JOC Article

Application of the Anomeric Samarium Route for the Convergent Synthesis of the *C*-Linked Trisaccharide α-D-Man-(1→3)-[α-D-Man-(1→6)]-D-Man and the Disaccharides α-D-Man-(1→3)-D-Man and α-D-Man-(1→6)-D-Man

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Received May 17, 2002

Studies are reported on the assembly of the branched *C*-trisaccharide, α-D-Man-(1→3)-[α-D-Man-(1→6)]-D-Man, representing the core region of the asparagine-linked oligosaccharides. The key step in this synthesis uses a SmI_2-mediated coupling of two mannosylpyridyl sulfones to a C3,C6-diformyl branched monosaccharide unit, thereby assembling all three sugar units in one reaction and with complete stereocontrol at the two anomeric carbon centers. Subsequent tin hydride-based deoxygenation followed by a deprotection step produces the target *C*-trimer. In contrast to many of the other *C*-glycosylation methods, this approach employes intact carbohydrate units as *C*-glycosyl donors and acceptors, which in many instances parallels the well-studied *O*-glycosylation reactions. The synthesis of the *C*-disaccharides α-D-Man-(1→3)-D-Man and α-D-Man-(1→6)-D-Man is also described, they being necessary for the following conformational studies of all three carbohydrate analogues both in solution and bound to several mannose-binding proteins.

Introduction

Carbohydrate−protein interactions represent key cellular recognition events that are associated with many human-inflicting diseases, ranging from inflammation and viral and bacterial infections to cancer.[1] With a growing understanding of the precise function cell surface carbohydrates play in such disorders, numerous carbohydrate-related pharmaceuticals have now been developed and have entered into clinical studies.[2] An important requisite for the rational design and understanding of how such sugar-based drugs operate involves an extensive knowledge of the conformational behavior and flexibility of the natural carbohydrates in solution and especially when protein bound.[3−5] In particular, such information could lead to the design of less flexible analogues whereby their binding efficiency is substantially increased due to reduced entropic costs in the recognition process. Replacement of the exocyclic oxygen atoms in an oligosaccharide with methylene groups affords the analogous *C*-linked glycoside,[6] thereby introducing a new handle for studying the conformational preferences around the interglycosyl linkage, where mobility of such sugars is highest.[7,8] Of course, O to CH_2 substitution will undoubtedly lead to an alteration in both the size and the electronic properties around the glycosidic linkage, eliminating the exoanomeric effect. In this context, such methylene-bridged analogues have been reported to occupy additional conformations around the interglycosidic linkage that are not observed for the parent *O*-glycosides.[8,9]

To provide further insight into the usefulness of *C*-linked saccharides as tools for studying carbohydrate−protein interactions, it is imperative that an ensemble

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10.1021/jo020339z CCC: $22.00
Published on Web 08/14/2002

of such compounds be available. Owing to the synthetic challenge of assembling *C*-oligosaccharides, which in essence requires the construction of a minimum of two carbon−carbon bonds in a stereoselective fashion, most of the conformational and biological studies have been restricted to the use of *C*-disaccharides.[6,10] Less prominent, therefore, are reported cases on the synthesis of more complex methylene-linked glycosides, namely *C*-oligosaccharides. Whereas, two reports have demonstrated the straightforward but linear assembly of *C*-(1→6)-tetra- and pentaglycosides composed of repeating units of galactose,[11,12] access to branched *C*-oligosaccharides represents a more formidable synthetic challenge. An example has been illustrated by the Kishi group in their partial de novo approach to the *C*-linked mimics of the central trisaccharide unit of the type II(H) cellular antigen.[7h,l] Armstrong and co-workers have also applied the de novo route combined with combinatorial chemistry techniques to access a library of *C*-trimer analogues of the Lewis type I blood group determinant.[13]

It has previously been shown that reductive samariation of glycosylpyridyl sulfones in the presence of carbonyl substrates represents an effective means of generating 1,2-*trans*-*C*-glycosides of manno-, gluco-, galacto- and fucopyransosides, as well as the 1,2-cis-stereoisomer of

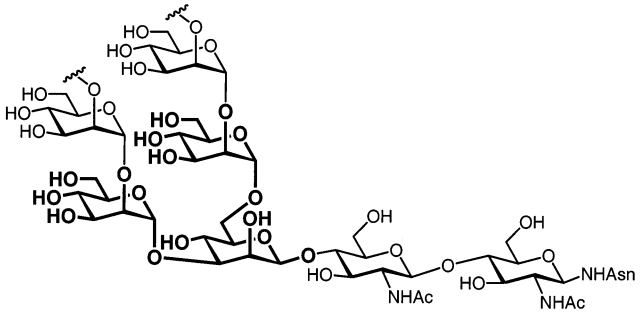

FIGURE 1. The core region of the asparagine-linked oligosaccharides.

N-acetylgalactosamine and -glucosamine.[14−17] When the same coupling reaction is performed with a *C*-formyl-branched monosaccharide as the carbonyl substrate, this route provides a rapid entry to *C*-disaccharides following a radical deoxygenation step.[14a,e,h−j,16,17] The similarities of this approach with the more conventional *O*-glycoside syntheses through the use of intact and appropriately functionalized carbohydrate units are apparent and therefore suggested the possibility of extending this methodology to the preparation of more elaborate *C*-linked sugars such as the branched oligosaccharides. To illustrate this potential, we present our first work in this area directed to the synthesis of the *C*-linked analogue of the trisaccharide α-D-Man-(1→3)-[α-D-Man-(1→6)]-D-Man, representing the core branching region of the aspargine-linked oligosaccharides (Figure 1).[18] The convergent nature of the synthetic route chosen, in addition to the total α-stereoselectivity at C1 in the carbon−carbon bond forming event, makes this approach a simple and an attractive alternative for accessing these interesting glycoside mimics. As a spin-off of this work, we also disclose the synthesis of the previously unknown *C*-

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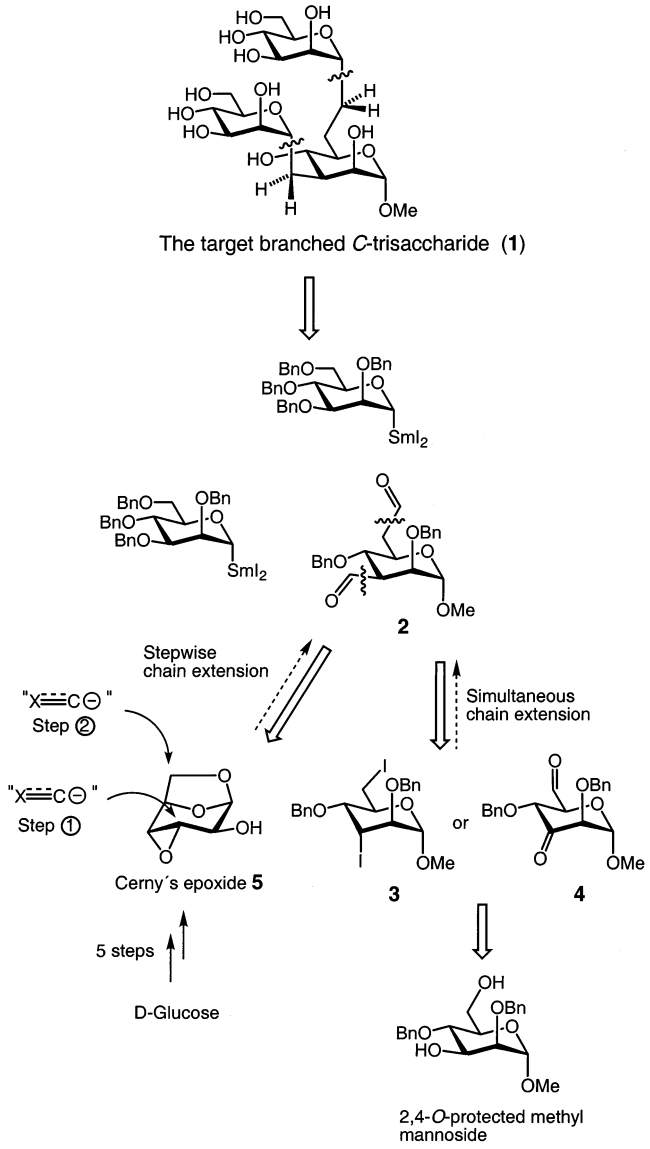
disaccharides α-D-Man-(1→3)-D-Man and α-D-Man-(1→6)-D-Man.[19−21]

Results and Discussion

The Synthetic Planning. In our earlier work, we established the configurational stability of anomeric samarium species obtained from the direct reduction of mannosylpyridyl sulfones in the presence of the single-electron reducing agent samarium diiodide.[14,15] In the company of aliphatic aldehydes or ketones, α-*C*-glycosides are the sole coupling products generated in both good yields and with minimal *β*-elimination. With this in mind, inspection of the target *C*-linked mannostrioside clearly revealed that the most convergent route for its preparation, employs as the key step a simultaneous double samarium diiodide-promoted *C*-glycosylation of a di-C3,-C6-formyl branched mannopyranoside **2**, as illustrated in Scheme 1. Subsequent deoxygenation of the diol product and deprotection would then lead to the desired *C*-branched oligosaccharide. In this planned double-coupling reaction, we anticipated the first C−C bond-forming event to take place at the sterically less hindered C6-aldehyde group of **2**. As we have previously observed the efficiency of such coupling reactions to be sensitive to the sterical environment neighboring the aldehyde functionality, it gave some concern about how effective the second *C*-glycosylation would be at the C3 position in the *C*-(1→6)-disaccharide intermediate. Nevertheless, simple molecular modeling of the desired *C*-trisaccharide quickly exposed the inability of these two branching sugars to come in close contact with one another and hence sterical blocking of the second coupling step should not come into play.

To access the *C*-branched mannose derivative **2**, we initially contemplated introducing simultaneously masked equivalents of both formyl groups through the nucleophilic substitution of the diiodide **3** with either cyanide or an alkene/alkyne anion. Nevertheless, nucleophilic substitution at one of the ring carbons in a monosaccharide is not always evident due to sterical and electronic repulsion from the flanking protected hydroxyl groups.[22] Another approach could implement a double chain extension procedure from the dicarbonyl compound **4** involving a sequence of Wittig or Wittig-type reactions, stereoselective hydroboration, and finally oxidation.[16b,23] In the event of failure in these two cases, resort could be made to a stepwise route, exploiting the well-established diaxial opening of epoxides in 1,6-anhydrosugars with sp^1 or sp^2 carbon nucleophiles for the introduction of a masked C3-formyl group. Commencement of the synthesis could then take place with the crystalline Cerny's epoxide **5**,[24] easily obtainable from starch in five steps and only two chromatographic purifications. Subsequent opening of the anydrosugar and chain extension at C6 should then proceed without incident.

SCHEME 1



The Simultaneous Functionalization Route. Initial attempts to prepare the dialdehyde **2** were focused on the simultaneous functionalization at C3 and C6 of methyl mannopyranoside, as depicted in Scheme 2, due to the brevity of the synthetic route planned. The diiodide **3** was effectively prepared by starting with the selective tin oxide-promoted allylation of the mannopyranoside, affording diallyl ethers at the C3- and C6-positions.[25]

(19) For other examples of *C*-disaccharides containing an α-mannoside unit in the nonreducing end, see refs 7g, 10e, 14i,j, and Vauzeilles, B.; Cravo, D.; Mallet, J.-M.; Sinaÿ, P. *Synlett* **1993**, 522.

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(21) A recent report has disclosed both the synthesis of a single *C*-glycoside analogue of the branched mannotrioside at the Man-α-(1→6)-Man linkage and its affinity to concanavalin A: Tsuruta, O.; Yuasa, H.; Kurono, S.; Hashimoto, H. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 807.

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(23) For a few applications of this sequence en route to *C*-formyl-branched monosaccharides, see: (a) Preuss, R.; Schmidt, R. R. *Tetrahedron Lett.* **1989**, *30*, 3409. (b) Daley, S. M.; Armstrong, R. W. *Tetrahedron Lett.* **1989**, *30*, 5713. (c) Preuss, R.; Schmidt, R. R. *J. Carbohydr. Chem.* **1991**, *10*, 887. (d) Preuss, R.; Jung, K.-H.; Schmidt, R. R. *Liebiegs Ann. Chem.* **1992**, 377. (e) Schmidt, R. R.; Beyerbach, A. *Liebiegs Ann. Chem.* **1992**, 983. (f) Eisele, T.; Ishida, H.; Hummel, G.; Schmidt, R. R. *Liebiegs Ann. Chem.* **1995**, 2113. (g) Alzeer, J.; Cai, C.; Vasella, A. *Helv. Chim. Acta* **1995**, *78*, 242.

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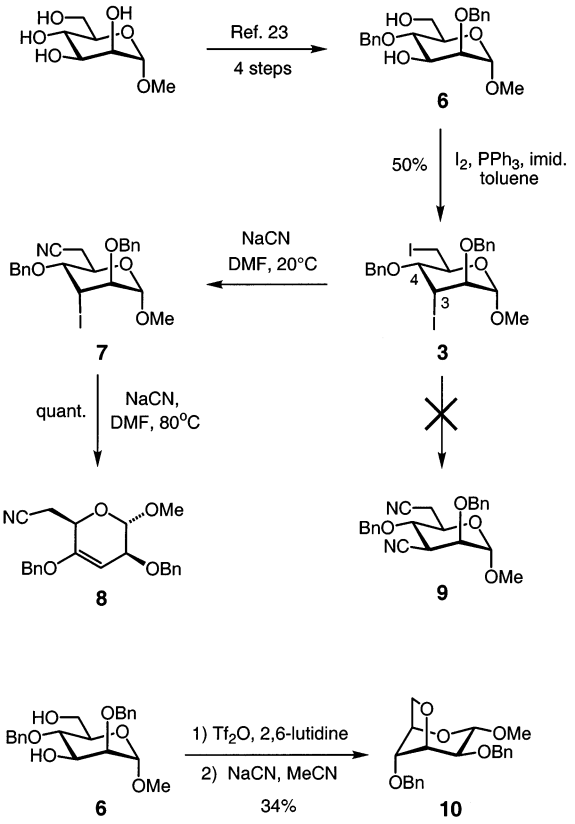
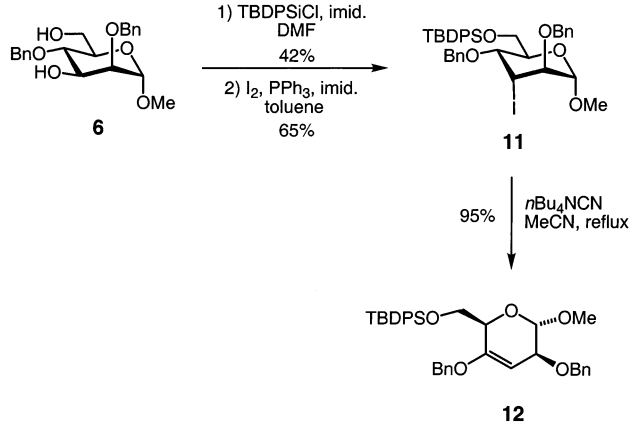
SCHEME 2



Subsequent standard benzylation and then deallylation with Pd/C and acetic acid produced the diol **6**. Transformation to the corresponding diiodide proceeded without incident under the conditions described by Garegg.[26] That indeed the axially oriented iodide at C3 was attained was confirmed by the small vicinal coupling constant between H3 and H4 ($J_{H3,H4} = 3.3$ Hz). Subjection of the diiodide **3** to excess sodium cyanide in DMF for 5 h at 20 °C led to a quantitative conversion of the C6-substituted product **7**. However, upon heating to 80 °C for an extra 2 h with additional NaCN, only the elimination product **8** could be isolated with no trace of the dinitrile **9**.

The diiodide **3** is obviously set up to undergo trans-β-elimination with the C4-proton, but Vasella and co-workers have previously reported the successful substitution of a C4-triflate in galactose with cyanide, even-though a *trans*-diaxial relationship exists between the C3- or C5-protons with the C4-triflate group.[23g] Attempts to prepare the corresponding ditriflate from **6** followed by its immediate subjection to sodium cyanide without isolation led only to the 3,6-anhydro sugar **10** as the main product and no traces of a product possessing a C3-nitrile group (Scheme 2).[27] To prevent the adverse elimination reaction, a stepwise approach to the dinitrile was conceived whereby installation of a bulky protecting group on the C6−OH would potentially prevent the C4 deprotonation. Hence, the iodide **11** was prepared with a

SCHEME 3



TBDPSi-ether at C6, but again its treatment with either NaCN or nBu$_4$NCN afforded predominantly the alkene **12** (Scheme 3).

An alternative route to the dialdehyde **2** calls for an initial chain extension at C3 and C6 with a Wittig or Tebbe reagent followed by a selective hydroboration/oxidation sequence.[16b,23] In this synthesis, the stereoselectivity of the hydroboration step at the C3 exocyclic C−C double bond is of little concern. It was assumed that eventually an axially oriented *C*-formyl group would freely equilibrate to the more stable equatorial position under mild basic conditions, as has previously been demonstrated in the preparation of other *C*-formyl branched sugars, including at the C3-position of a galactoside.[16b,23c−f,h] To test the feasibility of this approach, the model compound **13** was first subjected to oxidation with DMSO/Ac$_2$O, followed by Tebbe's reagent, affording the exocyclic alkene **14** in 70% yield for the two steps (Figure 4).

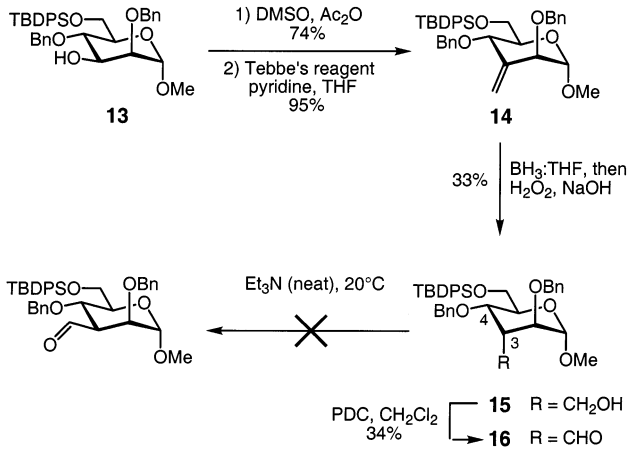
Attempted hydroboration with 9-BBN proved unrewarding and only led to unreacted starting material. On the other hand, with BH$_3$·THF a single primary alcohol **15** could be isolated after oxidation, though in a yield of 33%. The ^{1}H NMR spectrum of this branched monosaccharide revealed an axially oriented hydroxymethyl group due to the lack of a large $J_{H3,H4}$ vicinal coupling constant observed for the C3 proton at 2.28 ppm. To invert this undesired stereochemistry, the alcohol was first oxidized with PDC. The isomerization of an axially oriented formyl group on a sugar ring to the thermodynamically more stable equatorial position in neat triethylamine has been successfully carried out by Schmidt and co-workers.[23d,f] However, quite unexpectedly, upon treatment of the aldehyde **16** under the same conditions, the C3-aldehyde group remained reluctant to epimerize, as observed by the preservation of the small $J_{H3,H4}$ coupling constant of 4.4 Hz compared to approximately 9 Hz for the correct product (see below). Subsequently, these routes were abandoned and recourse was taken to the stepwise difunctionalization of the Cerny epoxide **5**.

The Stepwise Approach and Synthesis of Methyl α-1,3- and α-1,6-*C*-Mannobioside. Initial efforts were made to introduce a nitrile group at C3 of **5** owing to the previous successful epoxide openings in anhydrosugars with diethyl aluminum cyanide reported by Fraser-Reid

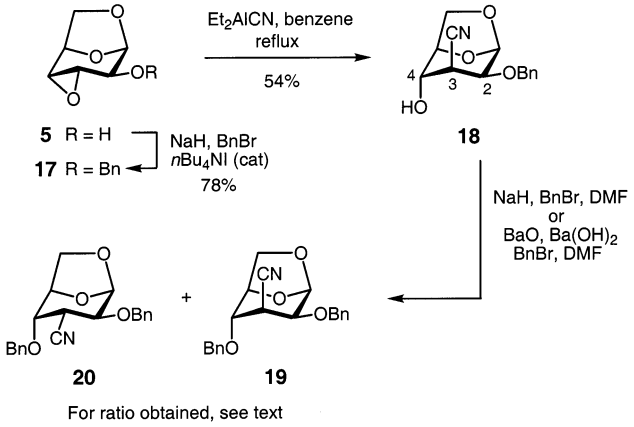
(26) Garegg, P.; Johansson, R.; Ortega, C.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 681.

(27) As in the previous cases (ref 23c−f,h), it was anticipated that the corresponding *C*-branched aldehyde obtained after DIBALH reduction of the axially oriented C3-cyanide would epimerize upon base treatment to the more favored equatorial position.

SCHEME 4



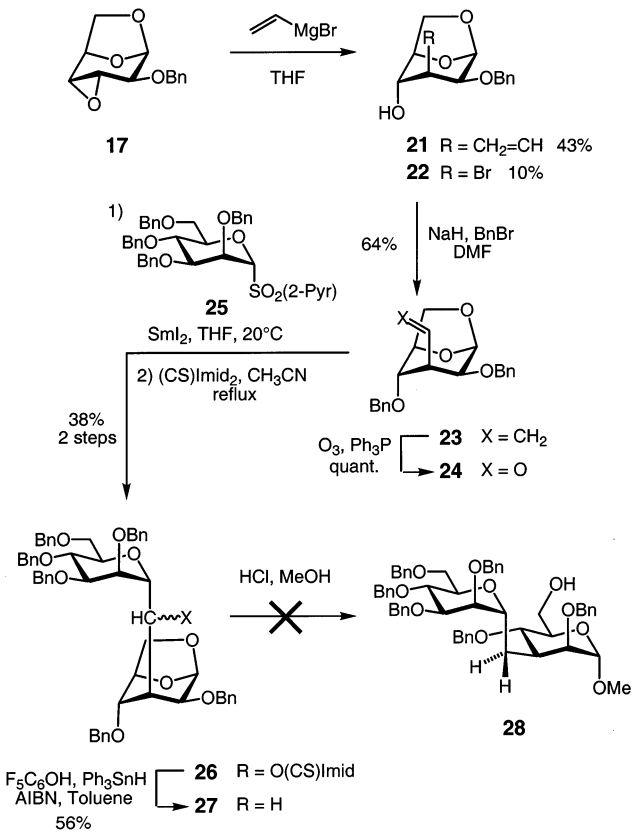
SCHEME 5



and co-workers.[28] Hence, protection of the C2-alcohol of **5** and then treatment of the epoxide **17** with Et_2AlCN in refluxing benzene afforded the expected C3-cyano compound **18** in 54% yield, as deduced by the $J_{H2,H3}$ (6.2 Hz) and $J_{H3,H4}$ (0.6 Hz) vicinal coupling constants (Scheme 5). Problems, however, arose in the second OH-protecting step, as attempted benzylation under standard conditions (NaH/BnBr/DMF) led to exclusive epimerization at C3. A large trans-diaxial vicinal coupling constant of 10.2 Hz was now observed between the H2 and H3 protons in compound **20**. This obstacle could only be partially remedied with the milder benzylating conditions employing $Ba(OH)_2$ as base, furnishing a 2:1 mixture of **20** and **19**. The unwanted epimerization at C3 could easily be solved by installation of a vinyl group instead as the formyl group equivalent (Scheme 6).[29] Therefore, the epoxide **17** was first treated with vinylmagnesium bromide, generating an inseparable 4:1 mixture of the alkene **21** and bromide **22**. Subsequent benzylation proceeded uneventfully in this case, leading to the crystalline **23** (mp 52−53 °C) after chromatographic separation.[30]

To access the *C*-glycoside analogue of α-D-Man-(1→3)-D-Man, necessary for the following conformation studies, attempts were undertaken to carry **23** through to this *C*-dimer. First, ozonolysis led to a quantitative yield of

SCHEME 6

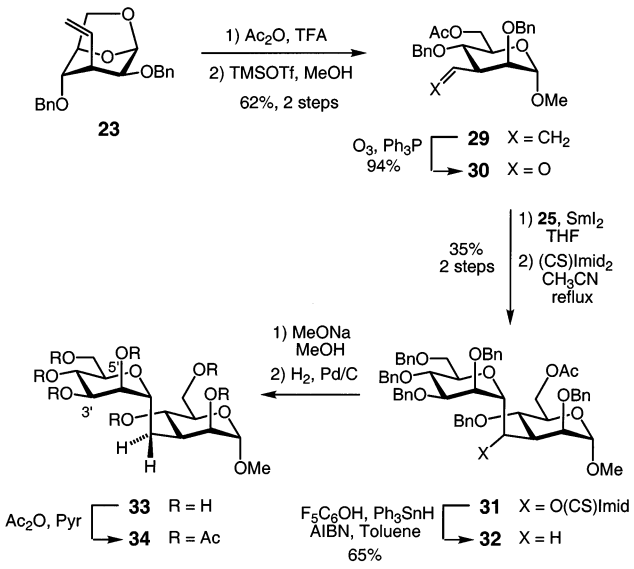


the corresponding aldehyde **24**. Coupling to the mannosylpyridyl sulfone **25** was then achieved by quickly adding a 0.1 M etheral solution of SmI_2 (3.5 equiv) to a mixture of **25** (1.5 equiv) with the aldehyde at 20 °C. Without chromatographic separation, the crude reaction mixture was immediately subjected to a large surplus of thiocarbonyldiimidazole in refluxing acetonitrile. This afforded a 38% yield of two diastereomeric thiocarbonylimidazole *C*-dimer derivatives (**26**) in a ratio of 2.7:1. The low yield in this coupling step was attributed to the steric congestion surrounding the aldehyde functionality. Deoxygenation was next achieved by employing our earlier described conditions for the removal of sterically hindered secondary alcohols.[14i] Treatment of **26** with pentafluorophenol, triphenyltin hydride, and AIBN in hot toluene led to a 56% yield of the *C*-disaccharide **27**. Unfortunately, all attempts to convert this compound directly to the fully protected α-1,3-*C*-mannobioside **28** via acid-catalyzed methanolysis failed, affording complex mixtures.

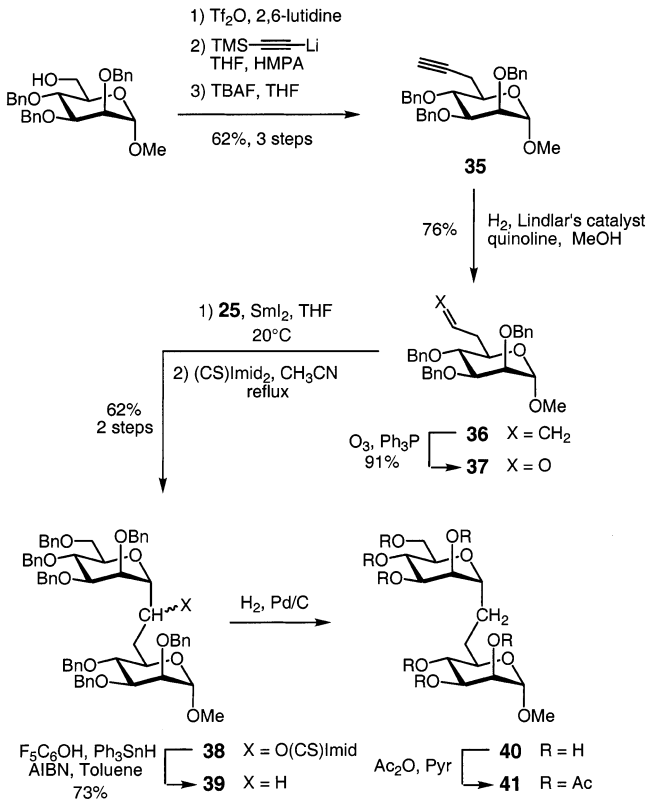
To circumvent this problem, we decided to promote the acid-catalyzed ring opening of the 1,6-anhydro bond in **23** prior to the *C*-glycosylation step, as shown in Scheme 7. In this manner, acetolysis of **23** in a 10:1 mixture of acetic anhydride and trifluoroacetic acid produced the corresponding C1,C6-diacetate, which underwent a clean TMSOTf-catalyzed glycosylation with methanol, affording exclusively the methyl α-mannoside **29** in a 62% overall yield. Following the preceding synthesis, ozonolysis to the aldehyde **30** and subsequent SmI_2-promoted coupling with **25** secured the *C*-glycoside **31** in this case as a sole diastereomer at C7 after functionalization with

(28) Mubarak, A.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 4265.
(29) Inghardt, T.; Frejd, T. *Synthesis* **1990**, 285.
(30) Upon benzylation of the mixture of compounds **21** and **22**, the bromide **22** cylized back to the epoxide **17**.

SCHEME 7



SCHEME 8



thiocarbonyldiimidazole. As previously observed with aldehyde **24**, this two-step sequence resulted only in a modest coupling yield of the *C*-dimer **31**, which was of some concern considering the extrapolation of this work to the *C*-trisaccharide **1**. At any rate, radical deoxygenation proceeded as expected, providing the fully protected *C*-disaccharide **32** in a 65% yield,[31] which was deprotected to the required *C*-dimer **33** via a classical two-step protocol. To facilitate its characterization, the methyl α-1,3-*C*-mannobioside was peracetylated with acetic anhydride to the heptaacetate **34**.

It is interesting to note the deviation of the nonreducing sugar in **34** from the normal $^4C_1$ chair conformation, as deduced by the medium size vicinal coupling constants observed between the H3′ and H4′ protons, as well as that of the H4′ and H5′ protons in the ^{1}H NMR spectrum ($J_{H3',H4'}$ = 5.4 Hz and $J_{H4',H5'}$ = 4.8 Hz). This result contradicts those observed for the analogous *C*-disaccharide of α-D-Man-(1→2)-D-Man, where both peracetylated monosaccharide units possess the normal ring conformation[14i] and hence clearly reflects the greater sterical congestion between the two sugars in the (1→3)-dimer. Consequently, it is not surprising that a lower yield for **31** was observed in the SmI_2-mediated coupling step compared to the same C−C bond-forming reaction in the synthesis of the methyl α-1,2-*C*-mannobioside. More importantly for the subsequent studies, upon deacetylation of **34** to the α-1,3-*C*-mannobioside, the $^4C_1$ chair conformation was restored for the nonreducing sugar, as illustrated by the large trans-diaxial coupling constants between the same ring protons ($J_{H3',H4'}$ = 9.4 Hz and $J_{H4',H5'}$ = 9.0 Hz).

To push forward to the *C*-trisaccharide, it was necessary at this stage to develop a second chain extension sequence at C6 of the central carbohydrate unit. Although exchange of the liberated C6-hydroxyl group in **29** to iodide followed by substitution with cyanide represented a plausible route, it was more convenient to introduce a second vinyl group in this position such that a single ozonolysis step would produce the dialdehyde **2**. In this context, we were attracted by a recent account disclosed by Clark et al. in their adaptation of the chiron approach toward the synthesis of the brevitoxin and ciguatoxin class of polycyclic ethers.[32] A three-step sequence was developed in this work for the introduction of a similar C6-functionalization on a sugar moiety.

To test this route, efforts were first made with the readily available methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside, thereby providing access to methyl α-1,6-*C*-mannobioside (Scheme 8). Treatment with triflic anhydride and lutidine afforded the unstable C6-triflate, which was immediately alkynylated with the lithium anion of trimethylsilylacetylene. Upon desilylation, the alkyne **35** was thus obtained. Partial hydrogenolysis then gave the alkene **36** and finally the aldehyde **37** upon ozonolysis.[33] Samarium diiodide-promoted coupling with the pyridyl sulfone **25** and thionocarbamate formation proceeded as expected, affording the *C*-dimer **38** as a 5:1 mixture of C7-diastereomers in a 62% yield. At last, radical deoxygenation to **39** and deprotection provided the *C*-glycoside analogue **40** of methyl α-1,6-mannobioside, characterized as its heptaacetate **41**. Not unexpectedly, both the sugar rings occupy in this case the normal chair conformation.

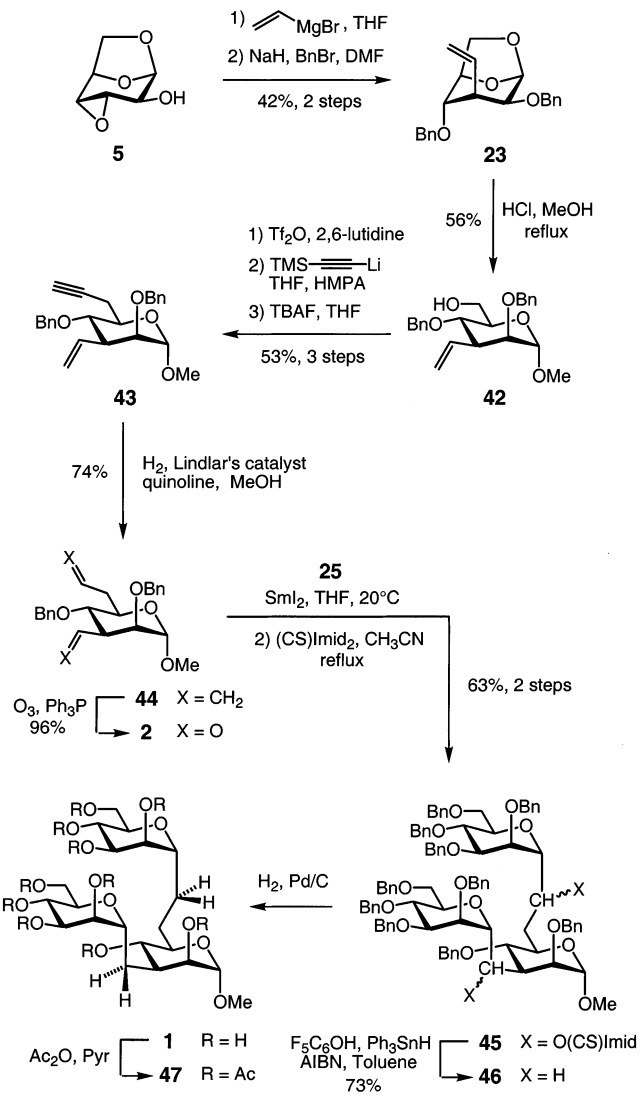
Synthesis of the Dialdehyde 2 and Completion of the *C*-Trisaccharide. With the successful preparation of the two *C*-disaccharides **33** and **44**, we felt confident this synthetic approach could now be carried through to the requisite *C*-trisaccharide. This necessitated the ad-

(31) The protected *C*-dimer **32** could undoubtedly have been carried through to the target *C*-trisaccharide via an initial deactylation and chain-extending sequence followed by a second *C*-glycosylation step.

(32) Clark, J. S.; Hamelin, O. *Angew. Chem., Int. Ed.* **2000**, *39*, 372.

(33) Interestingly, when phenylacetylene was introduced, selective hydrogenation of the triple bond failed.

SCHEME 9



ditional functionalization at C6 of the C3-branched mannoside **29**. As illustrated in Scheme 9, several modifications of the original synthesis of this compound were however made in order to shorten the number of the synthetic steps. First, introduction of the C3-vinyl group was accomplished directly on the epoxide **5** with excess of the vinyl Grignard reagent, whereafter benzylation of the diol afforded **23**. Second, simple methanolysis with concentrated HCl in refluxing methanol for 4 days opened the anhydro-ring, leading directly to the desired alcohol **42** as a single methyl glycoside in a 56% yield. This reaction proved to be somewhat delicate and required careful monitoring by TLC analysis. In most cases, the methanolysis never reached completion and the starting anhydrosugar was recovered. Nevertheless, with these adjustments the number of steps required for the synthesis of **42** was reduced by three. Elongation of the alcohol **42** with acetylene via a similar sequence as described above for the synthesis of the *C*-(1→6)-dimer then led to the dialkene **44** after selective hydrogenation with Lindlar's catalyst. Finally, ozonolysis afforded the dialdehyde **2** in near quantitative yield, as revealed by the two signals at 9.80 and 9.63 ppm in the ^{1}H NMR spectrum.

The crucial dicoupling step was next performed by the quick addition of 10 equiv of the lanthanide reducing agent directly to a mixture of the dialdehyde **2** with a large excess of the pyridyl sulfone **25** (4.7 equiv). The crude product mixture from this instantaneous coupling reaction was thereafter refluxed in acetonitrile with excess thiocarbonyldiimidazole for 12 h, followed by the slow concentration of the reaction mixture under heating. This latter procedure is important for the successful functionalization of the exocyclic hydroxyl groups. To our delight, with this two-step protocol a respectable 63% yield was obtained for the functionalized *C*-trisaccharide **45** as a mixture of inseparable diastereomers. Conversely, when these dithionocarbamates were treated under the above-described deoxgenation conditions, a single *C*-trisaccharide product **46** was furnished in a 53% yield. Further, Pd-catalyzed hydrogenation afforded the target *C*-oligosaccharide **1**, which was characterized as its undecaacetate **47**, as previously described. The assignment of the α-configuration for both of the nonreducing sugars was made on the related pattern observed for the proton coupling constants between the *C*-trisaccharide and the two *C*-disaccharides.

Conclusions

The *C*-trisaccharide analogue of the core region α-D-Man-(1→3)-[α-D-Man-(1→6)]-D-Man of the asparagine-linked oligosaccharides has been synthesized using a SmI_2-promoted reductive *C*-glycosylation as the key reaction for assembling the three monosaccharide units in a single step. The two *C*-disaccharides α-D-Man-(1→3)-D-Man and α-D-Man-(1→6)-D-Man were also prepared as model studies to the *C*-trisaccharide, in addition to allowing for a comparative study of the conformational behavior of all three *C*-oligosaccharides.

In comparison to many of the previous *C*-oligosaccharides syntheses, this highly convergent approach to the branched trisaccharide is distinguished by its use of glycosyl donors and acceptors, where the key coupling step occurs at the anomeric center, in a manner similar to the well-studied *O*-glycosylation reactions. Our approach should also be applicable to the synthesis of mixed branched oligosaccharides via a stepwise introduction of the two sugar units on to the central glycoside. This has already been partially demonstrated in the synthetic approach to the *C*-disaccharide α-D-Man-(1→3)-D-Man with the protected *C*-dimer **32**. A second glycosyl donor other than mannose could have been installed at the C6-position after liberation of C6-hyroxyl group and chain extension.

Experimental Procedure

General Methods. The SmI_2-promoted coupling reactions were performed under Ar, while all other reactions were carried out under N_2. THF was dried and freshly distilled over sodium/benzophenone. Dichloromethane was freshly distilled over P_2O_5. HMPA was dried over CaH_2 and distilled. DMF was distilled and stored over molecular sieves (4 Å). The following compounds were prepared according to literature procedures: samarium diiodide,[34] the mannosylpyridyl sulfone **25**,[14e] and the Cerny epoxide **5**.[24]

(34) Namy, J. L.; Girard, P.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

1,6:3,4-Dianhydro-2-*O*-benzyl-*β*-D-altropyranose (17). NaH (112 mg, 60% in mineral oil, 2.8 mmol) was added to a cooled (0 °C) solution of the Cerny epoxide **5** (225 mg, 1.56 mmol) in THF (11 mL). After vigorous stirring for 20 min, benzyl bromide (285 μL, 2.4 mmol) and Bu_4NI (157 mg, 0.48 mmol) were added and the mixture was stirred for another 2 h. The reaction was quenched with MeOH and diluted with diethyl ether. The organic phase was washed four times with water and once with brine, dried ($MgSO_4$), and evaporated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:2) yielded 280 mg (78%) of **17** as a colorless syrup: IR (film) 2957, 2894, 1639, 1497, 1454 cm^{-1}; ^1H NMR (200 MHz) δ = 7.40−7.28 (5H, m), 5.31 (1H, dd, J = 2.4, 2.6 Hz), 4.74 (1 H, d, J = 12.1 Hz), 4.68 (1H, m), 4.65 (1H, d, J = 12.1 Hz), 4.11 (1H, d, J = 7.4 Hz), 3.85 (1H, dd, J = 4.4, 7.4 Hz), 3.63 (1H, dd, J = 0.8, 2.8 Hz), 3.11 (1H, bd, J = 3.9 Hz), 3.05 (1H, dd, J = 3.9, 2.4 Hz); ^{13}C NMR (50 MHz) δ = 137.2, 128.6, 128.1, 98.2, 72.1, 72.0, 70.0, 67.4, 50.2, 49.7; MS (EI) *m*/*z* 234 (M), 143 (M − CH_2Ph).

1,6-Anhydro-2,4-di-*O*-benzyl-3-deoxy-3-*C*-vinyl-*β*-D-mannopyranose (23) from Epoxide 17. Vinylmagnesium bromide (6 mL, 1.0 M in THF, 6.0 mmol) was added dropwise to a solution of the epoxide **17** (281 mg, 1.2 mmol) in THF (3.5 mL). The mixture was refluxed for 8 h, whereafter it was cooled to 20 °C and then added to an aqueous saturated solution of NH_4Cl (30 mL). The mixture was extracted with EtOAc, and the organic phase was washed with water, dried ($MgSO_4$), and concentrated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:1) yielded 168 mg of a mixture of an approximately 4:1 mixture of the alkene **21** and the bromide **22**. For **21**: ^1H NMR (200 MHz) δ = 7.32 (5H, m), 6.32 (1H, ddd, J = 8.4, 10.4, 17.3 Hz), 5.47 (1H, bs), 5.28 (1H, ddd, J = 1.4, 1.4, 17.3 Hz), 5.25 (1H, ddd, J = 1.4, 1.4, 10.4 Hz), 4.62 (1H, d, J = 12.0 Hz), 4.46 (1H, m), 4.41 (1H, d, J = 12.0 Hz), 3.98 (1H, d, J = 7.8 Hz), 3.79 (1H, dd, J = 5.4, 7.8 Hz), 3.78 (1H, bs), 3.70 (1H, dd, J = 1.5, 6.9 Hz), 3.09 (1H, ddddd, J = 1.4, 1.4, 1.4, 6.9, 8.4 Hz), 2.43 (1H, bs); ^{13}C NMR (50 MHz) δ = 137.1, 136.4, 136.2, 127.9, 127.8, 127.4, 127.2, 117.9, 100.7, 76.5, 74.0, 73.0, 69.6, 64.6, 47.0; MS (EI) *m*/*z* 262 (M), 171 (M − CH_2Ph).

To a cooled (0 °C) solution of the above mixture (154 mg) in DMF (4.6 mL) was carefully added NaH (36 mg, 60% in mineral oil, 0.90 mmol). After stirring for 20 min, benzyl bromide (105 μL, 0.88 mmol) was added and the mixture was stirred for another 2 h. The reaction mixture was then quenched by the addition of MeOH and diluted with diethyl ether. The organic phase was washed four times with water and once with brine, dried ($MgSO_4$), and evaporated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:8) yielded the benzyl ether **23** (104 mg, 64%) as colorless crystals: mp 52−53 °C; IR (film) 2922, 1636, 1454 cm^{-1}; ^1H NMR (200 MHz) δ = 7.40−7.25 (10H, m), 6.33 (1H, ddd, J = 8.4, 10.4, 18.8 Hz), 5.48 (1H, bs), 5.17 (1H, ddd, J = 1.4, 1.4, 10.4 Hz), 5.10 (1H, ddd, J = 1.4; 1.4; 18.8 Hz), 4.70 (1H, d, J = 12.4 Hz), 4.60 (1H, d, J = 12.4 Hz), 4.60 (1H, d, J = 11.8 Hz), 4.51 (1H, m), 4.41 (1H, d, J = 11.8 Hz), 3.84 (1H, dd, J = 0.8, 7.8 Hz), 3.76 (1H, dd, J = 1.6, 7.0 Hz), 3.72 (1H, dd, J = 5.4, 7.8 Hz), 3.44 (1H, bs), 3.13 (1H, ddddd, J = 1.4, 1.4, 1.4, 7.0, 8.4 Hz); ^{13}C NMR (50 MHz) δ = 137.7, 137.7, 137.3, 128.4−127.6, 117.8, 101.0, 80.8, 75.0, 74.1, 71.0, 70.3, 65.2, 44.2; HR-MS (ES) calcd for $C_{22}H_{24}O_4Na$ (M + Na) 375.1572, found 375.1570.

1,6-Anhydro-2,4-di-*O*-benzyl-3-deoxy-3-*C*-vinyl-*β*-D-mannopyranose (23) from Epoxide 5. Vinylmagnesium bromide (8.33 mL, 1.0 M in THF, 8.33 mmol) was added dropwise to the Cerny epoxide **5** (400 mg, 2.78 mmol) dissolved in dry THF (4.5 mL) at 20 °C. The reaction mixture was heated to 60 °C for 4 h, after which TLC analysis indicated complete consumption of the starting material (MeOH:CH_2Cl_2, 1:20). The reaction mixture was quenched with a few drops of saturated aqueous NH_4Cl. The mixture was filtered through a 1−2 cm pad of silica gel with methanol as the eluent in order to remove the formed salts. The filtrate was evaporated to dryness in vacuo, and the resulting oil was redissolved in CH_2Cl_2, dried ($MgSO_4$), and again evaporated to dryness. The resulting yellow oil was used in the next step without further purification. A pure sample was nevertheless obtained by column chromatography (MeOH:CH_2Cl_2, 1:20) to give 1,6-anhydro-3-deoxy-3-*C*-vinyl-*β*-D-mannopyranose as a colorless syrup: ^1H NMR (200 MHz) δ = 5.97 (1H, ddd, J = 10.0, 11.2, 16.2 Hz), 5.43 (1H, d, J = 2.0 Hz), 5.33 (1H, m), 5.31 (1H, m), 4.48 (1H, d, J = 5.0 Hz), 3.94 (1H, d, J = 8.2 Hz), 3.87 (1H, dd, J = 2.0, 8.6 Hz), 3.80 (1H, dd, J = 5.0, 8.2 Hz), 3.74 (1H, m), 2.90 (1H, dd, J = 8.6, 10.0 Hz), 2.61 (1H, bs), 2.07 (1H, bs); ^{13}C NMR (50 MHz) δ = 134.9, 122.1, 102.4, 77.2, 73.2, 67.5, 65.8, 50.7.

Benzylation of the crude 1,6-anhydro-3-deoxy-3-*C*-vinyl-*β*-D-mannopyranose (approximately 2.77 mmol) was performed according to the procedure outlined for the previous synthesis of **23**, with the following quantities: DMF (15 mL), NaH (60% in mineral oil, 416 mg, 10.4 mmol), benzyl bromide (0.99 mL, 8.33 mmol). Column chromatography (EtOAc:pentane, 1:10) yielded 412 mg of **23** (42% for two steps).

Methyl 6-*O*-Acetyl-2,4-di-*O*-benzyl-3-deoxy-3-*C*-formyl-α-D-mannopyranoside (30). Trifluoroacetic acid (245 μL) was added to a solution of **23** (98 mg, 0.23 mmol) in Ac_2O (2.5 mL), and the mixture was stirred overnight. The crude material obtained by coevaporation with toluene was dissolved in dry CH_2Cl_2 (3.0 mL). MeOH (113 μL, 2.78 mmol) and crushed 4 Å molecular sieves (approximately 200 mg) were added, and the mixture was stirred for 1 h. After cooling to 0 °C, TMSOTf (72 μL, 0.37 mmol) was added dropwise. After 45 min at 0 °C, the reaction mixture was diluted with CH_2Cl_2 and then filtered through Celite. The organic phase was washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:6) yielded 73 mg of methyl glycoside **29** (62% for two steps) isolated as a colorless syrup: ^1H NMR (200 MHz) δ = 7.40−7.28 (10H, m), 6.11 (1H, ddd, J = 9.4, 10.3, 17.4 Hz), 5.31 (1H, dd, J = 2.2, 17.4 Hz), 5.20 (1H, dd, J = 2.2, 10.3 Hz), 4.71 (1H, d, J = 1.5 Hz), 4.66 (1H, d, J = 11.8 Hz), 4.62 (1H, d, J = 10.4 Hz), 4.51 (1H, d, J = 11.8 Hz), 4.39 (1H, dd, J = 2.2, 11.7 Hz), 4.38 (1H, d, J = 10.4 Hz), 4.29 (1H, dd, J = 5.1, 11.7 Hz), 3.83 (1H, ddd, J = 2.2, 5.1, 9.9 Hz), 3.71 (1H, dd, J = 9.9, 9.9 Hz), 3.57 (1H, dd, J = 1.5, 2.9 Hz), 3.40 (3H, s), 2.78 (1H, ddd, J = 2.9, 9.4, 9.4 Hz), 2.11 (3H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 171.1, 138.2, 137.9, 136.5, 128.5, 128.4, 128.2, 127.9, 127.8, 118.6, 97.2, 79.5, 74.0, 73.5, 72.8, 70.0, 64.0, 54.8, 47.5, 21.1.

Ozone was bubbled through a solution of the alkene **29** (51 mg, 0.12 mmol) dissolved in dry CH_2Cl_2 (16 mL) and MeOH (4.0 mL) at −78 °C until a blue color was obtained. After removal of the excess ozone by bubbling nitrogen through the solution for 5−10 min at −78 °C, triphenylphosphine (56 mg, 0.28 mmol) was added, and the reaction mixture was warmed to 20 °C over a period of 15 min. Stirring was continued for an additional 30 min, and the solvents were removed by evaporation to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:4) gave **30** (48 mg, 94%) as a colorless syrup, which was immediately used in the subsequent step. A small sample was characterized by NMR spectroscopy: ^1H NMR (200 MHz) δ = 9.61 (1H, d, J = 1.2 Hz), 7.36−7.27 (10H, m), 4.76 (1H, bs), 4.76 (1H, d, J = 10.6 Hz), 4.63 (1H, d, J = 12.2 Hz), 4.52 (1H, d, J = 10.6 Hz), 4.43 (1H, dd, J = 2.4, 12.2 Hz), 4.42 (1H, d, J = 12.2 Hz), 4.30 (1H, dd, J = 5.0, 12.2 Hz), 4.18 (1H, dd, J = 10.0, 10.0 Hz), 3.98 (1H, dd, J = 1.8, 3.2 Hz), 3.79 (1H, ddd, J = 2.4, 5.0, 10.0 Hz), 3.37 (3H, s), 2.94 (1H, ddd, J = 1.2, 3.4, 10.0 Hz), 2.10 (3H, s); ^{13}C NMR (50 MHz) δ = 200.8, 171.0, 137.6, 137.3, 128.6, 128.1, 127.9, 96.5, 74.7, 74.5, 72.3, 70.1, 69.5, 63.4, 54.9, 54.5, 21.0.

Methyl 6-*O*-Acetyl-2,4-di-*O*-benzyl-3-deoxy-3-*C*-(1′-(2′,3′,-4′,6′-tetra-*O*-benzyl-1′-deoxy-α-D-mannopyranosyl)(oxythiocarbonylimidazolylmethylene)-α-D-mannopyranoside (31). The aldehyde **30** (45 mg, 0.105 mmol) and pyridyl sulfone **25** (120 mg, 0.181 mmol) were loaded into an oven-dried flask and flushed with argon for 5 min. A 0.1 M solution of freshly prepared samarium diiodide in THF was added until

a permanent dark blue color persisted (approx 5 mL, 0.51 mmol). The reaction mixture was quenched by the addition of aqueous saturated NH_4Cl and then diluted with CH_2Cl_2. The organic phase was filtered through a small Celite pad, dried ($MgSO_4$), and concentrated to dryness in vacuo. A short column (EtOAc:pentane, 1:3) gave the crude 1,3-*C*-disaccharide, which was redissolved in dry distilled MeCN (2 mL). Thiocarbonyldiimidazole (187 mg, 1.05 mmol) was added, and the mixture was refluxed overnight. The solvent was thereafter slowly evaporated off by continued heating. The residue obtained was subjected to column chromatography (EtOAc:pentane, 1:2), yielding 35 mg of **31** (35% for two steps) as a thick colorless syrup: ^{1}H NMR (200 MHz) δ = 8.25 (1H, s), 7.50 (1H, s), 7.40−7.08 (30H, m), 6.80 (1H, s), 6.43 (1H, dd, J = 1.4, 2.6 Hz), 4.90 (1H, d, J = 10.6 Hz), 4.69 (1H, d, J = 1.4 Hz), 4.53−4.31 (11H, m), 4.23 (1H, dd, J = 4.8, 12.2 Hz), 4.18 (2H, m), 4.11 (1H, bd, J = 1.4 Hz), 4.07 (1H, dd, J = 9.2, 11.4 Hz), 3.94−3.63 (6H, m), 3.57 (1H, dd, J = 4.4, 10.2 Hz), 3.30 (3H, s), 2.97 (1H, ddd, J = 2.6, 5.2, 10.6 Hz), 2.10 (3H, s).

Methyl 2,4,6-Tri-*O*-acetyl-3-deoxy-3-*C*-(1′-(2′,3′,4′,6′-tetra-*O*-acetyl-1′-deoxy-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (34). To a solution of **31** (35 mg, 0.033 mmol) in dry distilled toluene (2.0 mL) were added pentafluorophenol (12 mg, 0.066 mmol), triphenyltin hydride (22 mg, 0.436 mmol), and a catalytic amount of AIBN (approximately 2 mg). The reaction mixture was refluxed for 30 min. The solvent was removed by evaporation in vacuo, and the residue was redissolved in acetonitrile and washed twice with pentane to remove the residual tin compounds. The acetonitrile phase was evaporated to dryness in vacuo, and subsequent column chromatography (EtOAc:pentane, 1:3) gave 20 mg of **32** (65%) as a colorless thick syrup: ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.44−7.10 (30H, m), 4.69 (1H, d, J = 11.1 Hz), 4.64 (1H, d, J = 1.8 Hz), 4.58−4.44 (11H, m), 4.38 (1H, dd, J = 2.1, 11.7 Hz), 4.23 (1H, d, J = 5.4, 11.7 Hz), 4.12 (1H, m), 3.84−3.61 (7H, m), 3.52 (1H, dd, J = 9.9; 9.9 Hz), 3.51 (1H, dd, J = 3.2, 5.1 Hz), 3.32 (3H, s), 2.17 (1H, m), 2.10 (3H, s), 1.82 (2H, m).

A catalytic amount of freshly prepared NaOMe in MeOH was added to the protected *C*-disaccharide **32** dissolved in MeOH (1.0 mL). After stirring overnight at 20 °C and concentration to dryness in vacuo, the residue was redissolved in MeOH (6 mL), and glacial acetic acid (1 mL), and 10% Pd/C (30 mg) were added. The reaction was stirred overnight under an atmosphere of hydrogen, filtered through a pad of Celite, and then coevaporated three times with toluene. A single product was detected by TLC analysis (R_f = 0.28, MeOH:CH_2Cl_2, 1:1): ^{1}H NMR (D_2O, 500 MHz) δ 4.60 (1H, d, J = 1.3 Hz), 4.02 (1H, ddd, J = 1.9, 4.9, 8.8 Hz), 3.86 (1H, dd, J = 1.9, 3.4 Hz), 3.85 (1H, dd, J = 1.3, 2.1 Hz), 3.82 (1H, dd, J = 2.0, 11.5 Hz), 3.79 (1H, dd, J = 2.1, 11.5 Hz), 3.76 (1H, dd, J = 3.4, 9.0 Hz), 3.68 (1H, dd, J = 6.2, 11.5 Hz), 3.68 (1H, dd, J = 5.6, 11.5 Hz), 3.59 (1H, dd, J = 9.0, 9.4 Hz), 3.56 (1H, ddd, J = 2.1, 6.2, 9.4 Hz), 3.55 (1H, ddd, J = 2.0, 5.6, 10.3 Hz), 3.43 (1H, dd, J = 9.8, 10.3 Hz), 3.37 (3H, s), 2.00−1.77 (3H, m); ^{13}C NMR (125 MHz) δ 100.3, 78.2, 73.8, 72.1, 71.3, 70.5, 69.3, 68.4, 67.7, 60.6 (2C), 39.2, 22.9.

The free 1,3-*C*-disaccharide **33** was dissolved in pyridine (4 mL) and Ac_2O (2 mL) and left standing overnight. Coevaporation three times with toluene and column chromatography (EtOAc:pentane, 1:3) yielded 7 mg (54% for three steps) of **34** as a colorless thick syrup: ^{1}H NMR (C_6D_6, 300 MHz) δ = 5.58 (1H, dd, J = 3.3, 5.4 Hz), 5.44 (1H, dd, J = 10.4, 10.4 Hz), 5.31 (1H, dd, J = 3.3, 7.2 Hz), 5.29 (1H, bs), 5.18 (1H, dd, J = 4.8, 5.4 Hz), 4.78 (1H, dd, J = 7.8, 11.4 Hz), 4.72 (1H, s), 4.44 (1H, dd, J = 5.1, 12.0 Hz), 4.22−4.12 (2H, m), 4.06 (1H, ddd, J = 2.5, 5.7, 7.8 Hz), 3.99 (1H, dd, J = 3.5, 11.4 Hz), 3.89 (1H, m), 2.97 (3H, s), 2.58 (1H, m), 1.86 (3H, s), 1.81 (3H, s), 1.72 (3H, s), 1.68 (3H, s), 1.63 (3H, s), 1.54 (3H, s), 1.50 (3H, s), 1.40−1.24 (2H, m); ^{13}C NMR (50 MHz) δ 170.8, 170.6, 170.5, 170.1, 169.7, 97.3, 72.3, 72.0, 71.7, 70.3, 69.0, 68.4, 68.1, 67.4, 63.0, 61.5, 55.1, 36.5, 27.7, 21.2, 20.9, 20.7; MS (EI) *m*/*z* 648 (M).

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-*C*-ethynyl-α-D-mannopyranoside (35). Trifluoromethanesulfonic anhydride (109 μL, 0.646 mmol) was slowly added to a solution of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (200 mg, 0.431 mmol) and 2,6-lutidine (63 μL, 0.538 mmol) in CH_2Cl_2 (2 mL) and cooled to −40 °C. After stirring for 1 h, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$, and the resulting mixture was extracted three times with diethyl ether. The combined organic phases were dried ($MgSO_4$) and evaporated to dryness in vacuo, keeping the temperature below 30 °C. The crude product was purified by rapid column chromatography (EtOAc:pentane, 1:15), giving 205 mg (80%) of methyl 2,3,4-tri-*O*-benzyl-6-trifluoromethansulfonyl-α-D-mannopyranoside as a colorless syrup, which was immediately used for the next step.

*n*BuLi (827 μL, 1.6 M in THF, 1.32 mmol) was added dropwise to a solution of trimethylsilylacetylene (170 μL, 1.20 mmol) dissolved in THF (0.5 mL) and HMPA (60 μL) at −78 °C. After stirring for 15 min, the triflate (205 mg, 0.344 mmol) in THF (1.0 mL) was added dropwise. The reaction mixture was slowly warmed to 20 °C and stirred overnight. After quenching by the addition of saturated aqueous NH_4Cl, the mixture was extracted three times with diethyl ether. The combined organic phases were dried ($MgSO_4$) and concentrated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:15) gave 112 mg (60%) of the disubstituted alkyne as a colorless syrup: ^{1}H NMR (200 MHz) δ = 7.40−7.22 (15H, m), 4.93 (1H, d, J = 10.8 Hz), 4.73 (1H, d, J = 1.8 Hz, H1), 4.70 (1H, d, J = 12.6 Hz), 4.67 (1H, d, J = 12.6 Hz), 4.61 (1H, d, J = 10.8 Hz), 4.58 (2H, s), 3.85−3.76 (2H, m), 3.76 (1H, dd, J = 1.8, 2.8 Hz), 3.64 (1H, ddd, J = 2.8, 7.4, 10.0 Hz), 3.31 (3H, s), 2.71 (1H, dd, J = 2.8, 17.2 Hz), 2.52 (1H, dd, J = 7.4, 17.2 Hz), 0.10 (9H, s); ^{13}C NMR (50 MHz) δ = 138.7, 138.7, 138.6, 128.6−127.8, 104.1, 99.1, 86.3, 80.5, 77.8, 75.6, 75.1, 73.0, 72.3, 70.6, 54.7, 23.3, 0.4; HR-MS (ES) calcd for $C_{33}H_{40}O_5SiNa$ (M + Na) 567.2543, found 567.2542.

Tetra-*n*-butylammonium fluoride (1.0 M in THF, 578 μL, 0.578 mmol) was added to a cooled solution (0 °C) of the above alkyne (105 mg, 0.193 mmol) in THF (1.0 mL) followed by stirring overnight. The reaction mixture was diluted with ether, and the organic phase was washed with water and brine and then dried ($MgSO_4$) and evaporated to dryness in vacuo. This afforded 81.6 mg (62%, 3 steps) of **35** as a slightly yellow syrup, which was sufficiently pure both by TLC analysis and ^{1}H NMR to be used without any further purification: ^{1}H NMR (200 MHz) δ = 7.40−7.22 (15H, m), 5.00 (1H, d, J = 11.0 Hz), 4.79 (1H, d, J = 1.6 Hz), 4.75 (2H, s), 4.68 (1H, d, J = 11.0 Hz), 4.63 (2H, s), 3.90 (2H, m), 3.82 (1H, dd, J = 1.8, 2.2 Hz), 3.72 (1H, m), 3.36 (3H, s), 2.73 (1H, ddd, J = 3.0, 3.0, 17.0 Hz), 2.57 (1H, ddd, J = 2.6, 7.0, 17.0 Hz), 2.06 (1H, dd, J = 2.6, 3.0 Hz); ^{13}C NMR (50 MHz) δ = 138.6, 138.6, 138.5, 128.6−127.8, 99.1, 81.1, 80.3, 77.6, 75.6, 74.8, 72.8, 72.2, 70.2, 70.1, 54.9, 22.0.

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-*C*-vinyl-α-D-mannopyranoside (36). A flask was charged with Lindlar's catalyst (5% palladium on $CaCO_3$ poisoned with lead, 36 mg, 0.017 mmol). The flask was thereafter evacuated under vacuum and filled with hydrogen three times. To this flask was added a solution of alkyne **35** (81 mg, 0.171 mmol) and quinoline (11 μL, 0.089 mmol) dissolved in EtOAc (1.0 mL). After 5 min at 20 °C, the reaction was stopped by filtering off the catalyst through a pad of Celite. Evaporation to dryness in vacuo and column chromatography (EtOAc:pentane, 1:20) gave 62 mg (76%, 78% corrected) of **36** as a colorless syrup and 1.5 mg (2%) of recovered starting material: ^{1}H NMR (200 MHz) δ = 7.45−7.25 (15H, m), 5.97 (1H, dddd, J = 6.4, 7.2, 10.0, 17.2 Hz), 5.17 (1H, dddd, J = 1.8, 1.8, 1.8, 17.2 Hz), 5.11 (1H, dddd, J = 1.8, 1.8, 1.8, 10.0 Hz), 4.98 (1H, d, J = 10.8 Hz), 4.76 (2H, s), 4.72 (1H, d, J = 1.8 Hz), 4.66 (1H, d, J = 10.8 Hz), 4.63 (2H, s), 3.89 (1H, dd, J = 3.2, 9.0 Hz), 3.81 (1H, dd, J = 1.8, 3.2 Hz), 3.75 (1H, dd, J = 8.8, 9.0 Hz), 3.63 (1H, ddd, J = 2.6, 8.0, 8.8 Hz), 3.30 (3H, s), 2.66 (1H, m), 2.38 (1H,

ddd, J = 7.2, 8.0, 14.6 Hz); ^{13}C NMR (50 MHz) δ = 138.8, 138.8, 138.5, 135.3, 128.6−127.8, 117.1, 99.1, 80.6, 78.5, 75.4, 74.8, 72.9, 72.3, 71.5, 54.8, 36.1; HR-MS (ES) calcd for $C_{30}H_{34}O_5Na$ (M + Na) 497.2304, found 497.2303.

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-*C*-formyl-α-D-mannopyranoside (37). Ozonolysis was performed according to the procedure outlined for the synthesis of compound **30**, with the following quantities: alkene **36** (58 mg, 0.12 mmol) dissolved in dry CH_2Cl_2 (4 mL) and MeOH (1 mL), triphenylphosphine (74 mg, 0.28 mmol). Column chromatography (EtOAc:pentane, 1:10) gave 30 (53 mg, 91%) as a colorless syrup: ^{1}H NMR (200 MHz) δ = 9.74 (1H, dd, J = 2.2, 2.2 Hz), 7.40−7.20 (15H, m), 4.96 (1H, d, J = 11.0 Hz), 4.72 (1H, d, J = 12.4 Hz), 4.70 (1H, d, J = 12.4 Hz), 4.64 (1H, d, J = 1.6 Hz), 4.61 (2H, s), 4.58 (1H, d, J = 11.0 Hz), 4.12 (1H, ddd, J = 4.0, 9.0, 9.2 Hz), 3.90 (1H, dd, J = 3.0, 9.4 Hz), 3.80 (1H, dd, J = 1.6, 3.0 Hz), 3.72 (1H, dd, J = 9.2, 9.4 Hz), 3.33 (3H, s), 2.79 (1H, ddd, J = 2.2, 4.0, 16.4 Hz), 2.63 (1H, ddd, J = 2.2, 9.0, 16.4 Hz); ^{13}C NMR (50 MHz) δ = 200.5, 138.5, 138.5, 138.3, 128.6−127.8, 99.3, 80.4, 76.6, 75.3, 74.7, 73.1, 72.2, 67.1, 55.2, 46.2; HR-MS (ES) calcd for $C_{29}H_{32}O_6Na$ (M + Na) 499.2097, found 499.2099.

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-*C*-(1′-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-deoxy-α-D-mannopyranosyl)(oxythiocarbonylimidazolylmethylene)-α-D-mannopyranoside (38). Samarium diiodide (9.6 mL, 0.10 M in THF, 0.96 mmol) was added to a solution of the pyridyl sulfone **25** (291 mg, 0.437 mmol) and aldehyde **37** (52 mg, 0.109 mmol) dissolved in THF (1.0 mL) under argon. After stirring for 10 min, the reaction mixture was quenched with aqueous saturated NH_4Cl. CH_2Cl_2 was added, and the organic phase was filtered through a Celite pad, dried ($MgSO_4$), and concentrated to dryness in vacuo. The residue was redissolved in MeCN (2.0 mL), and thiocarbonyldiimidazole (291 mg, 1.64 mmol) was added. After refluxing overnight, the reaction mixture was concentrated to dryness in vacuo. Column chromatography (EtOAC:pentane, 1:8 to 1:4) gave 75 mg (62%, 2 steps) of **38** as a thick colorless syrup. A 5:1 ratio of diastereomers at the newly created C-7-stereocenter was obtained. For the major diastereomer: ^{1}H NMR (200 MHz) δ = 8.34 (1H, s), 7.56 (1H, m), 7.40−7.10 (35H, m), 6.92 (1H, m), 6.13 (1H, ddd, J = 3.0, 5.2, 8.6 Hz), 4.88 (1H, d, J = 11.2 Hz), 4.71 (1H, d, J = 12.4 Hz), 4.69 (1H, d, J = 12.4 Hz), 4.67 (1H, d, J = 12.4 Hz), 4.61 (1H, d, J = 12.4 Hz), 4.59 (1H, d, J = 11.2 Hz), 4.59 (1H, d, J = 1.4 Hz), 4.51 (2H, s), 4.49 (2H, s), 4.48 (1H, d, J = 12.0 Hz), 4.40 (1H, d, J = 9.4 Hz), 4.39 (1H, d, J = 12.0 Hz), 4.36 (1H, d, J = 9.4 Hz), 4.29 (1H, dd, J = 2.0, 7.6 Hz), 4.13 (1H, dd, J = 5.8, 9.2 Hz), 3.91−3.58 (9H, m), 3.09 (3H, s), 2.49 (1H, ddd, J = 2.2, 8.6, 11.8 Hz), 2.10 (1H, ddd, J = 5.2, 8.8, 11.8 Hz); ^{13}C NMR (50 MHz) δ = 138.5, 138.9, 138.6, 138.5, 138.5, 138.2 138.2, 137.8, 137.5, 130.7, 128.6−127.6, 118.1, 99.5, 80.0, 80.0, 78.8, 75.1, 75.0, 74.8, 74.8, 74.8, 74.3, 73.4, 73.0, 72.9, 72.3, 72.3, 71.1, 69.9, 68.9, 68.8, 55.7, 31.2; HR-MS (ES) calcd for $C_{67}H_{70}N_2O_{11}SNa$ (M + Na) 1133.4598, found 1133.4612.

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-*C*-(1′-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-deoxy-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (39). To a solution of **38** (73 mg, 0.066 mmol) in toluene (4.0 mL) were added pentafluorophenol (24 mg, 0.131 mmol), triphenyltin hydride (44 μL, 0.171 mmol), and a catalytic amount of AIBN (5 mg, 0.030 mmol). This mixture was refluxed for 3 h, and then the solvent was removed by evaporation in vacuo. The residue was redissolved in acetonitrile and washed two times with pentane. After concentration to dryness in vacuo, column chromatography (EtOAc:pentane, 1:7) afforded 47 mg (73%) of **39** as a colorless syrup: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37−7.20 (35H, m), 4.91 (1H, d, J = 10.8 Hz), 4.76 (1H, d, J = 10.8 Hz), 4.73 (1H, d, J = 12.4 Hz), 4.70 (1H, d, J = 12.4 Hz), 4.65 (1H, d, J = 12.4 Hz), 4.63 (1H, d, J = 1.2 Hz), 4.61 (1H, d, J = 12.0 Hz), 4.59 (1H, d, J = 12.4 Hz), 4.59 (2H, s), 4.58 (1H, d, J = 11.2 Hz), 4.53 (2H, s), 4.51 (1H, d, J = 11.2 Hz), 4.50 (1H, d, J = 12.0 Hz), 4.05 (1H, ddd, J = 3.2, 3.6, 7.6 Hz), 3.96 (1H, dd, J = 6.8, 7.5 Hz), 3.81 (1H, dd, J = 3.2, 9.2 Hz), 3.77 (1H, dd, J = 3.2, 6.8 Hz, H3_), 3.76 (1H, dd, J = 1.2, 3.2 Hz), 3.75−3.70 (3H, m), 3.63 (1H, dd, J = 9.2, 9.2 Hz), 3.59 (1H, dd, J = 3.2, 3.2 Hz), 3.47 (1H, ddd, J = 1.6, 8.8, 9.2 Hz), 3.20 (3H, s), 1.95−1.80 (2H, m), 1.71 (1H, m), 1.41 (1H, m); ^{13}C NMR (50 MHz) δ = 138.8, 138.7, 138.6, 138.6, 138.6, 138.5, 138.5, 128.5−127.6, 99.0, 80.4, 79.0, 78.5, 76.0, 75.5, 75.2, 74.8, 74.5, 73.6, 73.5, 73.1, 72.9, 72.2, 72.2, 71.5, 71.3, 69.5, 54.8, 28.1, 25.7; HR-MS (ES) calcd for $C_{63}H_{68}O_{10}Na$ (M + Na) 1007.4710, found 1007.4724.

Methyl 6-Deoxy-6-*C*-(1′-(1′-deoxy-α-D-mannopyranosyl)-methylene)-α-D-mannopyranoside (40). A mixture of the perbenzylated 1,6-*C*-disaccharide **39** (47 mg, 0.048 mmol) and 10% Pd/C (67 mg) in MeOH (6.0 mL) and glacial acetic acid (1.0 mL) was stirred under an atmosphere of hydrogen overnight. The reaction mixture was filtered through Celite and coevaporated three times with toluene. TLC analysis revealed a single product (R_f = 0.48, MeOH:CH_2Cl_2, 1:1): ^{1}H NMR (D_2O, 500 MHz) δ = 4.61 (1H, bs), 4.03 (1H, bdd, J = 4.3, 9.0 Hz), 3.89−3.85 (2H, m), 3.85 (1H, dd, J = 1.7, 9.8 Hz), 3.82 (1H, bd, J = 12.6 Hz), 3.76 (1H, dd, J = 2.8, 8.7 Hz), 3.66 (1H, bd, J = 12.6 Hz), 3.56 (1H, dd, J = 8.7, 9.7 Hz), 3.56−3.54 (2H, m), 3.40 (1H, dd, J = 9.8, 9.9 Hz), 3.37 (3H, s), 2.05−1.77 (4H, m); ^{13}C NMR (125 MHz) δ 100.2, 78.1, 73.9, 72.2, 71.9, 70.8, 70.2, 70.1, 69.9, 67.9, 60.9, 27.2, 23.7; HR-MS (ES) calcd for $C_{14}H_{26}O_{10}Na$ (M + Na) 377.1424, found 377.1435.

Methyl2,3,4-Tri-*O*-acetyl-6-deoxy-6-*C*-(1′-(1′-deoxy-2′,3′,4′,-6′-tetra-*O*-acetyl-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (41). The free 1,6-*C*-disaccharide **40** was dissolved in pyridine (4.0 mL) and Ac_2O (2.0 mL), and left standing overnight. Coevaporation three times with toluene and column chromatography (EtOAc:pentane, 1:3) yielded 19 mg (63%, two steps) of **41** as a colorless thick syrup: ^{1}H NMR (400 MHz) δ = 5.29 (1H, dd, J = 3.6, 9.6 Hz), 5.27−5.23 (2H, m), 5.20 (1H, dd, J = 8.4, 8.4 Hz), 5.16 (1H, dd, J = 2.8, 3.2 Hz), 5.10 (1H, dd, J = 9.6, 10.0 Hz), 4.65 (1H, d, J = 1.6 Hz), 4.37 (1H, dd, J = 6.4, 12.0 Hz), 4.08 (1H, dd, J = 2.8, 12.0 Hz), 3.96 (1H, ddd, J = 3.2, 3.2, 10.8 Hz), 3.88 (1H, ddd, J = 2.8, 6.4, 8.4 Hz), 3.76 (1H, ddd, J = 2.6, 7.6, 9.6 Hz), 3.39 (3H, s), 2.16 (3H, s), 2.13 (3H, s), 2.12 (3H, s), 2.07 (3H, s), 2.05 (3H, s), 2.05 (1H, m), 2.03 (3H, s), 1.99 (3H, s), 1.68−1.57 (3H, m); ^{13}C NMR (50 MHz) δ 170.9, 170.5, 170.3, 170.2, 170.2, 170.1, 169.9, 98.6, 74.7, 71.0, 70.4, 69.8, 69.4, 69.3, 69.2, 69.0, 67.1, 62.5, 55.3, 27.0, 23.9, 21.2 (2C), 21.0 (3C), 20.9 (2C); HR-MS (ES) calcd for $C_{28}H_{40}O_{17}Na$ (M + Na) 671.2163, found 671.2158.

Methyl 2,4-Di-*O*-benzyl-3-deoxy-3-*C*-vinyl-α-D-mannopyranoside (42). Concentrated aqueous hydrochloric acid (0.2 mL) was added to a solution of **23** (50.0 mg, 0.142 mmol) in MeOH (3.5 mL) and heated to reflux for 2 days. Another portion of concentrated HCl (0.2 mL) was added and the mixture was refluxed for a further 2 days. The reaction mixture was neutralized by the addition of saturated aqueous $NaHCO_3$ (3 mL). After extracting with CH_2Cl_2, the combined organic phases were dried ($MgSO_4$) and concentrated to dryness in vacuo. Column chromatography (EtOAc:pentane, 1:10 to 1:4) gave first 12 mg (23%) of recovered starting material **23** and then 24 mg (43%, corrected yield: 56%) of **42** as a colorless syrup: ^{1}H NMR (200 MHz) δ = 7.45−7.25 (10H, m), 6.09 (1H, ddd, J = 9.2, 10.2, 17.2 Hz), 5.31 (1H, ddd, J = 0.6, 1.2, 17.2 Hz), 5.20 (1H, dd, J = 1.2, 10.2 Hz), 4.68 (1H, d, J = 1.6 Hz), 4.63 (2H, s), 4.60 (1H, d, J = 10.6 Hz), 4.49 (1H, d, J = 10.6 Hz), 3.90−3.75 (2H, m), 3.85 (1H, dd, J = 6.8, 9.6 Hz), 3.67 (1H, ddd, J = 3.4, 6.0, 6.8 Hz), 3.53 (1H, dd, J = 1.6, 2.8 Hz), 3.38 (3H, s), 2.78 (1H, ddd, J = 2.8, 9.2, 9.6 Hz), 2.03 (1H, bs); ^{13}C NMR (50 MHz) δ = 138.3, 138.3, 136.8, 128.5−127.8, 118.5, 97.5, 79.8, 74.3, 73.6, 73.2, 72.1, 62.8, 54.9, 47.4; HR-MS (ES) calcd for $C_{23}H_{28}O_5Na$ (M + Na) 407.1834, found 407.1839.

Methyl 2,4-Di-*O*-benzyl-3,6-dideoxy-6-*C*-ethynyl-3-*C*-vinyl-α-D-mannopyranoside (43). The triflation and ethynylation sequence was performed according to the procedure

outlined for the synthesis of compound **35**, with the following quantities (a) for the triflation step: alcohol **42** (69.5 mg, 0.181 mmol) in CH_2CH_2 (2.0 mL), 2,6-lutidine (182 μL, 1.56 mmol), and trifluoromethanesulfonic anhydride (315 μL, 1.87 mmol). Column chromatography on a short column (EtOAc:pentane, 1:25) gave 62 mg (66%) of methyl 2,4-di-*O*-benzyl-3-deoxy-6-*O*-triflouromethanesulfonyl-3-*C*-vinyl-α-D-mannopyranoside as a colorless oil. The following quantities were used (b) for the ethynylation step: trimethylsilylacetylene (220 μL, 1.56 mmol) in THF (1.0 mL), *n*BuLi (1.02 mL, 1.6 M in hexanes, 1.64 mmol), and HMPA (54 μL, 0.31 mmol). Column chromatography (EtOAc:pentane, 1:40 to 1:15) afforded 40.3 mg of methyl 2,4-di-*O*-benzyl-3,6-dideoxy-6-*C*-trimethylsilylethynyl-3-*C*-vinyl-α-D-mannopyranoside as a colorless syrup along with also 4.1 mg of the desilylated product **43**. This gave a total yield of 53% for the two steps. Characterization of the 6-*C*-trimethylsilylethynyl compound: ^{1}H NMR (200 MHz) δ = 7.39−7.29 (10H, m), 6.10 (1H, ddd, J = 9.2, 10.0, 17.2 Hz), 5.29 (1H, ddd, J = 0.6, 2.0, 17.2 Hz), 5.18 (1H, dd, J = 2.0, 10.0 Hz), 4.73 (1H, d, J = 1.2 Hz), 4.66 (1H, d, J = 11.6 Hz), 4.64 (1H, d, J = 10.4 Hz), 4.49 (1H, d, J = 11.6 Hz), 4.46 (1H, d, J = 10.4 Hz), 3.79−3.60 (2H, m), 3.51 (1H, dd, J = 1.2, 3.2 Hz), 3.41 (3H, s), 2.76 (1H, ddd, J = 0.6, 3.2, 9.2 Hz), 2.74 (1H, dd, J = 2.8, 17.0 Hz), 2.54 (1H, dd, J = 7.2, 17.0 Hz), 0.13 (9H, s); ^{13}C NMR (50 MHz) δ = 138.1, 138.0, 136.5, 128.2−127.5, 118.1, 103.9, 96.9, 86.0, 79.6, 76.2, 74.0, 72.7, 70.3, 54.3, 47.6, 23.2, 0.0; HR-MS (ES) calcd for $C_{28}H_{36}O_4SiNa$ (M + Na) 487.2281, found 487.2274. The following quantities were used (c) for the desilylation step: THF (0.5 mL) and tetra-*n*-butylammonium fluoride (259 μL, 1.0 M in THF, 0.259 mmol). This yielded 33.4 mg (100%) of the alkyne **43** as a pale yellow syrup, which according to TLC and ^{1}H NMR was sufficiently pure for the next step: ^{1}H NMR (200 MHz) δ = 7.40−7.25 (10H, m), 6.10 (1H, ddd, J = 9.2, 10.0, 17.2 Hz), 5.28 (1H, ddd, J = 0.6, 2.0, 17.2 Hz), 5.17 (1H, dd, J = 2.0, 10.0 Hz), 4.72 (1H, d, J = 1.4 Hz), 4.66 (1H, d, J = 11.8 Hz), 4.65 (1H, d, J = 10.4 Hz), 4.50 (1H, d, J = 11.8 Hz), 4.46 (1H, d, J = 10.4 Hz), 3.79−3.62 (2H, m), 3.51 (1H, dd, J = 1.4, 3.0 Hz), 3.40 (3H, s), 2.80−2.69 (1H, m), 2.70 (1H, ddd, J = 2.6, 2.6, 17.0 Hz), 2.54 (1H, ddd, J = 2.6, 6.6, 17.0 Hz), 2.05 (1H, dd, J = 2.6, 2.6 Hz); ^{13}C NMR (50 MHz) δ = 138.4, 138.3, 136.7, 128.5−127.8, 118.5, 97.4, 81.3, 79.8, 76.4, 74.3, 72.9, 70.2, 70.1, 54.8, 47.7, 22.1; HR-MS (ES) calcd for $C_{25}H_{28}O_4Na$ (M + Na) 415.1885, found 415.1883.

Methyl 2,4-Di-*O*-benzyl-3,6-dideoxy-3,6-di-*C*-vinyl-α-D-mannopyranoside (44). The hydrogenation step was performed according to the procedure outlined for the synthesis of compound **36**, with the following quantities: alkyne **43** (38 mg, 0.171 mmol) in EtOAc (0.5 mL), quinoline (6 μL, 0.050 mmol), and Lindlar's catalyst (5% palladium on $CaCO_3$ poisoned with lead, 20 mg, 9.6 μmol). Column chromatography (EtOAc:pentane, 1:25) gave 28 mg (74%, 77% corrected) of **44** as a colorless syrup and 1.4 mg of recovered starting material: ^{1}H NMR (200 MHz) δ = 7.37−7.25 (10H, m), 6.09 (1H, ddd, J = 9.4, 10.0, 17.2 Hz), 5.95 (1H, dddd, J = 6.4, 7.2, 10.2, 17.2 Hz), 5.26 (1H, ddd, J = 0.6, 2.0, 17.2 Hz), 5.16 (1H, dd, J = 2.0, 10.0 Hz), 5.14 (1H, dddd, J = 0.8, 0.8, 0.8, 17.2 Hz), 5.08 (1H, dddd, J = 0.8, 0.8, 0.8, 10.2 Hz), 4.65 (1H, d, J = 11.8 Hz), 4.64 (1H, d, J = 1.6 Hz), 4.61 (1H, d, J = 10.6 Hz), 4.50 (1H, d, J = 11.8 Hz), 4.44 (1H, d, J = 10.6 Hz), 3.65 (1H, ddd, J = 3.0, 8.4, 9.4 Hz), 3.51 (1H, dd, J = 9.4, 9.4 Hz), 3.49 (1H, dd, J = 1.6, 3.0 Hz), 3.33 (3H, s), 2.73 (1H, ddd, J = 3.0, 9.4, 9.4 Hz), 2.63 (1H, ddddd, J = 0.8, 0.8, 3.0, 6.4, 15.4 Hz), 2.32 (1H, ddddd, J = 0.8, 7.2, 8.4, 15.4 Hz); ^{13}C NMR (50 MHz) δ = 138.1, 138.1, 136.7, 135.7, 128.2−127.6, 118.0, 116.7, 97.0, 79.6, 77.0, 72.7, 71.2, 54.4, 47.5, 36.1; HR-MS (ES) calcd for $C_{25}H_{30}O_4Na$ (M + Na) 417.2042, found 417.2041.

Methyl 2,4-Di-*O*-benzyl-3,6-dideoxy-3,6-di-*C*-formyl-α-D-mannopyranoside (2). Ozonolysis was performed according to the procedure outlined for the synthesis of compound **30**, with the following quantities: dialkene **44** (98.1 mg, 0.249 mmol) dissolved in dry CH_2Cl_2 (4 mL) and MeOH (1 mL), and triphenylphosphine (150 mg, 0.572 mmol). Column chromatography (EtOAc:pentane, 1:5) gave the dialdehyde **2** (96 mg, 96%) as a colorless syrup: ^{1}H NMR (200 MHz) δ = 9.80 (1H, dd, J = 1.6, 2.6 Hz), 9.63 (1H, d, J = 1.2 Hz), 7.37−7.25 (10H, m), 4.83 (1H, d, J = 10.8 Hz), 4.68 (1H, d, J = 1.4 Hz), 4.63 (1H, d, J = 11.8 Hz), 4.55 (1H, d, J = 10.8 Hz), 4.44 (1H, d, J = 11.8 Hz), 4.18 (1H, ddd, J = 3.8, 8.6, 9.4 Hz), 4.00 (1H, dd, J = 1.4, 3.0 Hz), 3.99 (1H, dd, J = 9.4, 9.4 Hz), 3.41 (3H, s), 2.98 (1H, ddd, J = 1.2, 3.0, 9.4 Hz), 2.83 (1H, ddd, J = 1.6, 3.8, 16.4 Hz), 2.69 (1H, ddd, J = 2.6, 8.6, 16.4 Hz); ^{13}C NMR (50 MHz) δ = 200.7, 200.3, 137.7, 137.3, 128.7−128.1, 96.5, 74.8, 74.8, 73.5, 72.6, 66.7, 55.3, 54.8, 46.0; MS (ES) *m*/*z* 453.0 (M + MeOH + Na), 485.0 (M + 2MeOH + Na).

Methyl 2,4-Di-*O*-benzyl-3,6-dideoxy-3,6-*C*-di-(1′/1″-(2′/2″,3′/3″,4′/4″,6′/6″-tetra-*O*-benzyl-1′/1″-deoxy-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (46). The dialdehyde **2** (21 mg, 0.053 mmol) and the pyridyl sulfone **25** (164 mg, 0.246 mmol) were coevaporated with benzene in an oven-dried flask and dried on the vacuum line for approximately 15 min. Samarium diiodide (5.4 mL, 0.10 M in THF, 0.542 mmol) was added directly to this mixture under argon. After stirring for 15 min, the reaction mixture was quenched with aqueous saturated NH_4Cl. CH_2Cl_2 was added, and the organic phase was filtered through a Celite pad, dried ($MgSO_4$), and concentrated to dryness in vacuo. Column chromatography on a short column afforded 71 mg of a thick colorless syrup, which contained the coupling product as determed by MS (ES): *m*/*z* 1469.0 (M + Na).

The crude product was dissolved in MeCN (1.0 mL), and thiocarbonyldiimidazole (219 mg, 1.23 mmol) was added. After refluxing overnight, the solvent was slowly evaporated off by continued heating. The residue obtained was subjected to column chromatography (EtOAc:pentane, 1:3 to 1:1), yielding 52 mg (63% for two steps) of the dithionocarbamate **45** as a thick colorless syrup. MS (ES) *m*/*z* 1667.7 (M + H), 1689.8 (M + Na), 1705.8 (M + K).

To a solution of **45** (140 mg, 0.084 mmol) in toluene (4.0 mL) were added pentafluorophenol (62 mg, 0.34 mmol), triphenyltin hydride (111 mg, 0.44 mmol), and a catalytic amount of AIBN (3 mg). This mixture was refluxed for 2.5 h, and then the solvent was removed by evaporation in vacuo. The residue was redissolved in acetonitrile and washed two times with pentane. After concentration to dryness in vacuo, column chromatography (acetone:CH_2Cl_2, 1:100 to 1:40) afforded 64 mg (53%) of the trisaccharide **46** as a colorless syrup: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36−7.15 (50H, m), 4.76 (1H, d, J = 11.2 Hz), 4.71 (1H, d, J = 11.6 Hz), 4.64 (1H, d, J = 12.4 Hz), 4.59 (1H, bs), 4.55 (1H, d, J = 12.4 Hz), 4.55 (2H, s), 4.54 (1H, d, J = 11.6 Hz), 4.52 (1H, d, J = 11.2 Hz), 4.51 (2H, s), 4.50 (1H, d, J = 10.8 Hz), 4.49 (2H, s), 4.48 (1H, d, J = 10.8 Hz), 4.48 (2H, s), 4.45 (1H, d, J = 10.8 Hz), 4.44 (1H, d, J = 11.6 Hz), 4.43 (1H, d, J = 10.8 Hz), 4.41 (1H, d, J = 11.6 Hz), 4.10 (1H, ddd, J = 4.0, 4.4, 8.4), 4.05 (1H, ddd, J = 4.0, 4.0, 9.2), 3.96 (1H, dd, J = 7.2, 7.6), 3.84−3.66 (10H, m), 3.64 (1H, bs), 3.59 (1H, dd, J = 3.2, 3.2), 3.53−3.47 (2H, m), 3.24 (3H, s), 2.11−2.04 (1H, m), 2.00−1.89 (1H, m), 1.85−1.62 (4H, m), 1.44−1.34 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 138.6, 138.6, 138.5, 138.5, 138.4, 138.4, 138.4, 138.4, 138.4, 138.3, 128.6−127.7, 97.0, 79.6, 79.6, 78.4, 77.6, 77.5, 76.4, 76.2, 75.2, 75.2, 74.6, 74.1, 73.6, 73.6, 73.5, 73.5, 73.2, 73.0, 72.3, 72.3, 72.3, 72.0, 71.7, 71.7, 69.7, 69.4, 54.9, 28.6, 26.9, 25.6, 25.6; HR-MS (ES) calcd for $C_{91}H_{98}O_{14}Na$ (M + Na) 1437.6854, found 1437.6859.

Methyl 3,6-Dideoxy-3,6-*C*-di-(1′/1″-deoxy-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (1). A mixture of the perbenzylated *C*-trisaccharide **46** (63 mg, 0.045 mmol) and 10% Pd/C (47 mg) in MeOH (6.0 mL) and glacial acetic acid (1.0 mL) was stirred under an atmosphere of hydrogen overnight. The reaction mixture was filtered through Celite and coevaporated three times with toluene. TLC analysis revealed a single product (R_f = 0.30, MeOH:CH_2Cl_2, 1:1): ^{1}H NMR (D_2O, 800 MHz) δ = 4.60 (1H, d, J = 1.2 Hz), 4.06 (1H, ddd, J = 1.7, 4.6, 9.2 Hz), 3.94 (1H, ddd, J = 1.9, 3.6, 10.8

Hz), 3.91−3.90 (2H, m), 3.90 (1H, dd, J = 1.9, 3.4 Hz), 3.86 (1H, dd, J = 2.3, 12.1 Hz), 3.84 (1H, dd, J = 2.4, 12.2 Hz), 3.84 (1H, dd, J = 3.4, 9.5 Hz), 3.80 (1H, dd, J = 3.3, 8.7 Hz), 3.71 (1H, dd, J = 6.3, 12.2 Hz), 3.70 (1H, dd, J = 6.0, 12.1 Hz), 3.63 (1H, dd, J = 9.5, 9.5 Hz), 3.62 (1H, dd, J = 8.7, 9.6 Hz), 3.60 (1H, ddd, J = 2.3, 6.0, 9.6 Hz), 3.55 (1H, ddd, J = 2.6, 9.4, 10.1 Hz), 3.54 (1H, ddd, J = 2.4, 6.3, 9.5 Hz), 3.40 (3H, s), 3.32 (1H, dd, J = 9.7, 10.1 Hz), 2.02 (1H, ddd, J = 10.3, 10.5, 10.8 Hz), 1.93 (1H, ddd, J = 9.2, 9.2, 15.7 Hz), 1.89−1.82 (3H, m), 1.62−1.55 (2H, m); ^{13}C NMR (125 MHz) δ 99.8, 77.8, 77.7, 73.1, 73.0, 72.2, 71.1, 71.0, 70.1, 70.0, 69.1, 68.2, 67.2, 67.1, 60.5, 60.4, 39.0, 26.9, 24.1, 22.5; HR-MS (ES) calcd for $C_{21}H_{38}O_{14}Na$ (M + Na) 537.2159, found 537.2172.

Methyl 2,4-Di-*O*-acetyl-3,6-dideoxy-3,6-*C*-di-(1′/1″-(2′/2″,3′/3″,4′/4″,6′/6″-tetra-*O*-acetyl-1′/1″-deoxy-α-D-mannopyranosyl)methylene)-α-D-mannopyranoside (47). The free *C*-trisaccharide **1** was dissolved in pyridine (4 mL) and Ac_2O (2 mL) and left standing overnight. Coevaporation three times with toluene and column chromatography (EtOAc:pentane, 1:2 to 1:1) yielded **47** as a colorless thick syrup: ^{1}H NMR (400 MHz) δ = 5.25 (1H, dd, J = 3.2, 8.4 Hz), 5.21 (1H, dd, J = 8.4, 8.4 Hz), 5.18 (1H, dd, J = 3.6, 7.6 Hz), 5.15 (1H, dd, J = 3.2, 3.2 Hz), 5.07 (1H, dd, J = 6.0, 7.6 Hz), 4.99−4.94 (2H, m), 4.87 (1H, dd, J = 10.0, 10.8 Hz), 4.59 (1H, bs), 4.45 (1H, dd, J = 7.6, 12.0 Hz), 4.36 (1H, dd, J = 6.4, 12.0 Hz), 4.07 (1H, d, J = 12.0 Hz), 4.07 (1H, d, J = 12.0 Hz), 3.97−3.91 (2H, m), 3.89−3.82 (2H, m), 3.68−3.62 (1H, m), 3.36 (3H, s), 2.32 (1H, m), 2.15 (3H, s), 2.12 (3H, s), 2.11 (3H, s), 2.11 (3H, s), 2.11−2.08 (1H, m), 2.10 (3H, s), 2.08 (3H, s), 2.08 (3H, s), 2.06 (3H, s), 2.05 (3H, s), 2.02 (3H, s), 1.70−1.46 (5H, m); ^{1}H NMR (400 MHz, benzene-d_6) δ = 5.53 (1H, dd, J = 3.0, 6.0 Hz), 5.48 (1H, dd, J = 3.6, 8.8 Hz), 5.45 (1H, dd, J = 7.6, 8.8 Hz), 5.38 (1H, dd, J = 3.2, 3.6 Hz), 5.28 (1H, dd, J = 3.0, 6.4 Hz), 5.25 (1H, dd, J = 1.6, 2.4 Hz), 5.23 (1H, dd, J = 9.2, 10.4 Hz), 5.17 (1H, dd, J = 4.8, 6.0 Hz), 4.72 (1H, dd, J = 7.2, 11.6 Hz), 4.64 (1H, d, J = 1.6 Hz), 4.48 (1H, dd, J = 7.2, 12.0 Hz), 4.16 (1H, ddd, J = 4.8, 6.4, 7.6 Hz), 4.04 (1H, dd, J = 2.8, 12.0 Hz), 4.00 (2H, m), 3.95 (1H, ddd, J = 3.2, 3.6, 10.4 Hz), 3.89 (1H, ddd, J = 2.8, 7.2, 7.6 Hz), 3.69 (1H, ddd, J = 2.8, 9.2, 9.2 Hz), 2.96 (3H, s), 2.54 (1H, m), 2.06 (1H, m), 1.88 (3H, s), 1.84 (3H, s), 1.81 (3H, s), 1.81 (2H, m), 1.67 (3H, s), 1.65 (3H, s), 1.65 (3H, s), 1.61 (3H, s), 1.58 (3H, s), 1.57 (3H, s), 1.57 (1H, m), 1.49 (3H, s), 1.30 (2H, m); HR-MS (ES) calcd for $C_{41}H_{58}O_{24}Na$ (M + Na) 957.3215, found 957.3216.

Acknowledgment. We are indebted to the Danish National Science Foundation (THOR Program), the University of Aarhus, and the Carlsberg Foundation for generous financial support.

Supporting Information Available: Experimental details for the synthesis of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside; ^{1}H NMR spectra for compounds **1**, **2**, **17**, **21**, **23**, **29**−**34**, TMS−**35**, **36**−**47;** and ^{13}C NMR spectra for compounds **2**, **17**, **21**, **23**, **29**, **30**, **32**, **34**, TMS−**35**, **36**−**39**, **41**−**46**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO020339Z