacological activity and medicinal uses. Yamada *et al.*[9] have reported that ALR-5IIa-1-1, an arabino-3,6-galactan, which was purified from the rhizomes of medicinal herb *Atractylodes lancea* DC, possesses intestinal immune system modulating activity in mice. The analysis of the structure–activity relationships of ALR-5IIa-1-1 by glycosidase digestions revealed that the β-(1→6)-linked 3-branched tetrasaccharide portion **14** [β-D-Gal*p*-(1→6)-[α-L-Ara*f*-(1→3)]-β-D-Gal*p*-(1→6)-β-D-Gal*p*, Scheme 2] in the non-reducing terminal side of ALR-5IIa-1-1 largely contributes to expression of the activity.[10]

We chose 3,6-branched arabinogalactosyl glycoside **14** as our initial synthetic target for its relatively structural simplicity would enable us to easily verify the basic principles of the designed one-pot synthesis method. To date, chemical synthesis of some structurally different AG-type oligosaccharides has been reported.[11] In general, the published works are typical examples of oligosaccharide synthesis involving tediously selective protection and deprotection steps and



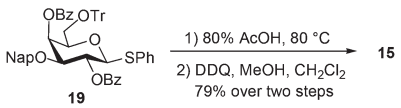
Scheme 2 Retrosynthetic analysis of tetraarabinogalactan **14**.

laborious intermediate purifications. We describe herein an alternative approach to **14** on the basis of the use of 3,6-dihydroxy D-thioglycoside **15** as a key intermediate. We envisaged that, due to the reactivity difference between the primary and the secondary OH groups, the glycosylation events of the former should be preferable over the later in regioselective glycosylation reaction. As retrosynthetically shown in Scheme 2, the reaction sequence for **14** involves three steps: (i) chemo- and regioselective glycosylation of the primary alcohol of thiogalactoside **15** in the presence of the secondary one with trichloroacetimidate **16**,[12] followed by (ii) coupling of the resulting disaccharide thioglycoside with acceptor **17**[11e] based on the difference in reactivity between the secondary OH on donor and the primary OH on acceptor, and (iii) glycosylation of the remaining secondary alcohol of **15** with donor **18**[8] to give the protected form of **14**.

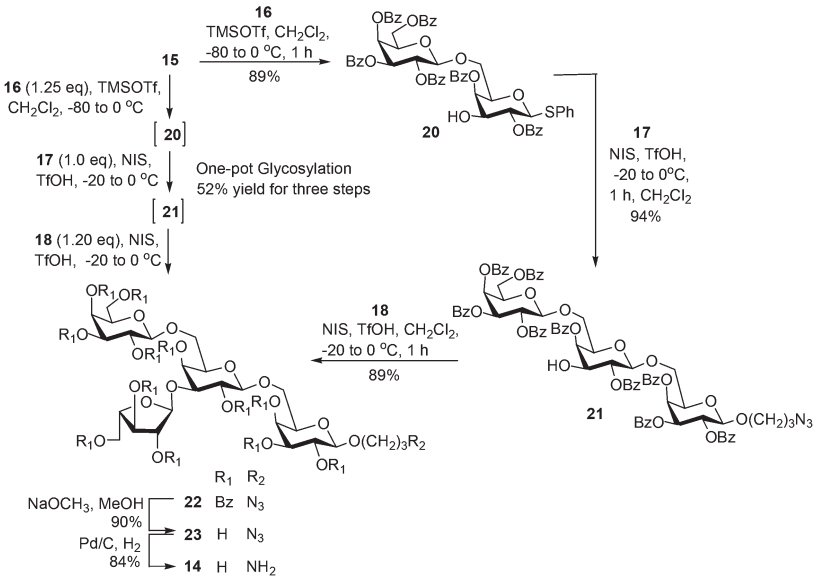
Preparation of D-galactose diol derivative **15** was performed as detailed in Scheme 3. Selective 6-*O*-detritylation of the known suitably protected β-D-galactothiopyranoside **19**[11e] under acidic hydrolysis followed by oxidative cleavage of the 2-naphthylmethyl (Nap) group in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded the desired **15** in 79% yield over two steps.

Stepwise synthesis of the protected tetrasaccharide **22** was undertaken (Scheme 4). We first examined the glycosylation of the primary alcohol of thioglycoside 3,6-diol **15** with 1.25 equivalents of trichloroacetimidate donor **16**. Trimethylsilyl triflate (TMSOTf), a versatile promoter for the chemoselective activation of glycosyl trichloroacetimidate donors over thioglycosyl acceptors[13] was chosen as the catalyst. Treatment of **15** with **16** (1.25 equiv.) in the presence of a catalytic amount of TMSOTf (0.1 equiv.) and 4 Å molecular sieves (MS) in dry dichloromethane (CH_2Cl_2) at −80 to 0 °C for 1 h provided (1→6)-linked disaccharide alcohol **20** as a single β-isomer in good 89% yield. The stereochemical outcome resulted from the neighboring group participation of the benzoyl group at the C-2 position of the donor. The regioselectivity in this process was assured by gHMBC experiment of **20**, namely, the strong correlation observed between the C-6 signal (δ_C 61.7 ppm) and the anomeric H-1′ resonance (δ_H 4.93 ppm, d, J_{H1-H2} = 8.0 Hz) confirmed a (1→6) linkage. Products arising from the C-3 glycosylation and the intermolecular aglycon transformation[14] of **15** were not isolated. Next, condensation of **20** with primary OH-containing galactoside **17** was investigated. We adopted the combination of *N*-iodosuccinimide (NIS) and catalytic triflic acid (TfOH), one of the most common reagent systems for activation of thioglycosides,[13] as coupling promoter. Thus, treatment of thioglycoside **20** (1.25 equiv.) with acceptor **17** (1.0 equiv.) under the promotion of NIS (1.20 equiv.), TfOH (0.1 equiv.), and 4 Å MS in CH_2Cl_2 at −20 to 0 °C for 1 h furnished trisaccharide alcohol **21** in excellent 94% yield. Importantly, no other coupled product was detected under these reaction conditions. Finally, through the same thioglycoside activation conditions, the desired protected **22** was obtained in 89% yield *via* glycosylation of the remaining secondary alcohol of **21** with 2,3,5-perbenzoylated L-arabinofuranose thioglycoside **18**.

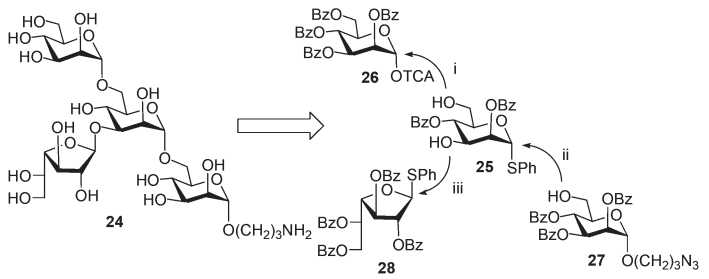
The one-pot synthesis of **22** was carried out with the same reaction sequence as in the preliminary tests in Scheme 4. In the event, imidate **16** was used to regioselectively and chemoselectively condense with diol **15** by activation with cat.



Scheme 3 Preparation of monosaccharide building block **15**.



Scheme 4 Synthesis of tetrasaccharide **14**.



Scheme 5 Retrosynthetic analysis of tetrasaccharide **24**.

TMSOTf at −80 °C in CH_2Cl_2. On gradual warming to approximately 0 °C, disaccharide **20**, as the only detected product, was visible on TLC. Next, the reaction mixture was re-cooled to −20 °C and subsequent addition of the acceptor **17** along with NIS–TfOH activating reagents to the reaction flask drove the second glycosylation reaction to proceed, giving rise to the trisaccharide intermediate **21** as the sole product after 1 h. Finally, NIS–TfOH-mediated glycosylation of the remaining secondary OH group of **21** with donor **18** at −20 to 0 °C within 1 h completed the synthesis of the perbenzoylated **22**. Purification of the crude mixture was achieved by silica-gel column chromatography to provide tetrasaccharide **22** as a colorless oil in a good 52% overall yield based on **15**. All glycosylations leading to **22** proceeded with exclusive β-anomeric stereoselectivity as a result of neighboring group participation of C-2 benzoyl groups.

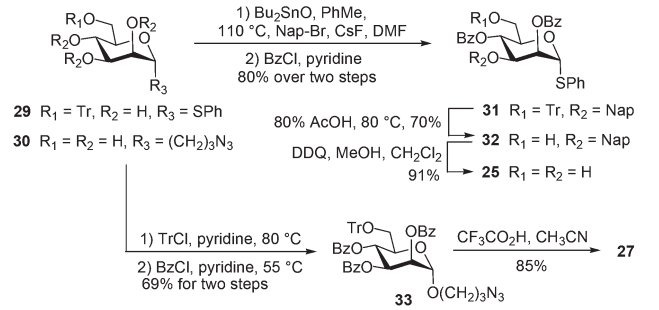
This four-component one-pot protocol illustrates the usefulness of the diol **15**, which is able to function consecutively as an acceptor, a donor, and an acceptor. Overall, when compared with the existing method, the approach greatly speeds up the preparation of the target molecule since the entire synthetic route can be accomplished without the need of protecting group manipulation and intermediate work-up, and thus offers a more practical access to the 3,6-branched arabinogalactan.

A complete deprotection of **22** was accomplished in two steps as follows. First, the benzoyl groups were cleaved by Zemplén transesterification ($NaOCH_3$, CH_3OH, rt, 2 h) to secure **23** in 90% yield. Next, the azido group of polyol **23** was reduced by Pd–C-catalyzed hydrogenolysis (H_2, Pd–C, CH_3OH, 30 °C, 24 h) to produce the target tetrasaccharide **14** in 84% yield. The structures of the compounds **23** and **14** were confirmed by comparison of their ^1H and ^{13}C NMR data with those published in literature.[11e]

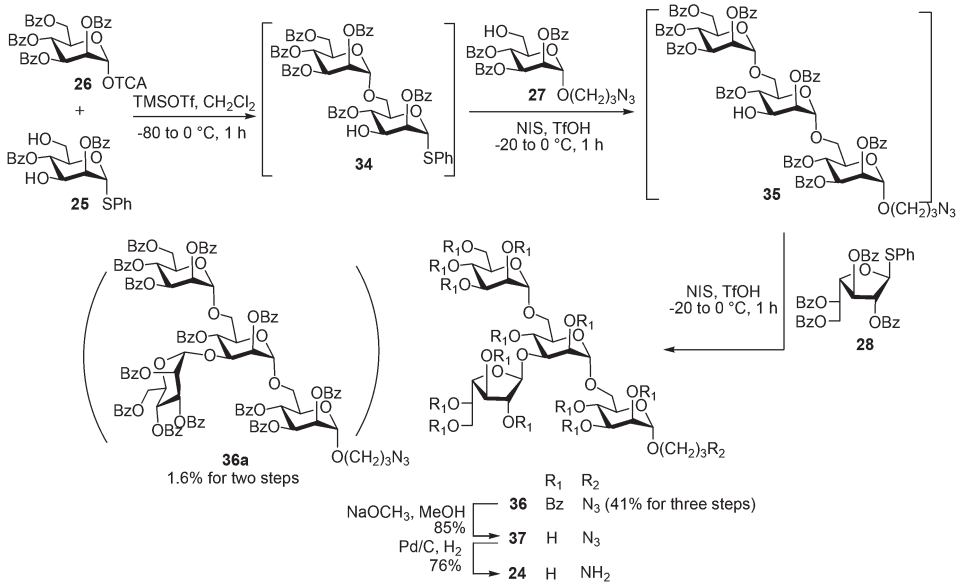
To ascertain the universality of this method, we next applied it to the synthesis of branched mannosides. The novel heterotetrasaccharide motif **24** [α-D-Man*p*-(1→6)-[β-D-Gal*f*-(1→3)]-α-D-Man*p*-(1→6)-α-D-Man*p*, Scheme 5] representing the repeating unit found in cell wall polysaccharide of the marine fungus *Lineolata rhizophorae*[15] was chosen as the target molecule. Here, we present a three-step one-pot synthetic route to **24** by taking advantage of 3,6-di-OHs D-mannose thioglycoside **25** as a core building block. As shown in Scheme 5, the sequence of its assembly also includes three consecutive glycosylation steps: (i) chemo- and regioselective coupling of the primary alcohol of **25** in the presence of the secondary one with trichloroacetimidate **26**,[16] followed by (ii) reaction of the resulting 6-*O*-glycosylated disaccharide thioglycoside with acceptor **27**, and (iii) condensation of the remaining secondary OH of **25** with donor **28**.[17]

The one-pot synthesis of tetrasaccharide **24** required the preparation of monosaccharide building blocks **25** and **27** (Scheme 6). Regioselective 3-*O*-monoalkylation of the known phenyl 1-thio-6-*O*-trityl-α-D-mannopyranoside (**29**)[18] with (2-naphthyl)-methyl (Nap) group *via* dibutylstannylene acetal formation[19] followed by 2,4-*O*-protection with benzoyl chloride (BzCl) formed **31** in 80% yield over two steps. Then, removal of the trityl (Tr) protecting group of **31** with 80% HOAc gave sugar **32** (70% yield) which was subsequently deprotected with DDQ to afford the corresponding monomer **25** (91% yield). In addition, the synthesis of compound **27** began with regioselective 6-*O*-tritylation of the known 2,3,4,6-tetraol **30**[20] followed by benzoylation to give mannose derivative **33** in 69% yield over two steps. Benzoate **32** was subsequently detritylated by acid hydrolysis to afford the required **27** in an 85% yield.

The successful implementation of the one-pot protocol with building blocks **25–28** is shown in Scheme 7. Thus, 1.25 equivalents of trichloroacetimidate **26** was regioselectively coupled to 1.0 equivalent of diol acceptor **25** activated with a catalytic amount of TMSOTf in the presence of 4 Å MS at −80 °C in CH_2Cl_2. On gradual warming to approximately 0 °C, a new spot, thiodisaccharide **34** was visible on TLC. Next, the reaction mixture was re-cooled to −20 °C and subsequent addition of the acceptor **27** (1.0 equiv.) along with NIS–TfOH to the mixture drove the second glycosylation to proceed and



Scheme 6 Preparation of monosaccharide building blocks **25** and **27**.



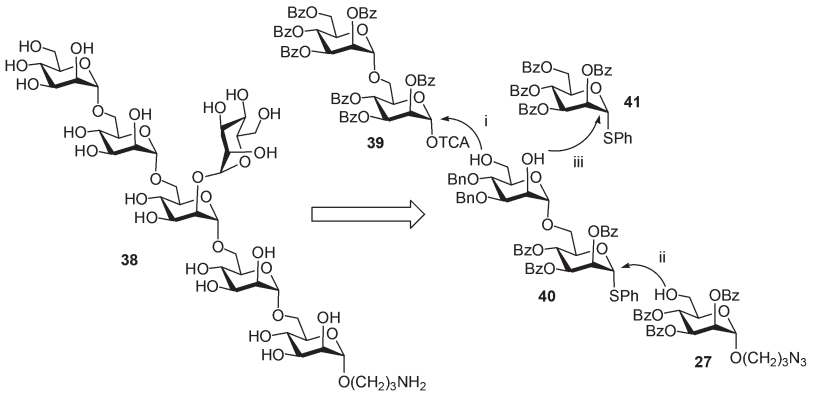
Scheme 7 Synthesis of tetragalactomannan **24**.

produced the trisaccharide **35** as a main product after 1 h. Finally, NIS–TfOH (cat.)-mediated reaction of the remaining secondary OH group of **35** with 1.2 equivalents of D-galactofuranosyl thioglycoside donor **28** at −20 to 0 °C within one hour completed the synthesis of the desired molecule. However, upon purification by silica gel column chromatography, the protected tetrasaccharide **36** along with a byproduct **36a** were acquired as colorless oils in 41% and 1.6% overall yield based on **25**, respectively. The tetrasaccharide **36a** turned out to be the result of the double glycosylation of **26** with diol **25** followed by coupling with glycosyl alcohol **27**. Further optimization of the reaction revealed that the amount of imidate **26** was critical to improving the regioselectivity of the first glycosylation step. Consequently, less amount of **26** (1.15 equiv.) was used instead and the one-pot synthesis process was repeated under the above-described glycosylation conditions, which led to the formation of **36** as the sole isolated product in an improved 45% overall yield after standard work-up and silica gel column chromatography.

The structure of **36** was elucidated through the use of ^{1}D (^{1}H, ^{13}C, 400 MHz) and ^{2}D NMR spectroscopy (gCOSY, HMQC, and gHMBC) and ESI-MS spectral analysis. The determination of the anomeric configuration of the mannopyranoses was performed according to Bock and Petersen.[21] Accordingly, the ^{1}H NMR spectrum of **36** showed the H-1 signals of the D-mannosidic linkages appeared as a singlet at δ_H 5.27, 5.18, and 4.82 ppm. In the ^{13}C NMR spectrum, three anomeric signals appeared at δ_C 98.0, 97.8, and 97.2 ppm, and the $^{1}J_{CH}$ coupling constants between anomeric carbons and hydrogens were determined to be 170.9, 171.6, and 171.6 Hz. Thus, these data confirm that all the mannosidic linkages are α. On the other hand, the H-1 and C-1 signals of the galactofuranosyl residue appeared as a singlet at δ_H 5.62 and at δ_C 102.6 ppm, respectively. Both are characteristic of β-galactofuranoside anomeric stereochemistry.[22] The structure of **36** was further confirmed by its high-resolution MS at *m/z* 2124.6001 $(M + Na)^+$, which was in accordance with the calculated exact mass of the molecule (calcd 2124.6008).

At last, deblocking of tetrasaccharide **36** was also effected in two steps involving debenzoylation by Zemplén transesterification (NaOMe, 85% yield) and the resulting polyol **37** was subjected to catalytic hydrogenation to give the deprotected saccharide **24** (76% yield).

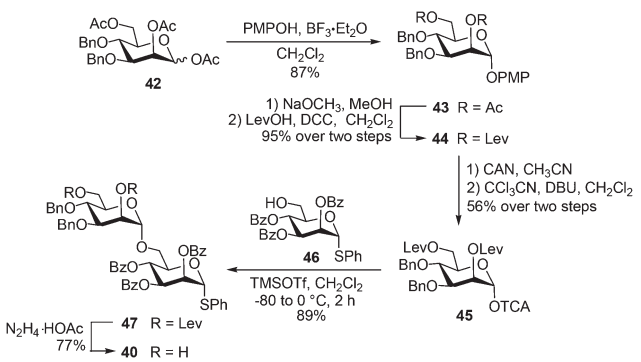
Success in the one-pot assembly of two branched tetrasaccharides led us to further explore the synthesis of sugar **38** containing more bulky architecture by use of all aspects of our regioselective glycosylation chemistry. Hexamannan motif **38**, which has α-(1→2) and α-(1→6) branch points at the central D-mannopyranose unit, is linked to the core arabinomannan (AM) domain from *Mycobacterium tuberculosis*, a human pathogen causing severe tuberculosis (TB) infection.[23] Such 2,6-branched mannan structures are very common and important component of cell surface polysaccharides of *Mycobacterium* species.[24] Synthesis of the molecule and its analogues will eventually help to find a carbohydrate antigen for vaccinations against TB.[25] In 2006, a thiol spacer-linked mannohexasaccharide fragment with the same sugar array of **38** was prepared by the Seeberger laboratory[26] to be used as an intermediate in the total synthesis of a core AM dodecasaccharide. Despite the flexible synthetic strategy they employed provided a ready access to several different TB AMs for structure–activity relationship studies, the tedious protecting group manipulation and intermediate purifications reduced its efficiency. We envisioned that the incorporation of our regioselective glycosylation method in the synthesis of **38** could simplify the complicated synthetic operation. Here, we present a new three-step one-pot procedure to **38** following the protocols similar to those used for the preparation of protected **22** and **36**. Retrosynthetic



Scheme 8 Retrosynthetic analysis of hexamannan **38**.

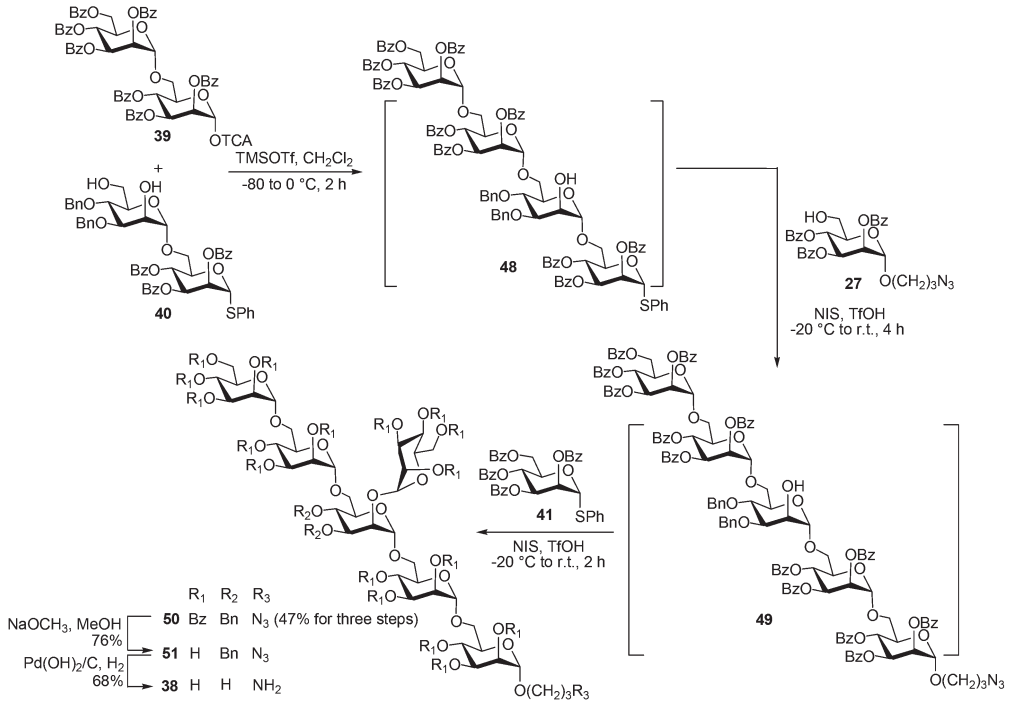
analysis indicated that the construction of **38**, as shown in Scheme 8, required the utility of four building blocks – dimannosyl trichloroacetimidate donor **39**[27] and 6-OH mannose acceptor **27** for the respective non-reducing and reducing terminal α-(1→6) mannan backbone, dimannose thioglycoside **40** with 2′,6′-hydroxy unprotected for the central 2,6-*O*-bis-glycosylated mannosyl block, and mannosyl thioglycoside donor **41**[28] for the α-(1→2) linked monosaccharide moiety.

The preparation of the core disaccharide alcohol **40** is depicted in Scheme 9. Compound **42**[29] was reacted with *p*-methylphenol (PMP-OH) under the promotion of boron trifluoride etherate ($BF_3{\cdot}Et_2O$) to yield glycoside **43** in good yield. Conventional modification of the 2- and 6-*O*-acetyl groups of **43** into Lev (levulinyl) function by methanolysis using $NaOCH_3$ in CH_3OH and subsequent esterification with levulinic acid (LevOH) furnished levulinate **44** in 95% over two steps. Oxidative cleavage of the *p*-methoxyphenyl (PMP) group at the anomeric carbon of **44** using ceric ammonium nitrate (CAN) in aqueous acetonitrile (CH_3CN) at 0 °C yielded an intermediate hemiacetal. Activation of the obtained crude hemiacetal was performed by treatment with trichloroacetonitrile (CCl_3CN) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2, thus forming imidate **45** as a single diastereomer (56% yield, two steps from **44**). TMSOTf-catalyzed chemoselective glycosylation of the obtained **45** with mannosyl thioglycoside **46**[30] resulted in a 89% yield of disaccharide thioglycoside **47**, which was easily elaborated into the corresponding **40** in 77% yield by exposure to hydrazine monoacetate ($N_2H_4{\cdot}HOAc$) at ambient temperature in CH_2Cl_2.



Scheme 9 Preparation of disaccharide building block **40**.

With all building blocks available, we carried out the one-pot glycosylation as shown in Scheme 10 to obtain **50**, a fully protected precursor of **38**. First, **39** (1.15 equiv.) was used to regioselectively glycosylate with disaccharide diol **40** (1.0 equiv.) by activation with TMSOTf (cat.) in CH_2Cl_2 at −80 °C to ambient temperature to deliver tetrasaccharide **48** as the only detected product. Next, the reaction mixture was re-cooled to −20 °C and subsequent addition of the acceptor **27** (1.0 equiv.) along with NIS–TfOH reagent system to the reaction mixture drove the second glycosylation to proceed and provided the pentasaccharide intermediate **49** as a main product after being stirred at room temperature for 4 h. Finally, reaction of the remaining axial secondary OH of **49** with donor **41** (1.2 equiv.) under NIS–TfOH activation conditions completed the synthesis of the desired **50**. After work-up and purification by column chromatography, **50** was acquired as a colorless oil in an acceptable 47% overall yield based on **40**. In contrast to the existing method, the usage of the regioselective one-pot glycosylation procedure realizes the rapid assembly of the target 2,6-*O*-disubstituted mannan structure, thereby improving the overall synthetic efficiency. The configuration of all mannosidic linkages could be assigned by the $^1J_{CH}$ coupling constants and the chemical shifts of the anomeric protons. In the ^{13}C NMR spectrum, all the anomeric carbon resonances appeared clearly in the range of δ_C 97.8 to 100.1 ppm, and the $^1J_{CH}$ values between anomeric protons and carbons are 169.9, 170.7, 170.9, 171.6, 172.1, and 172.1 Hz, proving that all D-glycosidic linkages are α. Furthermore, in the ^1H NMR spectrum, six anomeric proton resonances of the D-mannosidic linkages appeared as singlets at δ_H 5.26, 5.16, 5.13, 5.11, 5.11, and 5.07 ppm. The structure of **50** was further deduced by its high-resolution MS at *m*/*z* 3044.9050 $(M + Na)^+$, which was identical with the calculated exact mass of the molecule (calcd 3044.9046). Then, by means of the same two-step deprotection protocol, the target free homohexasaccharide **38** was synthesized *via* intermediate **51** as a white solid after size-



Scheme 10 Synthesis of hexamannan **38**.

exclusion chromatography on a Sephadex LH-20 column (Scheme 10).

Conclusions

In conclusion, presented here is the facile one-pot preparation of protected 3,6-branched D-galacto- and mannosides (**22** and **36**), and 2,6-branched D-mannoside (**50**). The synthesis features the highly regioselective glycosylation of the central 3,6- and 2,6-dihydroxy-D-galacto- and mannothioglycoside building units, by which sequential construction of three branched-type glycosidic bonds are achieved in a one-pot manner. The incorporation of the 3-aminopropyl function at the reducing end of the obtained carbohydrate molecules will allow for the attachment of these compounds to macromolecular devices for biological testing. This synthetic technology, which omits the protection/deprotection manipulations and purification of synthetic intermediate and permits the rapid assembly of both homo- and heteroglycan core structures, represents an important advance toward streamlining the synthesis of biologically relevant branched-chain oligosaccharides. Application of this new pathway to the synthesis of structurally diverse oligosaccharide libraries is currently under way.

Experimental section

All non-aqueous reactions were performed under a nitrogen atmosphere and monitored by thin layer chromatography (TLC) using Silica Gel GF_{254} plates with detection by charring with 10% (v/v) H_2SO_4 in EtOH or by UV detection. Solvents used in the reactions were distilled from appropriate drying agents prior to use. Silica gel (200–300 mesh) was used for column chromatography. Optical rotations were measured at 20 ± 1 °C for solutions in a 1.0 dm cell. Infrared absorption spectra were recorded as KBr discs using a FT-IR spectrophotometer. High resolution mass spectra (HRMS) were acquired in the ESI-TOF mode. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal reference. Chemical shifts (δ) are expressed in ppm downfield from the internal TMS absorption. Standard splitting patterns are abbreviated: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). *J* values are given in Hz.

Phenyl 2,4-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (15)

A solution of **19** (832 mg, 0.965 mmol) in 80% aq AcOH (9.7 mL) was stirred at 80 °C for 3 h and the mixture was then concentrated. The crude residue was dissolved in 4 : 1 DCM–MeOH (19.4 mL), and then DDQ (349 mg, 1.54 mmol) and H_2O (0.1 mL) were added. After being stirred for 1 d at room temperature, the mixture was evaporated. The residue was diluted with CH_2Cl_2, washed with satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (5 : 2, petroleum ether–EtOAc) to afford **15** (368 mg, 79% for two steps) as an amorphous solid. R_f 0.30 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +9.5 (*c* 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, 2H, *J* = 8.0 Hz), 7.92 (d, 2H, *J* = 8.0 Hz), 7.65 (t, 2H, *J* = 7.2 Hz), 7.44–7.52 (m, 6H), 7.29–7.40 (m, 3H), 5.57 (d, 1H, *J* = 3.6 Hz), 5.29 (t, 1H, *J* = 9.6 Hz), 4.91 (d, 1H, *J* = 9.6 Hz), 4.09–4.14 (m, 1H), 3.92 (t,

1H, J = 7.2 Hz), 3.76–3.83 (m, 1H), 3.53–3.59 (m, 1H), 2.74–2.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.6, 134.0, 133.7, 133.5, 130.7, 130.0, 129.9, 129.3, 128.8, 128.6, 128.5, 128.46, 128.4, 84.9, 77.7, 72.6, 71.4, 71.1, 60.5; IR (KBr) 3446, 2963, 2883, 1724, 1602, 1451, 1346 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{24}O_7S$ $[M + Na]^+$ 503.1140, found 503.1143.

Phenyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (20)

A mixture of trichloroacetimidate donor **16** (186 mg, 0.251 mmol), diol thioglycoside acceptor **15** (95 mg, 0.194 mmol), and freshly activated 4 Å molecular sieves (300 mg) in dry CH_2Cl_2 (4.0 mL) was cooled to −80 °C. The suspension was stirred for 15 min at the same temperature, then a solution of TMSOTf (4.6 μL, 0.025 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise. After being stirred for 1 h at the same temperature, the mixture was warmed gradually to 0 °C. The reaction was quenched with triethylamine, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated to give a residue, which was purified by column chromatography (8 : 3, petroleum ether–EtOAc) to afford **20** as a colorless syrup (185 mg, 89%). R_f 0.25 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +51.0 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, 2H, J = 8.4 Hz), 8.09 (d, 2H, J = 8.4 Hz), 7.97–8.02 (m, 4H), 7.90 (d, 2H, J = 8.4 Hz), 7.81 (d, 2H, J = 8.4 Hz), 7.24–7.66 (m, 23H), 5.97 (d, 1H, J = 3.2 Hz), 5.84 (dd, 1H, J = 8.0, 10.4 Hz), 5.66 (d, 1H, J = 2.8 Hz), 5.60 (dd, 1H, J = 3.2, 10.4 Hz), 5.25 (t, 1H, J = 9.6 Hz), 4.93 (d, 1H, J = 8.0 Hz), 4.80 (d, 1H, J = 10.0 Hz), 4.44 (dd, 1H, J = 8.4, 9.6 Hz), 4.22–4.22 (m, 2H), 3.99–4.13 (m, 3H), 4.44 (dd, 1H, J = 2.8, 10.4 Hz), 2.80 (d, 1H, J = 9.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 166.0, 165.9, 165.5, 165.47, 165.2, 133.9, 133.6, 133.5, 133.3, 133.25, 133.2, 131.0, 130.0, 129.95, 129.92, 129.74, 129.72, 129.7, 129.4, 129.2, 129.0, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 101.3, 84.9, 76.97, 72.8, 71.6, 71.3, 71.2, 70.8, 69.6, 68.1, 67.9, 61.7; IR (KBr) 3454, 2926, 2857, 1729, 1602, 1452, 1345 cm^{-1}; HRMS (ESI) calcd for $C_{60}H_{50}O_{16}S$ $[M + Na]^+$ 1081.2717, found 1081.2717.

3-Azidopropyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,4-di-*O*-benzoyl-1-thio-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (21)

A mixture of donor **20** (295 mg, 0.276 mmol), acceptor **17** (144 mg, 0.251 mmol), and freshly activated 4 Å molecular sieves (450 mg) in dry CH_2Cl_2 (10 mL) was cooled to −20 °C. The suspension was stirred for 15 min at −20 °C, then NIS (74 mg, 0.330 mmol), TfOH (2.5 μL, 0.028 mmol) were added and the resulting mixture was gradually warmed to 0 °C. The reaction mixture was stirred for 1 h at the same temperature, at the end of which time TLC indicated the complete consumption of the starting materials. The reaction was quenched with triethylamine, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated to give a residue, which was purified by column chromatography (2 : 1, petroleum ether–EtOAc) to afford protected trisaccharide **21** (361 mg, 94%) as a colorless syrup. R_f 0.18 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +81.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, 4H, J = 8.4 Hz), 7.92–8.04 (m, 10H), 7.77 (d, 4H, J = 8.4 Hz), 7.35–7.62 (m, 23H), 7.21–7.26 (m, 4 H), 5.90 (d, 1H, J = 3.2 Hz), 5.85 (d, 1H, J = 3.2 Hz), 5.65–5.71 (m, 3H), 5.50–5.57 (m, 2H), 5.32 (dd, 1H, J = 4.0, 9.6 Hz), 4.71 (d, 1H, J = 8.0 Hz), 4.66 (d, 1H, J = 8.0 Hz), 4.62 (d, 1H, J = 8.0 Hz), 4.16–4.25 (m, 2H), 4.03–4.13 (m, 3H), 3.94–3.98 (m, 2H), 3.90 (t, 1H, J = 6.0 Hz), 3.77 (dd, 1H, J = 7.2, 10.0 Hz), 3.64–3.69 (m, 1H), 3.61 (dd, 1H, J = 5.6, 10.0 Hz), 3.32–3.38 (m, 1H), 3.10 (t, 2H, J = 6.4 Hz), 2.77 (s 1H), 1.45–1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.2, 165.8, 165.4, 165.4, 165.3, 165.3, 165.3, 165.0, 133.5, 133.4, 133.3, 133.25, 133.2, 133.1, 133.0, 129.96, 129.8, 129.7, 129.6, 129.58, 129.5, 129.24, 129.2, 129.1, 128.9, 128.8, 128.61, 128.6, 128.42, 128.4, 128.2, 128.16, 101.3, 100.8, 100.7, 73.1, 72.8, 72.3, 71.5, 71.1, 70.2, 69.8, 68.6, 67.8, 66.6, 66.2, 61.4, 47.7, 28.6; IR (KBr) 3494, 2960, 2887, 2099, 1730, 1602, 1452, 1108 cm^{-1}; HRMS (ESI) calcd for $C_{84}H_{73}N_3O_{25}$ $[M + Na]^+$ 1546.4431, found 1546.4425.

3-Azidopropyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-[2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl-(1→3)]-2,4-di-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (22)

Prepared from thioglycoside **18** (102 mg, 0.184 mmol) and acceptor **21** (217 mg, 0.142 mmol) following the procedure similar to that for **20**→**21**. The resulting residue was purified by column chromatography (3 : 1, petroleum ether–EtOAc) to afford protected tetrasaccharide **22** (250 mg, 89%) as a colorless syrup. One-pot synthesis of the protected oligosaccharide **22**: A mixture of trichloroacetimidate **16** (312 mg, 0.420 mmol), 3,6-diol thioglycoside **15** (166 mg, 0.340 mmol), and freshly activated 4 Å molecular sieves (800 mg) in dry CH_2Cl_2 (7.4 mL) was stirred at room temperature for 15 min. Then the suspension was cooled to −80 °C, and a solution of TMSOTf (7.5 μL, 0.042 mmol) in CH_2Cl_2 (1 mL) was added dropwise. After being stirred for 1 h at the same temperature, the reaction was gradually warmed to room temperature. The reaction mixture was stirred for a further 1 h at the same temperature, at the end of which time TLC indicated the complete consumption of the starting materials. The resulting slurry was re-cooled to −20 °C, a solution of acceptor **17** (200 mg, 0.340 mmol) in CH_2Cl_2 (0.5 mL) was added. Then NIS (92 mg, 0.410 mmol) and TfOH (3.0 μL, 0.034 mmol) were added at −20 °C. The reaction mixture was stirred for 1 h at 0 °C, at the end of which time TLC indicated it was finished. A solution of thioglycoside donor **18** (232 mg, 0.420 mmol) in CH_2Cl_2 (0.5 mL) was added when the temperature was re-cooled to −20 °C. Then NIS (113 mg, 0.504 mmol) and TfOH (4 μL, 0.042 mmol) were added. After being stirred for 1 h at 0 °C, the reaction was quenched with triethylamine, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated to give a residue, which was purified by column chromatography (2 : 1, petroleum ether–acetone) to afford **22** (349 mg, 52% for three steps based on **17**) as an amorphous solid. R_f 0.18 (3 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +58.0 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–8.11 (m, 10H), 7.90–7.95 (m, 8H), 7.87 (d, 2H, J = 7.6 Hz), 7.77 (d, 2H, J = 7.6 Hz), 7.76 (d, 2H,

J = 7.6 Hz), 7.15–7.56 (m, 36H), 5.83–5.87 (m, 2H), 5.82 (d, 1H, J = 3.2 Hz), 5.63–5.71 (m, 3H), 5.49–5.55 (m, 3H), 5.30 (s, 1 H), 5.25 (s, 1 H), 4.97–5.03 (m, 2H), 4.72–4.76 (m, 1H), 4.74 (d, 1H, J = 8.0 Hz), 4.63 (d, 1H, J = 8.0 Hz), 4.60 (d, 1H, J = 8.0 Hz), 4.06–4.18 (m, 5H), 3.95–4.01 (m, 3 H), 3.56–3.74 (m, 3H), 3.26–3.31 (m, 1H), 3.06 (t, 1H, J = 6.8 Hz), 1.36–1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 165.8, 165.7, 165.44, 165.4, 165.3, 165.3, 165.25, 165.2, 165.0, 164.9, 164.6, 133.3, 133.15, 133.1, 133.0, 132.9, 132.8, 130.1, 130.0, 129.8, 129.7, 129.6, 129.55, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.39, 128.3, 128.2, 128.0, 107.6, 101.3, 101.2, 100.5, 82.5, 81.5, 77.5, 76.0, 73.0, 72.7, 71.6, 71.6, 71.5, 71.0, 69.84, 69.8, 69.5, 68.8, 68.1, 67.6, 66.3, 66.1, 63.2, 61.4, 47.7, 28.6; IR (KBr) 2931, 2858, 2099, 1729, 1602, 1452, 1108 cm^{-1}; HRMS (ESI) calcd for $C_{110}H_{93}N_3O_{32}$ [M + Na]$^+$ 1990.5640, found 1990.5641.

3-Azidopropyl β-D-galactopyranosyl-(1→6)-[α-L-arabinofuranosyl-(1→3)]-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside (23)[11e]

To a stirred solution of the **22** (290 mg, 0.147 mmol) in CH_3OH (14.7 mL) was added $NaOCH_3$ (29 mg) at 0 °C, and the resulting mixture was warmed gradually to room temperature. The mixture was stirred for 2 h at the same temperature at the end of which time TLC indicated it was finished. The reaction was quenched with acetic acid and the resulting mixture was concentrated to dryness. The resulting residue was purified by Sephadex LH-20 (1 : 2, CH_2Cl_2–MeOH) to afford compound **23** (95 mg, 90%) as a gray amorphous solid. $[\alpha]_D^{20}$ −22.4 (c 0.20, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.28 (s, 1H), 4.60 (d, 1H, J = 8.0 Hz), 4.52 (d, 1H, J = 8.0 Hz), 4.48 (d, 1H, J = 8.0 Hz), 4.22 (s, 1H), 4.16–4.26 (m, 2H), 3.68–4.16 (m, 20H), 3.57–3.62 (m, 2H), 3.54 (t, 2H, J = 6.8 Hz), 1.94–2.00 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 111.7, 105.8, 105.5, 105.2, 86.2, 83.7, 82.6, 78.9, 77.5, 76.2, 75.9, 75.1, 75.0, 73.1, 72.2, 71.6, 71.4, 71.0, 70.8, 69.8, 63.6, 63.4, 50.3, 30.6.

3-Aminopropyl β-D-galactopyranosyl-(1→6)-[α-L-arabinofuranosyl-(1→3)]-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside (14)[11e]

To a solution of compound **23** (85 mg, 0.118 mmol) in MeOH (11.8 mL) was added 10% Pd/C (17 mg). After being stirred for 24 h under H_2 at room temperature, the mixture was filtered through sephadex LH-20 (MeOH) to afford compound **14** (69 mg, 84%) as a gray amorphous solid. $[\alpha]_D^{20}$ −23.8 (c 0.10, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.27 (s, 1H), 4.58 (d, 1H, J = 7.6 Hz), 4.50 (d, 1H, J = 6.8 Hz), 4.48 (d, 1H, J = 6.8 Hz), 4.25 (s, 1H), 3.66–4.20 (m, 24H), 3.55–3.60 (m, 2H), 3.16 (t, 2H, J = 6.8 Hz), 2.01–2.07 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 111.6, 105.7, 105.4, 105.1, 86.1, 83.6, 82.5, 78.8, 77.5, 76.0, 75.9, 75.0, 74.8, 73.0, 72.95, 72.1, 71.7, 71.4, 70.9, 70.7, 70.3, 63.5, 63.3, 39.9, 29.5.

Phenyl 2,4-di-*O*-benzoyl-3-*O*-(2-naphthylmethyl)-6-*O*-trityl-1-thio-α-D-mannopyranoside (31)

To a solution of compound **29** (2.51 g, 4.88 mmol) in toluene (49 mL) was added dibutyltin oxide (2.1 g, 8.43 mmol). After being stirred for 3 h at 110 °C, the mixture was concentrated. The obtained residue was dissolved in dry DMF (49 mL). To the resulting solution were added CsF (1.45 g, 9.54 mmol) and 2-naphthylmethyl bromide (2.10 g, 9.59 mmol). After being stirred for 1 d at room temperature, the mixture was diluted with CH_2Cl_2, washed with water and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was directly used for the next step without further purification. To a solution of the obtained residue in pyridine (49 mL) was added benzoyl bromide (4.5 mL, 38.8 mmol). After being stirred for 2 h at 50 °C, the reaction was quenched with methanol, diluted with CH_2Cl_2, and then the mixture was washed with aq 1 M HCl, satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (10 : 1, petroleum ether–EtOAc) to afford compound **31** (3.354 g, 80%) as a pale yellow oil. R_f 0.45 (4 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +14.2 (c 1.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–8.17 (m, 3H), 7.71–7.80 (m, 3H), 7.57–7.65 (m, 5H), 7.36–7.53 (m, 14H), 7.20–7.29 (m, 4H), 7.07–7.15 (m, 8H), 5.98 (dd, 1H, J = 1.6, 3.2 Hz), 5.81 (t, 1H, J = 10.0 Hz), 5.75 (d, 1H, J = 1.6 Hz), 4.85 (d, 1H, J = 12.0 Hz), 4.67 (d, 1H, J = 12.0 Hz), 4.51–4.56 (m, 1H), 4.07 (dd, 1H, J = 3.2, 9.6 Hz), 3.29–3.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.1, 134.7, 133.6, 133.51, 133.5, 133.4, 133.0, 132.96, 132.9, 131.8, 130.2, 130.0, 129.8, 129.6, 129.5, 129.1, 128.6, 128.5, 128.4, 128.1, 127.9, 127.7, 127.6, 127.5, 126.8, 126.7, 125.9, 125.8, 86.1, 74.8, 71.7, 71.0, 70.3, 68.3, 62.7; IR (KBr) 2924, 2879, 1727, 1599, 1583, 1447, 1346 cm^{-1}; HRMS (ESI) calcd for $C_{56}H_{46}O_7S$ [M + Na]$^+$ 885.2862, found 885.2863.

Phenyl 2,4-di-*O*-benzoyl-3-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (32)

A solution of **31** (3.354 g, 3.89 mmol) in 80% aq AcOH (78 mL) was stirred at 80 °C for 3 h, then the mixture was concentrated. The crude residue was purified by column chromatography (6 : 1, petroleum ether–EtOAc) to afford **32** as a colorless syrup (1.69 g, 70.0%). R_f 0.50 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +9.7 (c 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, 2H, J = 8.0 Hz), 8.00 (d, 2H, J = 8.0 Hz), 7.79 (d, 1H, J = 8.4 Hz), 7.71 (s 1H), 7.58–7.65 (m, 4H), 7.41–7.54 (m, 9H), 7.26–7.35 (m, 4H), 6.04 (dd, 1H, J = 1.6, 3.2 Hz), 5.78 (d, 1H, J = 1.6 Hz), 5.77 (t, 1H, J = 10.0 Hz), 4.92 (d, 1H, J = 12.4 Hz), 4.75 (d, 1H, J = 12.4 Hz), 4.39 (dt, 1H, J = 3.2, 10.0 Hz), 4.26 (dd, 1H, J = 3.2, 9.6 Hz), 3.73–3.80 (m, 2H), 2.64 (s 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.6, 134.5, 133.5, 133.4, 133.0, 132.9, 132.8, 131.8, 129.93, 129.9, 129.2, 129.16, 128.9, 128.5, 128.4, 128.2, 127.9, 127.8, 127.5, 127.0, 126.0, 125.94, 125.9, 86.2, 74.1, 72.1, 71.1, 70.0, 68.3, 61.3; IR (KBr) 3526, 2926, 2877, 1724, 1602, 1452, 1345 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{32}O_7S$ [M + Na]$^+$ 643.1766, found 643.1770.

Phenyl 2,4-di-*O*-benzoyl-1-thio-α-D-mannopyranoside (25)

To a solution of **32** (1.6 g, 2.58 mmol) in 4 : 1 DCM–MeOH (52 mL) were added DDQ (932 mg, 4.12 mmol) and H_2O (0.25 mL). After being stirred for 1 d at room temperature, the

mixture was evaporated. The residue was diluted with CH_2Cl_2, washed with satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (7 : 2, petroleum ether–EtOAc) to yield **25** (1.13 g, 91%) as an amorphous solid. R_f 0.40 (2 : 1, petroleum ether–EtOAc). R_f 0.40 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +99.1 (*c* 1.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 2H), 8.06 (s, 2H), 7.41–7.62 (m, 8H), 7.25–7.34 (m, 3H), 5.71 (s, 1H), 5.80 (t, 1H, *J* = 1.6 Hz), 4.39–4.47 (m, 2H), 3.73–3.79 (m, 2H), 2.95 (s, 1H), 2.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 165.8, 133.7, 133.6, 132.8, 132.0, 129.9, 129.8, 129.2, 129.0, 128.8, 128.51, 128.5, 128.0, 85.9, 74.2, 71.6, 70.3, 69.3, 61.3; IR (KBr) 3447, 2923, 2877, 1722, 1602, 1451 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{24}O_7S$ $[M + Na]^+$ 503.1140, found 503.1140.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-6-*O*-trityl-α-D-mannopyranoside (33)

To a solution of **30** (1.01 g, 3.84 mmol) in pyridine (50 mL) were added Ph_3CCl (2.68 g, 9.60 mmol) and DMAP (46 mg, 0.38 mmol). The mixture was stirred for 1 d at 80 °C. Then benzoyl chloride (2.70 mL, 23.0 mmol) was added at 0 °C. The resulting mixture was warmed gradually to 55 °C. The reaction was stirred for 2 h at the same temperature, at the end of which time TLC indicated it was finished. The reaction was quenched with methanol, diluted with CH_2Cl_2, and then the mixture was washed with aq 1 M HCl, satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (8 : 1, petroleum ether–EtOAc) to afford compound **33** (2.17 g, 69% for two steps) as a yellow syrups. R_f 0.55 (3 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +99.1 (*c* 1.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, 2H, *J* = 7.6 Hz), 7.87 (d, 2H, *J* = 7.6 Hz), 7.77 (d, 2H, *J* = 7.6 Hz), 7.65 (t, 1H, *J* = 7.2 Hz), 7.41–7.52 (m, 10H), 7.26–7.35 (m, 4H), 7.09–7.18 (m, 9H), 6.10 (t, 1H, *J* = 10.0 Hz), 5.80 (dd, 1H, *J* = 2.8, 10.0 Hz), 5.72 (s, 1H), 5.16 (s, 1H), 4.21 (dd, 1H, *J* = 2.8, 10.0 Hz), 3.98–4.03 (m, 1H), 3.65–3.71 (m, 1H), 3.55 (t, 2H, *J* = 6.4 Hz), 3.44 (d, 1H, *J* = 10.4 Hz), 3.32 (dd, 1H, *J* = 4.8, 10.4 Hz), 2.02 (t, 2H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 165.5, 165.0, 143.6, 133.4, 133.1, 133.0, 129.9, 129.7, 129.6, 129.4, 129.2, 129.1, 128.6, 128.5, 128.2, 128.1, 127.7, 126.8, 97.6, 70.7, 70.5, 66.7, 64.7, 62.1, 48.3, 28.8; IR (KBr) 2930, 2877, 2098, 1725, 1601, 1452, 1112 cm^{-1}; HRMS (ESI) calcd for $C_{49}H_{43}N_3O_9$ $[M + Na]^+$ 840.2897, found 840.2901.

3-Azidopropyl 2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside (27)

To a solution of **33** (1.72 g, 2.11 mmol) in CH_3CN (21 mL) was added CF_3COOH (5.4 mL) dropwise at 0 °C and the resulting mixture was warmed gradually to 35 °C. The reaction was stirred for 4 h at the same temperature, at the end of which time TLC indicated it was finished. The reaction was quenched with methanol, diluted with CH_2Cl_2, and then the mixture was washed with satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (7 : 2, petroleum ether–EtOAc) to afford compound **27** (1.03 g, 85%) as colorless syrups. R_f 0.52 (3 : 2, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −103.4 (*c* 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, 2H, *J* = 8.4 Hz), 8.00 (d, 2H, *J* = 8.4 Hz), 7.84 (d, 2H, *J* = 8.4 Hz), 7.38–7.64 (m, 7H), 7.25–7.29 (m, 2H), 5.98 (dd, 1H, *J* = 3.6, 10.0 Hz), 5.87 (t, 1H, *J* = 10.0 Hz), 5.68 (q, 1H, *J* = 3.6 Hz), 5.12 (s, 1H), 4.02 (dd, 1H, *J* = 2.0, 8.8 Hz), 3.92–3.96 (m, 1H), 3.76–3.87 (m, 2H), 3.61–3.66 (m, 1H), 3.54 (t, 2H, *J* = 6.4 Hz), 2.65 (dd, 1H, *J* = 6.0, 8.4 Hz), 1.95–2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.5, 165.0, 133.7, 133.6, 133.2, 129.9, 129.6, 129.2, 129.0, 128.6, 128.5, 128.3, 127.9, 127.0, 97.8, 71.1, 70.5, 69.6, 67.1, 65.0, 61.3, 48.2, 28.7; IR (KBr) 3529, 2929, 2883, 1729, 1602, 1452, 1112 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{29}N_3O_9$ $[M + Na]^+$ 598.1801, found 598.1802.

One-pot synthesis of 3-azidopropyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl-(1→3)]-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside (36)

Using the same procedures as described for the one-pot preparation of **22**, trichloroacetimidate **26** (242 mg, 0.326 mmol), 3,6-diol thioglycoside **25** (136 mg, 0.283 mmol) were coupled first by activation with TMSOTf (6.0 μL, 0.033 mmol), then the resulting disaccharide thioglycoside **34** was glycosylated with the acceptor **27** (162 mg, 0.283 mmol) promoted by NIS (76 mg, 0.340 mmol) and TfOH (2.5 μL, 0.028 mmol) to give trisaccharide **35**. Finally, thioglycoside donor **28** (229 mg, 0.326 mmol) and NIS (49.1 mg, 0.218 mmol)–TfOH (1.6 μL, 0.018 mmol) were added to glycosylate with **35**. The resulting residue was purified by column chromatograph (2 : 1, petroleum ether–acetone) to afford **36** (268 mg, 45% for three steps based on **25**) as a colorless syrup. Data for disaccharide intermediate **34**: R_f 0.25 (3 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −12.6 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 2H, *J* = 8.0 Hz), 8.13 (d, 2H, *J* = 8.0 Hz), 8.00–8.05 (m, 6H), 7.89 (d, 2H, *J* = 8.0 Hz), 7.25–7.63 (m, 18H), 6.14 (t, 1H, *J* = 10.0 Hz), 6.04 (dd, 1H, *J* = 3.2, 10.0 Hz), 8.13 (t, 1H, *J* = 10.0 Hz), 5.79–5.83 (m, 3H), 5.14 (s, 1H), 4.87 (dd, 1H, *J* = 3.2, 10.0 Hz), 4.46 (td, 1H, *J* = 3.2, 4.8 Hz), 4.39 (dd, 1H, *J* = 2.0, 12.0 Hz), 4.23 (dd, 2H, *J* = 4.0, 10.8 Hz), 4.14 (dd, 1H, *J* = 4.0, 12.0 Hz), 3.79 (d, 1H, *J* = 10.8 Hz), 2.85 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.0, 165.9, 165.4, 165.13, 165.1, 133.8, 133.5, 133.45, 133.4, 133.1, 133.0, 131.9, 130.0, 129.9, 129.87, 129.8, 129.75, 129.7, 129.68, 129.6, 129.3, 129.2, 129.11, 129.1, 128.94, 128.9, 128.8, 128.6, 128.5, 128.4, 128.38, 128.3, 128.0, 97.7, 86.3, 74.4, 70.1, 70.1, 70.1, 70.0, 69.8, 68.8, 66.6, 66.3, 62.2; IR (KBr) 3437, 2926, 2872, 1728, 1602, 1451, 1369 cm^{-1}; HRMS (ESI) calcd for $C_{60}H_{50}O_{16}S$ $[M + Na]^+$ 1081.2717, found 1081.2721. Data for trisaccharide intermediate **35**: R_f 0.28 (2 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −30.3 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–8.18 (m, 6H), 7.97–8.04 (m, 8H), 7.85–7.90 (m, 4H), 7.26–7.58 (m, 27H), 6.23 (t, 1H, *J* = 10.0 Hz), 6.07 (t, 1H, *J* = 10.0 Hz), 5.94 (dd, 1H, *J* = 2.8, 11.6 Hz), 5.93 (dd, 1H, *J* = 2.0, 9.6 Hz), 5.72–5.77 (m, 2 H), 5.63 (d, 1H, *J* = 2.4 Hz), 5.55 (t, 1H, *J* = 2.0 Hz), 5.19 (s, 1H),

5.16 (d, 1H, J = 1.2 Hz), 4.86 (d, 1H, J = 1.2 Hz), 4.62 (td, 1H, J = 3.6, 10.0 Hz), 4.43 (d, 1H, J = 10.0 Hz), 4.39 (dd, 1H, J = 2.0, 8.0 Hz), 4.22–4.26 (m, 3H), 4.13 (dd, 1H, J = 4.0, 12.0 Hz), 3.95–4.00 (m, 2H), 3.84 (d, 1H, J = 9.6 Hz), 3.65–3.70 (m, 1H), 3.51 (t, 2H, J = 6.4 Hz), 3.45 (d, 1H, J = 10.0 Hz), 2.51 (d, 1H, J = 8.4 Hz), 1.99 (t, 2H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 165.98, 165.95, 165.56, 165.53, 165.5, 165.3, 165.2, 165.0, 133.7, 133.6, 133.57, 133.5, 133.4, 133.38, 133.2, 133.01, 133.0, 129.9, 129.87, 129.8, 129.77, 129.76, 129.7, 129.65, 129.3, 129.2, 129.17, 129.1, 129.0, 128.98, 128.73, 128.7, 128.5, 128.4, 128.3, 128.29, 97.8, 97.77, 97.2, 72.7, 70.4, 70.3, 70.1, 69.9, 69.89, 69.5, 69.2, 69.1, 68.7, 66.5, 66.4, 66.1, 65.8, 65.4, 65.0, 62.2, 48.2, 28.8; IR (KBr) 2925, 2875, 2098, 1727, 1601, 1451, 1106 cm^{-1}; HRMS (ESI) calcd for $C_{84}H_{73}N_3O_{25}$ $[M + Na]^+$ 1546.4431, found 1546.4425. Date for tetrasaccharide **36**: R_f 0.30 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −25.2 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 2H, J = 7.2 Hz), 8.19 (d, 2H, J = 7.2 Hz), 8.14 (d, 2H, J = 7.2 Hz), 8.09 (d, 2H, J = 7.2 Hz), 8.04 (d, 2H, J = 7.6 Hz), 7.99 (d, 4H, J = 8.0 Hz), 7.94 (d, 2H, J = 8.0 Hz), 7.82–7.92 (m, 8H), 7.77 (d, 2H, J = 7.2 Hz), 7.13–7.61 (m, 39H), 6.37 (t, 1H, J = 10.0 Hz), 6.14 (t, 1H, J = 10.0 Hz), 5.93–6.00 (m, 3H), 5.88 (d, 1H, J = 1.6 Hz), 5.83 (t, 1H, J = 10.0 Hz), 5.78 (d, 1H, J = 1.6 Hz), 5.64 (s, 1H), 5.62 (d, 1H, J = 2.0 Hz), 5.47 (d, 1H, J = 4.8 Hz), 5.35 (s, 1H), 5.27 (s, 1H), 5.18 (s, 1H), 4.97 (dd, 1H, J = 2.4, 12.0 Hz), 4.89 (dd, 1H, J = 3.2, 10.0 Hz), 4.82 (s, 1H), 4.68 (q, 1H, J = 4.0 Hz), 4.52–4.58 (m, 2H), 4.44–4.48 (m, 2H), 4.37 (td, 1H, J = 4.0, 10.8 Hz), 4.12–4.16 (m, 1H), 3.91–4.03 (m, 3H), 3.66–3.71 (m, 1H), 3.49 (t, 2H, J = 6.8 Hz), 3.39 (d, 1H, J = 9.2 Hz), 1.99 (t, 2H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.9, 165.61, 165.6, 165.59, 165.5, 165.3, 165.26, 165.2, 165.07, 165.06, 164.6, 133.6, 133.5, 133.4, 133.3, 133.2, 133.1, 133.05, 133.02, 133.0, 132.8, 130.1, 130.0, 129.95, 129.83, 129.8, 129.7, 129.68, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.16, 128.0, 102.6, 98.0, 97.8, 97.2, 82.4, 81.5, 77.3, 71.3, 70.6, 70.4, 70.2, 70.1, 70.0, 69.6, 69.4, 68.7, 67.9, 67.1, 66.5, 66.1, 66.0, 65.0, 64.1, 63.2, 62.5, 48.1, 28.8; IR (KBr) 2926, 2857, 2099, 1729, 1602, 1452, 1110 cm^{-1}; HRMS (ESI) calcd for $C_{118}H_{99}N_3O_{34}$ $[M + Na]^+$ 2124.6008, found 2124.6001. Date for byproduct **36a**: R_f 0.28 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −42.4 (c 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 2H, J = 7.2 Hz), 8.19 (d, 2H, J = 7.2 Hz), 8.24 (d, 2H, J = 7.6 Hz), 8.04–8.07 (m, 8H), 8.04 (t, 4H, J = 7.2 Hz), 7.95 (d, 2H, J = 7.6 Hz), 7.89 (d, 2H, J = 7.6 Hz), 7.86 (d, 2H, J = 7.6 Hz), 7.73 (d, 2H, J = 7.6 Hz), 7.69 (d, 2H, J = 7.2 Hz), 7.53–7.60 (m, 6H), 7.17–7.52 (m, 32H), 7.14 (t, 1H, J = 7.2 Hz), 6.21 (t, 1H, J = 10.0 Hz), 6.13 (td, 2H, J = 3.2, 10.0 Hz), 5.90–5.94 (m, 3H), 5.84 (s, 1H), 5.75 (s, 1H), 5.75 (dd, 1H, J = 2.8, 10.0 Hz), 5.56 (s, 1H), 5.44 (s, 1H), 5.38 (s, 1H), 5.26 (s, 1H), 5.14 (s, 1H), 4.81 (s, 1H), 4.74 (dd, 2H, J = 3.2, 9.6 Hz), 4.57 (t, 2H, J = 9.6 Hz), 4.41–4.48 (m, 3H), 4.18–4.31 (m, 4H), 3.95–4.02 (m, 2H), 3.89 (t, 1H, J = 10.4 Hz), 3.65–3.70 (m, 1H), 3.40–3.45 (m, 3H), 1.98 (t, 2H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.99, 165.9, 165.7, 165.53, 165.52, 165.5, 165.4, 165.2, 165.01, 165.0, 164.7, 164.6, 133.6, 133.4, 133.3, 133.1, 133.0, 132.97, 132.8, 130.1, 130.0, 129.9, 129.8, 129.74, 129.7, 129.65, 129.5, 129.24, 129.22, 129.14, 129.1, 129.04, 129.0, 128.9, 128.3, 128.23, 128.22, 128.2, 128.1, 99.8, 97.8, 97.4, 77.5, 71.8, 70.43, 70.4, 70.2, 70.12, 70.05, 69.5, 69.3, 68.7, 68.0, 66.5, 66.4, 66.1, 66.0, 65.0, 62.4, 62.3, 48.1, 29.5; IR (KBr) 2931, 2858, 2099, 1726, 1602, 1452, 1119 cm^{-1}; HRMS (ESI) calcd for $C_{118}H_{99}N_3O_{34}$ $[M + Na]^+$ 2124.6008, found 2124.5999.

3-Azidopropyl α-D-mannopyranosyl-(1→6)-[β-D-arabinofuranosyl-(1→3)]-α-D-mannopyranosyl-(1→6)-α-D-mannopyranoside (37)

Prepared from **36** (210 mg, 0.100 mmol) following the procedure similar to that for **22→23**. The resulting residue was purified by Sephadex LH-20 (1 : 2, CH_2Cl_2–MeOH) to afford compound **37** as an amorphous solid (64 mg, 85%). $[\alpha]_D^{20}$ +26.4 (c 0.80, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 5.22 (s, 1H), 5.00 (s, 1H), 4.98 (s, 1H), 4.93 (s, 1H), 4.26 (s, 1H), 4.22 (s, 1H), 4.11–4.15 (m, 2H), 3.65–4.05 (m, 22H), 3.60–3.75 (m, 4H), 3.55 (t, 2H, J = 6.0 Hz), 1.98 (s, 2H); ^{13}C NMR (100 MHz, D_2O) δ 102.5, 98.1, 97.5, 97.3, 81.0, 79.6, 75.2, 73.7, 70.8, 69.1, 69.0, 68.8, 68.1, 64.8, 63.9, 63.4, 62.9, 60.9, 60.0, 46.3, 26.0; HRMS (ESI) calcd for $C_{27}H_{47}N_3O_{21}$ $[M + Na]^+$ 772.2600, found 772.2593.

3-Aminopropyl α-D-mannopyranosyl-(1→6)-[β-D-arabinofuranosyl-(1→3)]-α-D-mannopyranosyl-(1→6)-α-D-mannopyranoside (24)

Prepared from **37** (42 mg, 0.056 mmol) following the procedure similar to that for **23→14**. The mixture was filtered through Sephadex LH-20 (MeOH). The filtrate was concentrated. The residue was lyophilized to give **24** (31 mg, 76%) as a white solid. $[\alpha]_D^{20}$ +21.0 (c 0.10, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.20 (s, 1H), 4.98 (s, 1H), 4.96 (s, 1H), 4.91 (s, 1H), 4.25 (s, 1H), 4.21 (s, 1H), 3.60–4.13 (m, 24H), 3.15–3.25 (m, 2H), 2.02–2.10 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 106.8, 102.4, 101.9, 101.7, 85.4, 83.9, 79.5, 78.0, 75.1, 73.3, 73.2, 73.0, 72.4, 69.1, 69.0, 68.4, 68.1, 67.8, 67.7, 67.1, 65.3, 46.1, 36.2, 28.5; HRMS (ESI) calcd for $C_{27}H_{49}NO_{21}$ $[M + H]^+$ 724.2875, found 724.2908.

p-Methoxyphenyl 2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (43)

To a solution of **42** (1.76 g, 3.62 mmol) in CH_2Cl_2 (18 mL) was added PMPOH (0.75 g, 6.05 mmol) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, then $BF_3{\cdot}Et_2O$ (0.75 mL, 5.94 mmol) was slowly added and the resulting mixture was warmed gradually to room temperature. The mixture was stirred for 2 h at the same temperature, at the end of which time TLC indicated that it was finished. The reaction was quenched with Et_3N and the mixture was concentrated. The crude product was purified by column chromatography (6 : 1, petroleum ether–EtOAc) to give **43** as a colorless syrup (1.73 g, 87%). R_f 0.25 (5 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +45.7 (c 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.38 (m, 10H), 6.97 (d, 2H, J = 9.2 Hz), 6.82 (d, 2H, J = 9.2 Hz), 5.56 (dd, 1H, J = 2.0, 3.2 Hz), 5.41 (d, 1H, J = 1.6 Hz), 4.95 (d, 1H, J = 10.8 Hz), 4.79 (d, 1H, J = 10.8 Hz), 4.63 (d, 1H, J = 10.8 Hz), 4.59 (d, 1H, J = 10.8 Hz), 4.37 (dd, 1H, J = 4.8, 12.0 Hz), 4.29 (dd, 1H, J = 2.0, 12.0 Hz), 4.22 (dd, 1H, J = 3.2, 9.6 Hz), 3.99–4.03 (m, 1H), 3.84 (d, 1H, J = 9.6 Hz), 3.76 (s, 3H), 2.19 (s, 3H), 2.02 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.2, 155.2, 149.7, 137.8, 137.6, 128.43, 128.4, 128.1, 128.0, 127.9, 117.8, 114.5, 96.8, 77.9, 75.2, 73.8, 71.9, 70.2, 68.3, 63.0, 55.6, 21.0, 20.8; IR (KBr) 2936, 2848, 1744, 1506, 1455, 1369 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{34}O_9$ $[M + Na]^+$ 573.2101, found 573.2099.

p-Methoxyphenyl 2,6-di-*O*-levulinoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (44)

To a solution of **43** (1.42 g, 2.58 mmol) in 1 : 2 DCM–MeOH (25.8 mL) was added CH_3ONa (2 8 mg, 0.520 mmol). The reaction was stirred at room temperature for 1 h, at the end of which time TLC indicated it was finished. The reaction was diluted with CH_2Cl_2, and then the mixture was washed with water and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude residue was dissolved in dry CH_2Cl_2 (25 mL), then DCC (7.0 g, 34.0 mmol) and LevOH (1.14 mL, 9.80 mmol) were added to the reaction. The resulting mixture was stirred for 4 h at room temperature, at the end of which time TLC indicated that it was finished. The reaction was diluted with CH_2Cl_2, and then the mixture was filtered through celite and concentrated *in vacuo*. The crude product was purified by column chromatography (2 : 1, petroleum ether–EtOAc) to give **44** as a colorless syrup (1.55 g, 95%). R_f 0.48 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +22.9 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.38 (m, 10H), 6.97 (d, 2H, *J* = 8.8 Hz), 6.81 (d, 2H, *J* = 9.2 Hz), 5.54 (dd, 1H, *J* = 2.0, 3.2 Hz), 5.40 (d, 1H, *J* = 1.6 Hz), 4.93 (d, 1H, *J* = 11.2 Hz), 4.77 (d, 1H, *J* = 11.2 Hz), 4.60 (dd, 1H, *J* = 2.0, 11.2 Hz), 4.37 (dd, 1H, *J* = 4.8, 11.6 Hz), 4.28 (dd, 1H, *J* = 1.6, 11.6 Hz), 4.19 (dd, 1H, *J* = 3.2, 8.8 Hz), 3.96–3.98 (m, 1H), 3.81 (t, 1H, *J* = 9.6 Hz), 3.75 (s, 3H), 2.66–2.76 (m, 6H), 2.52–2.57 (m, 2H), 2.17 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 206.2, 172.3, 172.0, 155.1, 149.6, 137.8, 137.7, 128.3, 128.1, 127.8, 117.7, 117.4, 96.6, 77.8, 75.2, 73.8, 71.7, 70.1, 68.5, 63.1, 55.5, 37.9, 37.7, 29.7, 29.7, 28.0, 27.7; IR (KBr) 2932, 2860, 1741, 1719, 1602, 1506, 1363 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{42}O_{11}$ $[M + Na]^+$ 685.2625, found 633. 685.2629.

3,4-Di-*O*-benzyl-2,6-di-*O*-levulinoyl-α-D-mannopyranosyl trichloroacetimidate (45)

To a solution of **44** (1.55 g, 2.34 mmol) in CH_3CN (37.5 mL) and H_2O (9.30 mL) was added CAN (3.20 g, 5.85 mmol). The reaction mixture was stirred at 0 °C for 40 min, at the end of which time TLC indicated it was finished. The mixture was diluted with EtOAc, and then the mixture was washed with satd aq $NaHCO_3$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude residue was dissolved in dry CH_2Cl_2 (11.8 mL), then Cl_3CCN (1.18 mL, mmol) and DBU (0.24 mL) were added. The mixture was stirred for 1 h at room temperature, at the end of which time TLC indicated it was finished. The reaction was concentrated and purified by column chromatography (5 : 3, petroleum ether–EtOAc) to give **45** (920 mg, 56% for two steps) as a colorless syrup. Compound **45** was unstable and should be used for the next step quickly. R_f 0.40 (1 : 1, petroleum ether–EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.26–7.35 (m, 10H), 6.24 (s, 1H), 5.47 (d, 1H, *J* = 2.0 Hz), 4.92 (d, 1H, *J* = 11.2 Hz), 4.73 (d, 1H, *J* = 11.2 Hz), 4.60 (t, 2H, *J* = 11.2 Hz), 4.29–4.36 (m, 2H), 3.99–4.04 (m, 2H), 3.86 (t, 1H, *J* = 10.0 Hz), 2.70–2.78 (m, 6H), 2.58 (t, 2H, *J* = 6.4 Hz), 2.16 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 205.9, 172.2, 171.6, 159.6, 137.6, 137.2, 128.3, 128.28, 128.2, 128.18, 127.83, 127.8, 94.7, 77.0, 75.3, 73.0, 72.2, 71.7, 67.2, 62.7, 37.7, 37.6, 27.8, 27.6; IR (KBr) 2932, 2858, 1739, 1715, 1599, 1118, 1092, 1030 cm^{-1}.

Phenyl 3,4-di-*O*-benzyl-2,6-di-*O*-levulinoyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-1-thio-α-D-mannopyranoside (47)

The donor **45** (810 mg, 1.15 mmol) and the acceptor **46** (560 mg, 0.959 mmol) were dried together under high vacuum for 0.5 h. The mixture was dissolved in CH_2Cl_2 (22 mL) and followed by addition of freshly activated 4 Å molecular sieves (1.50 g). The resulting slurry was cooled to −80 °C, then a solution of TMSOTf (22.0 μL, 0.118 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise. After being stirred for 2 h at the same temperature, the mixture was warmed gradually to 0 °C. The reaction was quenched with triethylamine, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated to give a residue, which was purified by column chromatography (2 : 1, petroleum ether–EtOAc) to afford **47** as a colorless syrup (960 mg, 89%). R_f 0.30 (3 : 2, petroleum ether–EtOAc). $[\alpha]_D^{20}$ +14.9 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, 2H, *J* = 8.0 Hz), 8.01 (d, 2H, *J* = 8.0 Hz), 7.86 (d, 2H, *J* = 8.0 Hz), 7.41–7.56 (m, 7H), 7.25–7.34 (m, 16H), 7.19 (t, 1H, *J* = 7.6 Hz), 6.03 (t, 1H, *J* = 10.0 Hz), 5.96 (q, 1H, *J* = 1.6 Hz), 5.84 (dd, 1H, *J* = 3.2, 10.4 Hz), 5.76 (d, 1H, *J* = 1.2 Hz), 5.37 (q, 1H, *J* = 1.6 Hz), 4.91 (d, 1H, *J* = 10.4 Hz), 4.80–4.82 (m, 2H), 4.56 (d, 1H, *J* = 11.2 Hz), 4.53 (d, 1H, *J* = 11.2 Hz), 4.35 (d, 1H, *J* = 10.4 Hz), 4.30 (dd, 1H, *J* = 4.8, 12 Hz), 4.18 (d, 1H, *J* = 10.4 Hz), 3.96–4.00 (m, 2H), 3.78–3.80 (m, 1H), 3.65–3.73 (m, 2H), 2.63–2.73 (m, 6H), 2.46–2.52 (m, 2H), 2.14 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 206.17, 172.3, 171.7, 165.4, 165.3, 165.25, 138.1, 137.8, 133.5, 133.45, 133.2, 133.1, 131.4, 129.8, 129.7, 129.6, 129.3, 129.1, 128.74, 128.7, 128.6, 128.4, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 97.7, 85.8, 78.3, 75.1, 73.6, 71.9, 71.6, 70.4, 69.7, 68.3, 67.0, 66.6, 63.1, 37.9, 37.7, 29.74, 29.7, 28.0, 27.6; IR (KBr) 2927, 2858, 1731, 1602, 1453, 1362 cm^{-1}; HRMS (ESI) calcd for $C_{63}H_{62}O_{17}S$ $[M + Na]^+$ 1145.3605, found 1145.3608.

Phenyl 3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-1-thio-α-D-mannopyranoside (40)

To a solution of **47** (960 mg, 0.855 mmol) in DCM (17 mL) and MeOH (0.3 mL) was added $AcOH{\cdot}NH_2NH_2$ (315 mg, 3.42 mmol). The reaction was stirred overnight at room temperature. Then the reaction mixture was quenched with acetone and concentrated to dryness. The resulting residue was purified by column chromatography (3 : 2, CH_2Cl_2–MeOH) to afford compound **40** (610 mg, 77%) as an amorphous solid. R_f 0.35 (1 : 1, petroleum ether–acetone). $[\alpha]_D^{20}$ +18.4 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, 2H, *J* = 8.0 Hz), 8.02 (d, 2H, *J* = 8.0 Hz), 7.89 (d, 2H, *J* = 8.0 Hz), 7.44–7.58 (m, 7H), 7.26–7.39 (m, 16H), 7.23 (t, 1H, *J* = 7.6 Hz), 4.92 (d, 1H, *J* = 1.2 Hz), 4.89 (d, 1H, *J* = 10.8 Hz), 4.78–4.83 (m, 1H), 4.66 (d,

1H, J = 10.8 Hz), 4.55 (d, 1H, J = 11.2 Hz), 4.50 (d, 1H, J = 11.2 Hz), 3.96–4.00 (m, 2H), 3.82–3.88 (m, 2H), 3.63–3.72 (m, 4H), 2.60 (s, 1H), 2.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.41, 165.4, 165.3, 138.3, 137.8, 133.6, 133.5, 133.1, 131.6, 129.81, 129.8, 129.7, 129.3, 129.2, 128.9, 128.8, 128.6, 128.48, 128.46, 128.3, 128.0, 127.9, 127.86, 127.7, 127.68, 99.2, 85.9, 80.0, 75.1, 73.7, 72.0, 71.9, 71.7, 70.5, 70.4, 68.1, 67.3, 66.4, 61.7; IR (KBr) 3430, 2925, 2858, 1730, 1600, 1451, 1362 cm^{-1}; HRMS (ESI) calcd for $C_{53}H_{50}O_{13}S$ $[M + Na]^+$ 949.2870, found 949.2850.

One-pot synthesis of 3-azidopropyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)]-3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside (50)

A mixture of trichloroacetimidate **39** (86 mg, 0.069 mmol), 2,6-diol thioglycoside **40** (56 mg, 0.061 mmol), and freshly activated 4 Å molecular sieves (300 mg) in dry CH_2Cl_2 (1.0 mL) was stirred at room temperature for 15 min. Then the suspension was cooled to −80 °C, and a solution of TMSOTf (1.3 μL, 0.007 mmol) in CH_2Cl_2 (0.3 mL) was added dropwise. After being stirred for 2 h at the same temperature, the reaction was gradually warmed to room temperature. The reaction mixture was stirred for a further 1 h at the same temperature, at the end of which time TLC indicated the complete consumption of the starting materials. The resulting slurry was re-cooled to −20 °C, a solution of acceptor **27** (35 mg, 0.061 mmol) in CH_2Cl_2 (0.2 mL) was added. Then NIS (17 mg, 0.075 mmol) and TfOH (1 μL, 0.011 mmol) were added at −20 °C. The reaction mixture was stirred for 4 h at room temperature, at the end of which time TLC indicated it was finished. A solution of thioglycoside donor **41** (50 mg, 0.073 mmol) in CH_2Cl_2 (0.2 mL) was added when the temperature was re-cooled to −20 °C. Then NIS (20 mg, 0.088 mmol) and TfOH (1.2 μL, 0.013 mmol) were added. After being stirred for 2 h at room temperature. The reaction was quenched with triethylamine, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated to give a residue, which was purified by column chromatography (2 : 1, petroleum ether–acetone) to afford **50** (86 mg, 47% for three steps based on **40**) as an amorphous solid. Data for tetrasaccharide intermediate **48**: R_f 0.30 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −7.9 (c 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, 2H, J = 8.0 Hz), 8.12 (d, 2H, J = 8.0 Hz), 8.01–8.05 (m, 8H), 7.85–7.95 (m, 8H), 7.14–7.61 (m, 45H), 6.30 (t, 1H, J = 10.0 Hz), 6.14 (t, 1H, J = 10.4 Hz), 6.12 (t, 1H, J = 10.4 Hz), 6.03 (dd, 1H, J = 3.2, 10.4 Hz), 6.01 (d, 1H, J = 3.2 Hz), 5.90 (td, 2H, J = 3.2, 8.0 Hz), 5.82–5.84 (m, 2H), 5.60 (dd, 1H, J = 1.6, 2.8 Hz), 5.13 (s, 1H), 5.05 (s, 1H), 5.05 (d, 1H, J = 2.8 Hz), 5.01 (s, 1H), 4.89 (s, 1H), 4.65–4.68 (m, 3H), 4.45 (dd, 1H, J = 2.0, 12.0 Hz), 4.31–4.37 (m, 2H), 4.22–4.28 (m, 2H), 4.14–4.16 (m, 1H), 4.08 (dd, 1H, J = 3.2, 9.2 Hz), 4.02 (dd, 1H, J = 4.0, 11.2 Hz), 3.94 (t, 1H, J = 9.2 Hz), 3.87 (dd, 1H, J = 6.4, 10.8 Hz), 3.74–3.79 (m, 1H), 3.68 (d, 1H, J = 10.0 Hz), 3.56 (d, 1H, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.5, 165.48, 165.43, 165.4, 165.39, 165.3, 165.2, 165.1, 138.6, 138.0, 133.5, 133.4, 133.2, 133.1, 133.02, 133.0, 131.9, 130.0, 129.9, 129.81, 129.79, 129.7, 129.69, 129.6, 129.58, 129.33, 129.31, 129.2, 129.17, 129.1, 129.05, 129.0, 128.95, 128.8, 128.5, 128.46, 128.4, 128.3, 128.2, 127.9, 127.8, 127.77, 127.6, 99.4, 97.9, 97.4, 86.2, 80.5, 75.0, 74.1, 72.2, 71.7, 70.9, 70.7, 70.4, 70.1, 70.0, 69.2, 68.8, 68.0, 66.7, 66.6, 66.41, 66.4, 66.3, 65.9, 62.4; IR (KBr) 3441, 2922, 2853, 1730, 1602, 1453 cm^{-1}; HRMS (ESI) calcd for $C_{114}H_{98}O_{30}S$ $[M + Na]^+$ 2001.5761, found 2001.5767. Data for pentasaccharide intermediate **49**: R_f 0.25 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −12.1 (c 1.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18–7.84 (m, 26H), 7.21–7.59 (m, 49H), 6.08–6.14 (m, 3H), 6.05 (d, 1H, J = 10.0 Hz), 6.01 (dd, 1H, J = 3.2, 10.0 Hz), 5.96 (dd, 1H, J = 3.2, 10.0 Hz), 5.93 (dd, 1H, J = 3.2, 10.0 Hz), 5.87 (dd, 1H, J = 3.2, 10.4 Hz), 5.82–5.84 (m, 1H), 5.74–5.77 (m, 2H), 5.68 (d, 1H, J = 1.6 Hz), 5.18 (s, 1H), 5.13 (d, 1H, J = 1.2 Hz), 5.04 (d, 1H, J = 12.0 Hz), 5.01 (s, 1H), 5.00 (s, 1H), 4.97 (s, 1H), 4.71 (d, 1H, J = 11.6 Hz), 4.61 (d, 1H, J = 11.6 Hz), 4.57 (d, 1H, J = 11.6 Hz), 4.42 (dd, 1H, J = 2.0, 12.0 Hz), 4.24–4.36 (m, 4H), 4.23 (dd, 1H, J = 4.0, 12.0 Hz), 4.12–4.16 (m, 1H), 4.03 (s, 1H), 4.00–3.85 (m, 6H), 3.80 (dd, 1H, J = 1.6, 10.0 Hz), 3.55–3.69 (m, 5H), 3.51 (d, 2H, J = 10.8 Hz), 1.99 (t, 2H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 165.6, 165.5, 165.46, 165.43, 165.42, 165.4, 165.33, 165.31, 165.2, 165.1, 138.6, 138.0, 133.5, 133.4, 133.3, 133.1, 133.0, 132.9, 130.0, 129.9, 129.8, 129.75, 129.7, 129.66, 129.4, 129.3, 129.25, 129.2, 129.1, 129.0, 128.95, 128.91, 128.7, 128.67, 128.5, 128.44, 128.39, 128.35, 128.3, 128.2, 128.1, 127.8, 127.7, 127.68, 127.6, 127.5, 99.5, 98.1, 98.0, 97.86, 97.85, 80.3, 74.9, 73.8, 71.4, 70.8, 70.5, 70.4, 70.3, 70.2, 70.1, 69.7, 69.1, 68.8, 67.8, 66.9, 66.63, 66.62, 66.4, 66.3, 65.5, 65.1, 62.3, 60.3, 48.2, 28.7; IR (KBr) 3436, 2924, 2853, 2099, 1729, 1602, 1452, 1106 cm^{-1}; HRMS (ESI) calcd for $C_{138}H_{121}N_3O_{39}$ $[M + Na]^+$ 2466.7475, found 2466.7483. Data for hexasaccharide **50**: R_f 0.25 (1 : 1, petroleum ether–EtOAc). $[\alpha]_D^{20}$ −12.1 (c 1.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–7.84 (m, 34H), 7.20–7.60 (m, 61H), 7.16 (t, 1H, J = 7.6 Hz), 7.11 (t, 1H, J = 7.6 Hz), 7.01–7.16 (m, 2H), 6.72–6.79 (m, 2H), 6.29 (q, 1H, J = 10.0 Hz), 6.06–16 (m, 3H), 6.05 (dd, 1H, J = 3.6, 10.0 Hz), 5.99 (dd, 1H, J = 2.8, 10.4 Hz), 5.83–5.94 (m, 4H), 5.74–5.76 (m, 2H), 5.26 (s, 1H), 5.16 (s, 1H), 5.13 (s, 1H), 5.11 (s, 2H), 5.07 (s, 1H), 4.92 (d, 1H, J = 12.0 Hz), 4.77 (t, 1H, J = 11.6 Hz),4.75 (d, 1H, J = 11.6 Hz), 4.71 (d, 1H, J = 11.6 Hz), 4.60 (d, 1H, J = 11.2 Hz), 4.38–4.45 (m, 2H), 4.30–4.32 (m, 2H), 4.22 (d, 1H, J = 10.0 Hz), 4.16 (dd, 2H, J = 3.6, 10.4 Hz), 3.93–4.08 (m, 5H), 3.67–3.86 (m, 5H), 3.48–3.63 (m, 5H), 2.04 (t 2H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.9, 165.6, 165.5, 165.45, 165.4, 165.3, 165.28, 165.24, 165.22, 165.04, 165.0, 164.8, 164.7, 138.9, 138.0, 133.5, 133.4, 133.36, 133.3, 133.27, 133.1, 132.9, 132.8, 132.14, 132.1, 130.0, 129.9, 129.86, 129.7, 129.66, 129.6, 129.34, 129.3, 129.1, 129.05, 129.0, 128.8, 128.7, 128.66, 128.4, 128.34, 128.3, 128.2, 128.1, 127.6, 127.4, 127.35, 100.1, 99.2, 98.3, 98.0, 97.84, 97.81, 80.4, 77.4, 74.9, 74.0, 72.6, 71.3, 70.7, 70.6, 70.4, 70.3, 70.2, 70.1, 69.8, 69.3, 69.0, 68.7, 66.8, 66.7, 66.4, 66.3, 66.2, 65.9, 65.3, 65.2, 62.5, 62.1, 48.2, 28.7; IR (KBr) 2928, 2853, 2099, 1730, 1603, 1453, 1105 cm^{-1}; HRMS (ESI) calcd for $C_{172}H_{147}N_3O_{48}$ $[M + Na]^+$ 3044.9046, found 3044.9058.

3-Azidopropyl α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→2)]-3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-α-D-mannopyranoside (51)

Prepared from **50** (302 mg, 0.100 mmol) following the procedure similar to that for **23→14**. The resulting residue was purified by Sephadex LH-20 (MeOH) to afford compound **51** (95 mg, 76%) as an amorphous solid. $[\alpha]_D^{20}$ +57.4 (*c* 1.25, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.35–7.45 (m, 10H), 5.18 (s, 1H), 5.02 (s, 1H), 4.95 (s, 1H), 4.92 (s, 1H), 4.86 (s, 2H), 4.78 (d, 1H, *J* = 11.6 Hz), 4.71 (d, 1H, *J* = 11.6 Hz), 4.63 (d, 1H, *J* = 10.8 Hz), 4.24 (s, 1H), 4.09 (s, 2H), 4.05 (s, 3H), 3.70–3.98 (m, 31H), 3.63 (d, 1H, *J* = 11.6 Hz), 3.52–3.55 (m, 1H), 3.32–3.33 (m, 2H), 1.84 (dd, 2H, *J* = 6.4, 12.4 Hz); ^{13}C NMR (100 MHz, D_2O) δ 134.9, 134.8, 126.3, 126.2, 126.0, 125.8, 125.7, 99.6, 97.6, 97.57, 97.05, 97.0, 95.6, 76.2, 73.1, 72.2, 71.4, 70.81, 70.8, 70.1, 69.4, 68.7, 68.5, 68.4, 68.1, 68.0, 67.8, 67.6, 67.4, 64.3, 64.2, 63.9, 63.7, 62.9, 62.7, 62.2, 58.6, 58.4, 45.5, 25.4; HRMS (ESI) calcd for $C_{53}H_{79}N_3O_{31}$ $[M + Na]^+$ 1276.4595, found 1276.4601.

3-Aminopropyl α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→2)]-α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-α-D-mannopyranoside (38)

To a solution of compound **51** (23 mg, 0.018 mmol) in MeOH (3.6 mL) were added 10% $Pd(OH)_2$/C (9 mg) and AcOH (0.36 mL). After being stirred under a hydrogen atmosphere of 30 atm at room temperature for 24 h, the mixture was neutralized and filtered. The filtrate was concentrated. The resulting residue was purified by Sephadex LH-20 (MeOH) to give **37** (15 mg, 68%) as a white solid. $[\alpha]_D^{20}$ +33.6 (*c* 0.25, H_2O); ^{1}H NMR (400 MHz, D_2O) δ 5.19 (s, 1H), 5.09 (s, 1H), 4.97 (s, 2H), 4.95 (s, 1H), 4.91 (s, 1H), 4.13 (s, 1H), 3.97–4.05 (m, 11H), 3.75–3.95 (m, 22H), 3.60–3.75 (m, 4H), 3.06–3.08 (m, 2H), 1.99 (t, 2H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, D_2O) δ 104.7, 102.4, 102.0, 101.8, 101.7, 100.5, 75.7, 75.1, 73.4, 73.3, 73.26, 73.2, 73.1, 72.9, 72.8, 72.4, 69.1, 69.0, 68.9, 68.3, 68.0, 67.9, 67.6, 63.5, 63.3, 40.0, 29.9; HRMS (ESI) calcd for $C_{39}H_{69}NO_{31}$ $[M + Na]^+$ 1070.3751, found 1070.3782.

Acknowledgements

We appreciate financial support from NSFC (21172156, 21021001), the National Basic Research Program of China (973 Program, 2010CB833202), Ministry of Education (NCET-08-0377, 20100181110082), and Sichuan Province (08ZQ026-029) of China.

Notes and references

1 (*a*) A. Varki, *Glycobiology*, 1993, **3**, 97–130; (*b*) R. A. Dwek, *Chem. Rev.*, 1996, **96**, 683–720; (*c*) S. Nishimura, in *Glycoscience: Chemistry and Chemical Biology*, ed. B. Fraser-Reid, K. Tatsuta and J. Thiem, Springer, Berlin, 2001, vol. 3, pp. 1993–2004.

2 (*a*) C. N. Scanlan, J. Offer, N. Zitzmann and R. A. Dwek, *Nature*, 2007, **446**, 1038–1045; (*b*) L.-X. Wang, *Curr. Opin. Drug Discovery Dev.*, 2006, **9**, 194–206; (*c*) D. A. Calarese, H. K. Lee, C.-Y. Huang, M. D. Best, R. D. Astronomo, R. L. Stanfield, H. Katinger, D. R. Burton, C. H. Wong and I. A. Wilson, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 13372–13377; (*d*) M. Mandal, V. Y. Dudkin, X.-D. Geng and S. J. Danishefsky, *Angew. Chem., Int. Ed.*, 2004, **43**, 2557–2561.

3 (*a*) D. Egert and N. Beuscher, *Planta Med.*, 1992, **58**, 163–172; (*b*) B. S. Paulsen, *Curr. Org. Chem.*, 2001, **5**, 939–950; (*c*) S. Alban, B. Classen, G. Brunner and W. Blaschek, *Planta Med.*, 2002, **68**, 1118–1124.

4 (*a*) J. K. Sharp, B. Valent and P. Albersheim, *J. Biol. Chem.*, 1984, **259**, 11312–11320; (*b*) J. K. Sharp, M. McNeil and P. Albersheim, *J. Biol. Chem.*, 1984, **259**, 11321–11336; (*c*) J. K. Sharp, P. Albersheim and B. Lindberg, *J. Biol. Chem.*, 1984, **259**, 11341–11345.

5 Selected examples. Stepwise approach: (*a*) N. Teumelsan and X.-F. Huang, *J. Org. Chem.*, 2007, **72**, 8976–8979; (*b*) A. Koizumi, N. Hada, A. Kaburaki, K. Yamano, F. Schweizer and T. Takeda, *Carbohydr. Res.*, 2009, **344**, 856–868. Layered approach: (*c*) X.-D. Geng, V. Y. Dudkin, M. Mandal and S. J. Danishefsky, *Angew. Chem., Int. Ed.*, 2004, **43**, 2562–2565. Regioselective strategy: (*d*) K. N. Jayaprakash, S. R. Chaudhuri, C. V. S. R. Murty and B. Fraser-Reid, *J. Org. Chem.*, 2007, **72**, 5534–5545; (*e*) K. N. Jayaprakash, J. Lu and B. Fraser-Reid, *Angew. Chem., Int. Ed.*, 2005, **44**, 5894–5898. Convergent strategy: (*f*) V. K. Rajput and B. Mukhopadhyay, *J. Org. Chem.*, 2008, **73**, 6924–6927; (*g*) R. Geurtsen, F. Côté, M. G. Hahn and G.-J. Boons, *J. Org. Chem.*, 1999, **64**, 7828–7835; (*h*) K. Pekari and R. R. Schmidt, *J. Org. Chem.*, 2003, **68**, 1295–1308; (*i*) Y. Xing and J. Ning, *Tetrahedron: Asymmetry*, 2003, **14**, 1275–1283; (*j*) J. Ning, L.-S. Heng and K.-F. Kong, *Carbohydr. Res.*, 2002, **337**, 1159–1164; (*k*) A. Düffels, L. G. Green, S. V. Ley and A. D. Miller, *Chem.–Eur. J.*, 2000, **6**, 1416–1430; (*l*) P. Grice, S. V. Ley, J. Pietruszka and H. W. M. Priepke, *Angew. Chem., Int. Ed.*, 1996, **35**, 197–200; (*m*) A. A. Karelin, Y. E. Tsvetkov, L. Paulovicová, S. Bystricky, E. Paulovicová and N. E. Nifantiev, *Carbohydr. Res.*, 2010, **345**, 1283–1290; (*n*) L. V. Backinowsky, P. I. Abronina, A. S. Shashkov, A. A. Grachev, N. K. Kochetkov, S. A. Nepogodiev and J. F. Stoddart, *Chem.–Eur. J.*, 2002, **8**, 4412–4423. Orthogonal protecting groups strategy: (*o*) T. J. Boltje, C.-X. Li and G.-J. Boons, *Org. Lett.*, 2010, **12**, 4636–4639; (*p*) C. H. Wong, X.-S. Ye and Z.-Y. Zhang, *J. Am. Chem. Soc.*, 1998, **120**, 7137–7138; (*q*) Y.-G. Du, M.-M. Zhang and F.-Z. Kong, *Org. Lett.*, 2000, **2**, 3797–3800. Solid-phase synthesis: (*r*) O. J. Plante, E. R. Palmacci and P. H. Seeberger, *Science*, 2001, **291**, 1523–1527; (*s*) K. C. Nicolaou, N. Winssinger, J. Pastor and F. DeRoose, *J. Am. Chem. Soc.*, 1997, **119**, 449–450.

6 Recent reviews on one-pot glycosylation: (*a*) B. Yu, Z.-Y. Yang and H.-Z. Cao, *Curr. Org. Chem.*, 2005, **9**, 179–194;

(*b*) Y.-H. Wang, X.-S. Ye and L.-H. Zhang, *Org. Biomol. Chem.*, 2007, **5**, 2189–2200.

7 For one-pot syntheses of branched oligopyranoses, see: (*a*) H. Yamada, T. Harada and T. Takahashi, *J. Am. Chem. Soc.*, 1994, **116**, 7919–7920; (*b*) H. Yamada, T. Kato and T. Takahashi, *Tetrahedron Lett.*, 1999, **40**, 4581–4584; (*c*) T. Takahashi, M. Adachi, A. Matsuda and T. Doi, *Tetrahedron Lett.*, 2000, **41**, 2599–2603; (*d*) H. Tanaka, N. Matoba and T. Takahashi, *Chem. Lett.*, 2005, 400–401; (*e*) H. Tanaka, M. Adachi, H. Tsukamoto, T. Ikeda, H. Yamada and T. Takahashi, *Org. Lett.*, 2002, **4**, 4213–4216; (*f*) H. Tanaka, M. Adachi and T. Takahashi, *Tetrahedron Lett.*, 2004, **45**, 1433–1436; (*g*) H. Tanaka, M. Adachi and T. Takahashi, *Chem.–Eur. J.*, 2005, **11**, 849–862; (*h*) A. Miermont, Y.-L. Zeng, Y.-Q. Jing, X.-S. Ye and X.-F. Huang, *J. Org. Chem.*, 2007, **72**, 8958–8961.

8 L.-M. Deng, X. Liu, X.-Y. Liang and J.-S. Yang, *J. Org. Chem.*, 2012, **77**, 3025–3037.

9 (*a*) K. W. Yu, H. Kiyohara, T. Matsumoto, H. C. Yang and H. Yamada, *Planta Med.*, 1998, **64**, 714–719; (*b*) K. W. Yu, H. Kiyohara, T. Matsumoto, H. C. Yang and H. Yamada, *Carbohydr. Polym.*, 2001, **46**, 147–156.

10 I. Taguchi, H. Kiyohara, T. Matsumoto and H. Yamada, *Carbohydr. Res.*, 2004, **339**, 763–770.

11 (*a*) A. Borbás, L. Jánossy and A. Lipták, *Carbohydr. Res.*, 1999, **318**, 98–109; (*b*) M. Csávás, A. Borbás, L. Jánossy, Gy. Batta and A. Lipták, *Carbohydr. Res.*, 2001, **336**, 107–115; (*c*) M. Csávás, A. Borbás, L. Szilágyi and A. Lipták, *Synlett*, 2002, 887–890; (*d*) M. Csávás, A. Borbás, L. Jánossy and A. Lipták, *Tetrahedron Lett.*, 2003, **44**, 631–635; (*e*) A. Fekete and A. Lipták, *Carbohydr. Res.*, 2009, **344**, 1434–1441; (*f*) G. Gu, F. Yang, Y.-G. Du and F.-Z. Kong, *Carbohydr. Res.*, 2001, **336**, 99–106; (*g*) J. Ning, H. Wang and Y. Yi, *Tetrahedron Lett.*, 2002, **43**, 7349–7352; (*h*) A. Li and F.-Z. Kong, *Carbohydr. Res.*, 2004, **339**, 1847–1856; (*i*) A. Li and F.-Z. Kong, *Carbohydr. Res.*, 2005, **340**, 1949–1962; (*j*) A. Li and F.-Z. Kong, *Bioorg. Med. Chem.*, 2005, **13**, 839–853.

12 (*a*) F. Bien and T. Ziegler, *Tetrahedron: Asymmetry*, 1998, **9**, 781–790; (*b*) P. Wayne and P. V. Murphy, *J. Org. Chem.*, 2010, **75**, 6747–6755.

13 K. Toshima and K. Tatsuta, *Chem. Rev.*, 1993, **93**, 1503–1531.

14 For examples of aglycon transfer reactions of thioglycosides, see: (*a*) H. Yu, B. Yu, X.-Y. Wu, Y.-Z. Hui and X.-W. Han, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1445–1453; (*b*) T. Zhu and G. J. Boons, *Carbohydr. Res.*, 2000, **329**, 709–715; (*c*) Z.-T. Li and J. C. Gildersleeve, *J. Am. Chem. Soc.*, 2006, **128**, 11612–11619.

15 M. I. Gimenez-Abián, J. A. Leal and A. Prieto, *Carbohydr. Res.*, 2007, **342**, 2599–2603.

16 M. A. Brimble, R. Kowalczyk and V. J. Muir, *Org. Biomol. Chem.*, 2008, **6**, 112–121.

17 G. C. Completo and T. L. Lowary, *J. Org. Chem.*, 2008, **73**, 4513–4525.

18 T. Ziegler and G. Lemanski, *Tetrahedron*, 2000, **56**, 563–579.

19 T. B. Grindley, *Adv. Carbohydr. Chem. Biochem.*, 1998, **53**, 17–142.

20 V. Ladmiral and D. M. Haddleton, *J. Am. Chem. Soc.*, 2006, **128**, 4823–4830.

21 (*a*) K. Bock and C. Petersen, *J. Chem. Soc., Perkin Trans. 2*, 1974, 293–297; (*b*) J. Ø. Duus, C. H. Gotfredsen and K. Bock, *Chem. Rev.*, 2000, **100**, 4589–4614.

22 (*a*) K. Mizutani, R. Kasai, M. Nakamura, O. Tanaka and H. Matsuura, *Carbohydr. Res.*, 1989, **185**, 27–38; (*b*) M. T. de Oliveira, D. L. Hughes, S. A. Nepogodiev and R. A. Field, *Carbohydr. Res.*, 2008, **343**, 211–220.

23 (*a*) P. J. Brennan, *Annu. Rev. Biochem.*, 1995, **64**, 29–63; (*b*) A. Vercellone, J. Nigou and G. Puzo, *Front. Biosci.*, 1998, **3**, 149–163; (*c*) D. Chatterjee, *Curr. Opin. Chem. Biol.*, 1997, **1**, 579–588; (*d*) T. L. Lowary, *J. Carbohydr. Chem.*, 2002, **21**, 691–722; (*e*) R. R. Gadikota, C. S. Callam, B. J. Appelmelk and T. L. Lowary, *J. Carbohydr. Chem.*, 2003, **22**, 459–480.

24 (*a*) T. L. Lowary, in *Glycoscience: Chemistry and Chemical Biology*, ed. B. Fraser-Reid, K. Tatsuta and J. Thiem, Springer, Berlin, 2001, p. 2005; (*b*) P. J. Brennan, *Tuberculosis*, 2003, **83**, 91–97.

25 (*a*) A. K. Pathak, V. Pathak, J. A. Maddry, W. J. Suling, S. S. Gurcha, G. S. Besra and R. C. Reynolds, *Bioorg. Med. Chem.*, 2001, **9**, 3129–3143; (*b*) A. K. Pathak, V. Pathak, W. J. Suling, S. S. Gurcha, C. B. Morehouse, G. S. Besra, J. A. Maddry and R. C. Reynolds, *Bioorg. Med. Chem.*, 2002, **10**, 923–928; (*c*) J. Han, R. R. Gadikota, P. R. McCarren and T. L. Lowary, *Carbohydr. Res.*, 2003, **338**, 581–588; (*d*) A. K. Pathak, V. Pathak, J. R. Riordan, W. J. Suling, S. S. Gurcha, G. S. Besra and R. C. Reynolds, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 4527–4530; (*e*) A. K. Pathak, V. Pathak, W. J. Suling, J. R. Riordan, S. S. Gurcha, G. S. Besra and R. C. Reynolds, *Bioorg. Med. Chem.*, 2009, **17**, 872–881.

26 A. Hölemann, B. L. Stocker and P. H. Seeberger, *J. Org. Chem.*, 2006, **71**, 8071–8088.

27 R. Kowalczyk and M. A. Brimble, *Synthesis*, 2009, 2210–2222.

28 O. Arjona, A. de Dios, C. Montero and J. Plumet, *Tetrahedron*, 1995, **51**, 9191–9200.

29 (*a*) R. Verduyn, J. J. A. Beliën and J. H. van Boom, *Tetrahedron Lett.*, 1991, **32**, 6637–6640; (*b*) R. N. Shah, *J. Carbohydr. Chem.*, 1987, **6**, 645–660.

30 M. K. Christensen, M. Meldal and K. Bock, *J. Chem. Soc., Perkin Trans. 1*, 1993, **13**, 1453–1460.