Samarium Diiodide Promoted *C*-Glycosylation: An Application to the Stereospecific Synthesis of α-1,2-*C*-Mannobioside and Its Derivatives

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Abstract: The synthesis of the *C*-glycoside analogue of the disaccharide Man(α1$\rightarrow$2)Man has been achieved in a highly stereoselective and efficient manner employing an approach which closely parallels *O*-glycoside synthesis. The key step included the samarium diiodide reduction of mannosyl pyridylsulfone **18** in the presence of the C2-formyl branched mannoside derivative **17a** to furnish the *C*-disaccharide derivative **19a** in high yield. An intramolecular formyl group transfer reaction by means of 5-*exo* radical cyclization and concomitant fragmentation yielded aldehyde **17a** stereospecifically. We also present a potentially viable alternative for the deoxygenation of sterically encumbered secondary alcohols. Attempts to extend this procedure to the synthesis of the *C*-trisaccharide of Man(α1$\rightarrow$2)Man(α1$\rightarrow$2)Man were frustrated by the inability of the disaccharide, pyridylsulfone derivative **43**, to undergo coupling with carbonyl substrates upon treatment with SmI_2, possibly owing to the sterically bulky C2 substituent.

Keywords: C–C coupling · carbanions · *C*-glycosides · radicals · samarium

Introduction

It is now well established that cell surface carbohydrates participate in key molecular recognition events with protein receptors.[1] Although such interactions are important elements for cell-to-cell recognition and binding, they may also be harmful in that they provide the initial steps in bacterial[2] and viral infections,[3] as well as cell adhesion in inflammation[4] and metastasis.[5] Strategies for the prevention of such diseases include the preparation of small, soluble carbohydrate-based pharmaceuticals which may inhibit this recognition event by preferential binding to the protein receptor. However, the low binding constants of carbohydrates with proteins and the potential instability of oligosaccharides to extra- and intracellular glycosidases have opened a new field for the development of carbohydrate mimics.[6]

An important class of glycomimetics includes the *C*-glycosides in which the interglycosidic linkage (for example in a disaccharide) has been substituted by a methylene group; this renders these analogues completely resistant to hydrolysis.[7] For these compounds to become promising drug candidates it is also apparent that the solution conformational behavior should be similar to that of the parent *O*-glycoside. Although initial investigations by Kishi and co-workers suggest this is true,[8] more rigorous studies performed by Jiménez-Barbero have demonstrated that certain *C*-glycosides are more flexible, possessing other non-*exo*-anomeric conformations.[9, 10] Nevertheless, for the evaluation of *C*-glycosides as inhibitors of the detrimental cellular interactions described above, a general and rapid approach for the efficient construction of a broad class of these mimics is required. Kishi's group has prepared a wealth of *C*-disaccharides and some *C*-trisaccharides in order to investigate their conformational properties.[8] The synthetic completion for each *C*-glycoside was in general brought about by the de novo synthesis of at least one of the pyranyl ring systems. Schmidt and co-workers used C1-lithiated glycals, and their coupling to branched sugars has proved to be a viable route to several β-*C*-disaccharides.[11] On the other hand, Sinaÿ and collaborators have provided a synthetic stratagem to *C*-disaccharides employing tin hydride promoted 8- and 9-*endo* radical cyclizations with disposable tethers that control the stereochemistry at the anomeric center.[12] Finally, the Armstrong group recently reported the preparation of stereochemically diverse *C*-disaccharides and trisaccharides by means of a nonstereoselective and partial de novo synthesis from noncarbohydrate precursors.[13]

In contrast, we demonstrate in this paper the use of anomeric organosamarium species as a possible route for the

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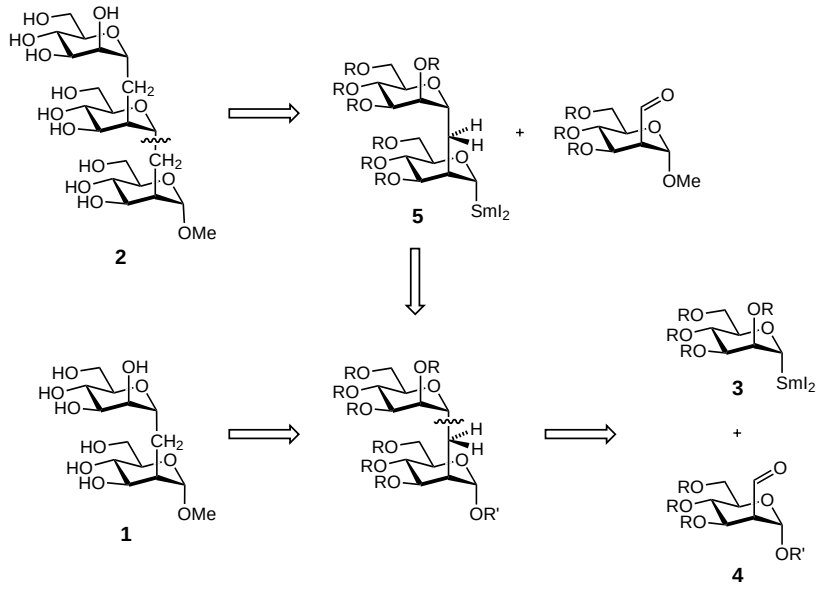
direct preparation of *C*-disaccharides, providing an example of *C*-disaccharide construction which parallels *O*-glycoside synthesis through the use of intact monosaccharide units as both donors and acceptors. We also disclose our attempts to extend this approach to the synthesis of a *C*-trisaccharide. The advantages and disadvantages of this methodology will be discussed.[14]

Results and Discussion

We have recently reported that reductive samariation of mannosyl and glucosyl pyridylsulfones in the presence of carbonyl substrates leads to the mild and stereospecific synthesis of 1,2-*trans*-*C*-glycosides, where β-elimination affording D-glucal is not a major concern in contrast to similar reactions performed with the corresponding C1 lithium derivatives.[15] In addition, this approach was successfully applied to the synthesis of a *C*-glycoside analogue of Man(α1→2)Glu employing a C2-formyl derivative of glucose.[15a,d] In order to expand this approach, we wished to synthesize the analogous *C*-glycoside of the disaccharide Man(α1→2)Man and the trisaccharide Man(α1→2)Man-(α1→2)Man, which are not only important constituents of *N*-glycoproteins but have also been identified as the principal capping residues of a major cell surface lipopolysaccharide of pathogenic mycobacteria strains (for example *Mycobacteria tuberculosis*), partly responsible for the recognition, uptake, and survival of mycobacteria in macrophages.[16, 17] We were also interested as to whether the conformational properties of this α-linked *C*-disaccharide and *C*-trisaccharide would be similar to those of the parent *O*-glycosides, and whether derivatives of the disaccharide could be potential inhibitors of Man(α1→2)Man glycosidases (for example the *N*-glycoprotein-trimming glycosidases).[9d]

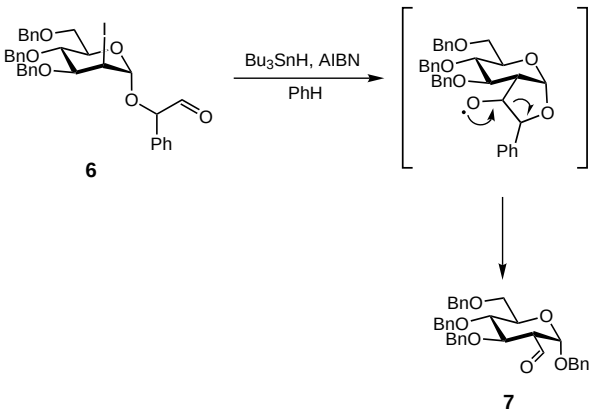
Our synthetic approach to the methyl *C*-mannobioside **1** and *C*-mannotrioside **2** is outlined in Scheme 1. The salient step of this synthesis involves the coupling of the mannosyl organosamarium species **3,** prepared by means of the SmI_2 reduction of the corresponding pyridylsulfone, with the C2-aldehydo-sugar **4**. Our earlier observations with **3** show that this organometallic species couples efficiently with carbonyl substrates without the competing β-elimination to give D-glucal.[15a,d,e] Subsequent dehydroxylation and deprotection would then lead to the desired *C*-disaccharide. Employing a suitable protecting group at the anomeric center of **4** would allow its selective demasking and derivatization to generate a new organosamarium species **5**, which could couple to aldehyde **4** (R′ = Me), thus extending our procedure to the preparation of *C*-trisaccharides in an iterative fashion. The interesting feature of this approach is its close resemblance to that of *O*-disaccharide and oligosaccharide synthesis.[18]



Scheme 1. Retrosynthetic analysis of the *C*-disaccharide Man(α1→2)Man (**1**) and the *C*-trisaccharide Man(α1→2)Man(α1→2)Man (**2**).

Although there were several potential routes to aldehyde **4**, we were particularly interested in adapting an approach for the preparation of C2-formyl substituted sugars as previously reported by Jung and Choe (Scheme 2).[19, 20] In this work, the authors demonstrated that substrate **6**, obtained by iodoglycosylation of tribenzylglucal with 1-phenylprop-2-enol and then ozonolysis, could easily undergo a 5-*exo* radical cyclization–fragmentation process resulting in the intramolecular transfer of a formyl group to C2 and generation of a more stable benzyl radical. The nice feature of this method is that

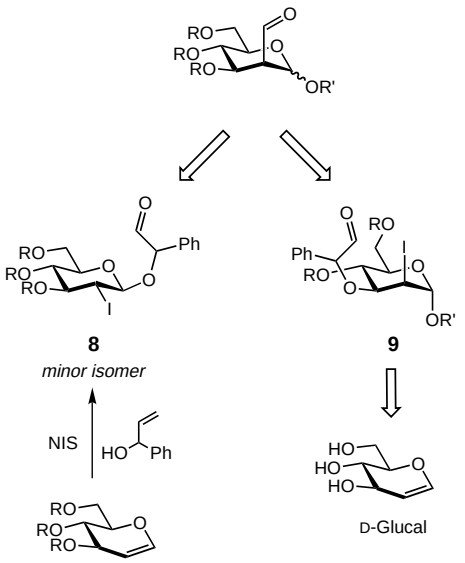
Abstract in Danish: *En C-glykosid analog af disaccharidet Man(α1→2)Man er blevet fremstillet på en effektiv og meget stereoselektiv måde ved brug af en C-glykosyleringsmetode som kan sammenlignes med tilsvarende O-glykosyleringreaktioner. Nøgle reaktionen i syntesen består af en kobling i højt udbytte mellem mannosyl pyridylsulfon **18** og et passende C2-formyl forgrenet kulhydrat **17a** i nærværelse af samariumdiiodid. **17a** kunne til gengæld fremstilles via en intramolekulær formyl gruppe overførsel ved hjælp af en 5-exo radikalcyklisering efterfulgt af en fragmenteringsproces. En alternativ metode til deoxygenering af sterisk hindrede sekundære alkoholer er også vist. Forsøg på at udvide denne C-glykosyleringsmetode til C-trisaccharider, såsom Man(α1→2)Man(α1→2)Man, var ikke frugtbar, da den samariumdiiodid-inducerede reaktion mellem pyridylsulfon **43** og **17a** eller cyclohexanone ikke gav nogen koblingsprodukter, muligvis på grund af den sterisk hindrende C2-substituent.*



Scheme 2. Preparation of a C2-branched sugar **7** as reported by Jung and Choe.[19]

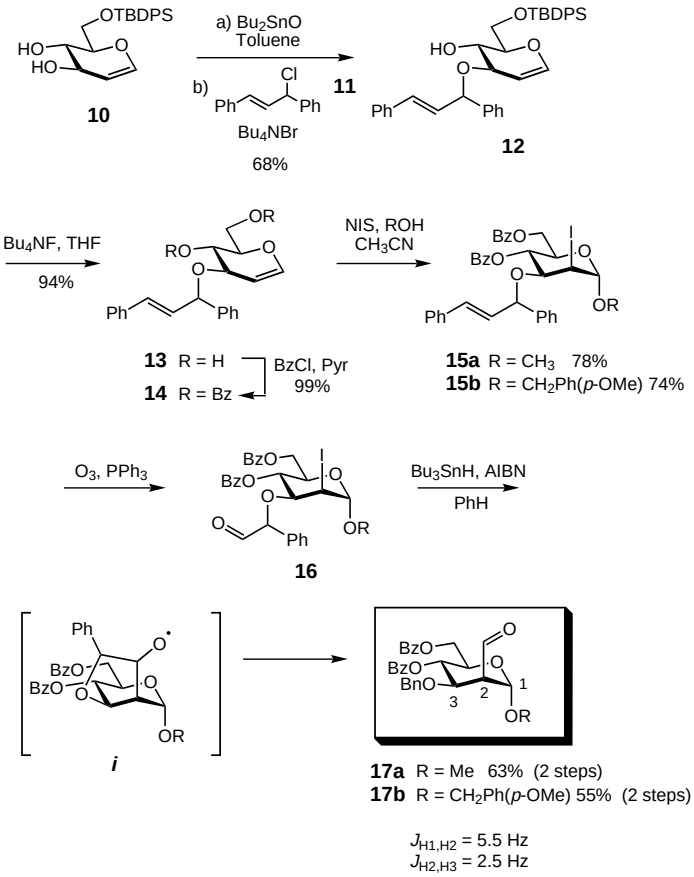
not only is the formyl group transferred stereospecifically to give the 1,2-*cis* relationship in **7** owing to the 5-membered cyclic intermediate in the transfer mechanism, but the original functionality at the anomeric center is itself transformed to the well-known benzyl protecting group.

This approach, suitable for the preparation of equatorial-oriented C2-aldehydosugars, would require some modification to allow the introduction of the formyl group in the axial position as required in our case. This gave us two choices, depicted in Scheme 3: we could either employ iodide **8** possessing diequatorial C1,C2-substituents, which is obtained as the minor isomer in approximately 20% yield under the iodoglycosylation reaction,[19] or attempt the formyl group transfer from the correctly disposed C3-hydroxy group as in **9**. The second option appeared to be the more profitable.



Scheme 3. Possible synthetic approaches to the 2-deoxy-*C*2-formyl-mannoside.

Synthesis of the C2-branched sugar 16: Selective functionalization of the C3-OH of D-glucal required initial protection of the primary alcohol (Scheme 4). Hence D-glucal was converted to the TBDPSi derivative **10** with TBDPSiCl and imidazole as previously reported.[21] In order to introduce the proper alkyl substituent necessary for the formyl group transfer, we decided to alkylate with the known chloride **11**[22] as any competing S_N2 and S_N2' reactions in this case would lead to the same product. Glucal **10** was therefore



Scheme 4. Synthesis of aldehydes **17a** and **17b** by means of a radical cyclization–fragmentation approach.

transformed to the corresponding stannylene with Bu_2SnO in refluxing toluene and then treated with nBu_4NBr and chloride **11** at 0 °C for 12 h, affording a 68% yield of the derivatized glucal **12**. Subsequent desilylation and benzoylation of the C4- and C6-hydroxy groups led to the dibenzoate **14** in an overall yield of 94%. Iodoglycosylation was achieved according to that previously published.[23] *N*-Iodosuccinimide was added to an acetonitrile solution of **14** and methanol at 0 °C to give a 78% yield of the methyl glycoside **15a**. Small amounts of the diequatorial C1,C2-isomer were also detected. Finally, **15a** was subjected to ozonolysis to furnish aldehyde **16**, which was immediately used in the following transfer step. Treatment with Bu_3SnH in refluxing benzene for 1 h and subsequent workup led to the isolation of a single aldehyde **17a** in 63% yield (2 steps). The configuration shown in **17a** was deduced from the following spectral observations. The small coupling constants between H1 and H2, and between H2 and H3 ($J_{H1,H2} = 5.5$ Hz, $J_{H2,H3} = 2.5$ Hz) in the ^1H NMR spectrum are consistent with a structure in which the formyl group occupies an axial orientation at the C2 position. A larger *trans*-diaxial H2,H3 coupling constant of approximately 9.0 Hz would have

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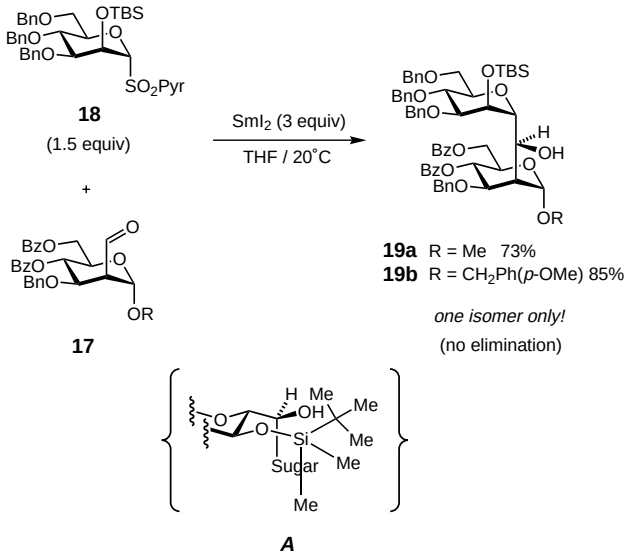
been expected if the formyl group was in the equatorial position as for **7**. The stereospecificity observed in the transfer step therefore implies that the cyclic oxyradical ***i*** is a true intermediate of this reaction. In addition, no epimerization to the more stable equatorial aldehyde was noted.

Coupling and completion of disaccharide 1: With aldehyde **17a** secured, the stage was set for the coupling between the two monosaccharide components. Following our earlier reported procedure for the SmI_2-promoted Barbier reactions with glycosyl pyridylsulfones,[15a,d,e] two equivalents of SmI_2 with respect to the pyridylsulfone were added quickly to a concentrated THF solution of the mannosyl derivative **18** (1.5 equiv) and aldehyde **17a**; this resulted in an immediate decoloration of the one-electron reducing agent signaling the completion of the reaction. As previously observed with pyridylsulfone **18**, no β-elimination occurred, but instead the *C*-disaccharide **19a** could be isolated in good yield as a sole diastereomer at the two newly created stereogenic centers after chromatographic purification (Scheme 5). While the

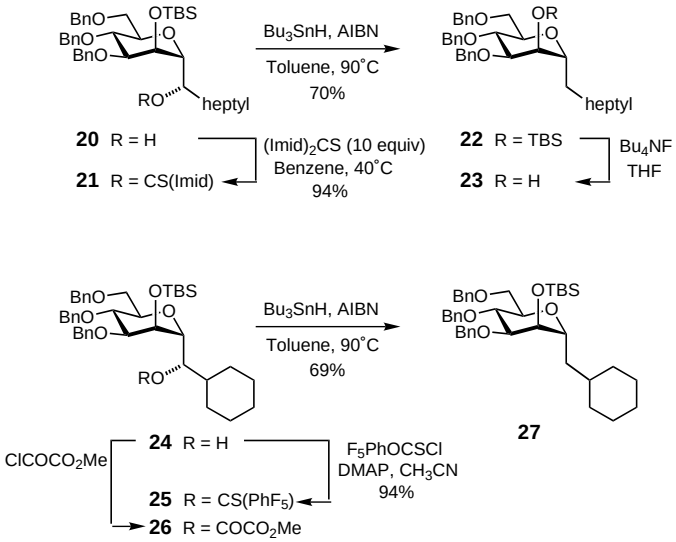


Scheme 5. Coupling of aldehyde **17** with the mannosyl pyridylsulfone **18**.

exclusive formation of the α-anomer was anticipated, the high stereoselectivity at the exocyclic stereocenter contradicts that observed with simple aldehydes, reflecting the large sterical encumbrance of the aldehyde substituent in **17**.[24] Based on the stereochemical assignments previously made for the major isomer obtained from the coupling of **18** with octanal, we tentatively attributed the (*S*)-configuration to the exocyclic stereocenter in **19a**.[15d]

In analogy with the *C*-mannosides previously obtained, the nonreducing sugar of **19a** had a skew-boat conformation, as seen from its ^{1}H NMR coupling constants ($J_{H1',H2'} = 8.5$ Hz, $J_{H2',H3'} = 3.0$ Hz, $J_{H3',H4'} = 4.0$ Hz, $J_{H4',H5'} = 3.0$ Hz). Although this was an expected observation, CPK models of this system suggested that the secondary alcohol used for transformation or deoxygenation was in a sterically demanding environment owing to the bulky TBS protecting group at the C2′-OH as shown in conformer **A** (Scheme 5).

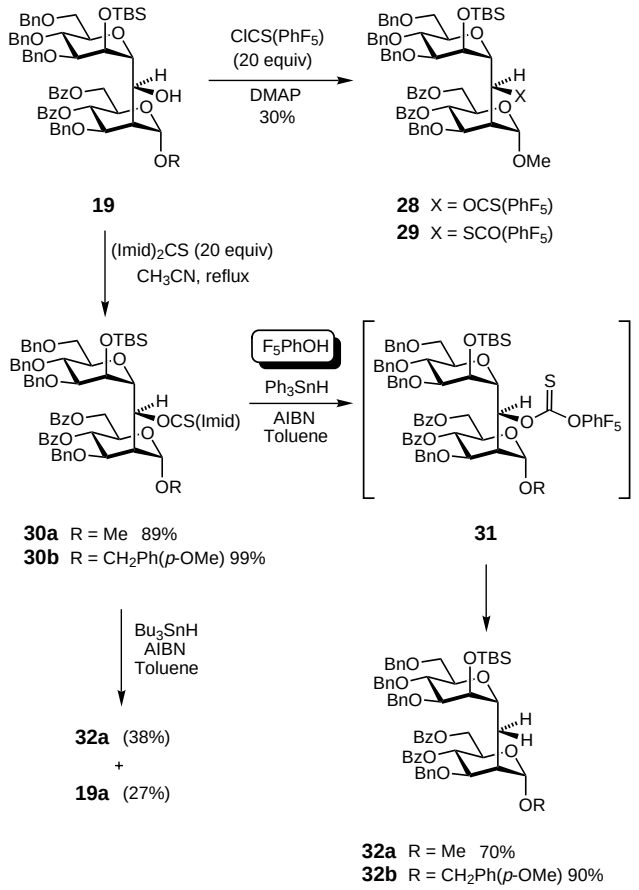
To test the ease of removal of the unwanted alcohol, we examined the model system **20** prepared earlier by the coupling of **18** with *n*-octanal (Scheme 6). Treatment of **20** with thiocarbonyldiimidazole (10 equiv) in benzene at 40 °C for 12 h, led to its smooth conversion to the thiocarbonyl derivative **21** in 94 % yield. Deoxygenation employing the standard protocol (Bu_3SnH, AIBN) in toluene at 90 °C led to the expected *C*-glycoside **22** in 70 % yield, which could also be desilylated to the alcohol **23**. However, we quickly discovered that the secondary alcohol in **19a** was quite resistant to functionalization. Attempted thiocarbonylation employing similar conditions as above were fruitless, even upon refluxing in toluene for 12 h.



Scheme 6. Model studies for the deoxygenation of the exocyclic hydroxy group.

With the purpose of investigating other dehydroxylation systems, we converted the model compound **24** to the highly radicophilic thionocarbonate **25** in an 82 % yield employing commercially available pentafluorophenyl chlorothionoformate (3 equiv) and DMAP (5 equiv) in acetonitrile (Scheme 6).[25] Deoxygenation in refluxing toluene with Bu_3SnH proceeded quickly (15 min) affording the *C*-glycoside **27** in 69 % yield. Although **24** could easily be transformed to the methyl oxalolate **26** in quantitative yields, a known procedure for deoxygenating tertiary alcohols,[26] the subsequent radical deoxygenation step with **26** led only to the formation of a complex mixture.

When alcohol **19a** was subjected to similar thiocarbonylating conditions, 20 equivalents of the chlorothionoformate were required for the reaction to reach completion, and the products, approximately 30 % yield, were not only the desired thionocarbonate **28** but also the rearranged product, the thiocarbonate **29**, in a ratio of 1 to 3, respectively (Scheme 7). The driving force behind this rearrangement is likely to be the combination of some strain energy release on going from the sp^3 C–O bond to the longer sp^3 C–S bond and the formation of the stronger C=O bond.[27] Although **29** could be reduced, we did not pursue this route due to the inefficiency of the thiocarbonylating step.

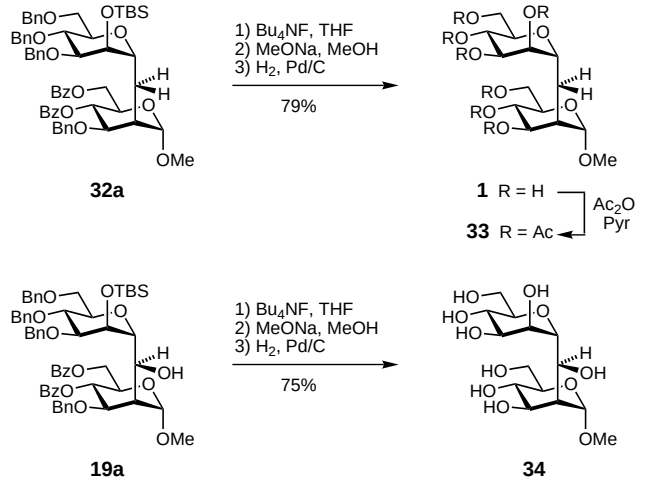


Scheme 7. Deoxygenation of the *C*-disaccharide **19**.

Finally, we returned to the use of thiocarbonyldiimidazole, and treated **19a** with 20 equivalents of the thiocarbonylating reagent in refluxing acetonitrile (Scheme 7). Whereas only a little conversion was noted (TLC analysis) after 10 hours, it was found that slowly concentrating the solution to near-dryness at 100 °C led to the conversion of **19a** to the desired thiocarbonylimidazole derivative **30a** in high yield after chromatographic purification. Having surmounted this obstacle we were immediately confronted with a second. Subjecting **30a** to the radical deoxygenation conditions with Bu_3SnH in hot toluene afforded only a 38% yield of the *C*-disaccharide **32a** along with the alcohol **19a** (27%). The use of the more reactive triphenyltin hydride did not improve the reduction yields. The sterically encumbering environment surrounding the thionocarbamate was most likely the cause for this poor yield. We reasoned that increasing the radicophilicity of the C=S bond could be a possible remedy to this problem. It was hoped that treatment of **30a** with pentafluorophenol under the tin hydride reduction conditions would lead to the in situ formation of **31a**, and that its high reactivity with the tin radical would supercede its rearrangement to the thiocarbonate **29**. Indeed, when **30a** was treated with pentafluorophenol (2 equiv), triphenylstannane (2.5 equiv) and AIBN in hot toluene, a gratifying 70% yield of the protected *C*-disaccharide **32a** could be isolated. This procedure therefore represents a potential alternative for the effective reductive deoxygenation of sterically inaccessible secondary hydroxy groups.

It is interesting to note the conformational consequences of the dehydroxylation step on the nonreducing sugar of the *C*-mannobioside. Absence of functionality at C7 restores the normal $^4C_1$ chair conformation for the nonreducing sugar as seen from the larger *trans*-diaxial coupling constants between H3′ and H4′ and between H4′ and H5′ in the ^{1}H NMR spectrum of **32a** ($J_{H3',H4'} = 7.4$ Hz, $J_{H4',H5'} = 7.4$ Hz) compared with **19a**.

A three-step deprotection sequence involving desilylation, debenzoylation and hydrogenolysis finally afforded the methyl *C*-mannobioside **1** in an overall yield of 79%, completing this highly convergent and stereoselective synthesis of a *C*-disaccharide (Scheme 8). To simplify the characterization, **1** was converted to its heptaacetate **33**, which clearly displayed two conformationally normal monosaccharide units.



Scheme 8. The final steps to the *C*-disaccharides **1** and **34**.

In order to examine the conformational influence of substituents at the methylene bridge of the α-*C*-disaccharide, the hydroxy derivative **34** was prepared from **19a** employing a similar three-step deprotection protocol as used above (Scheme 8).[9d] We also focused our attention on the preparation of the fluoro derivative **35**, and the recent work of Motherwell and co-workers on the mild formation of alkyl fluorides employing xanthate esters and 4-methyl(difluoroiodo)benzene seemed particularly appealing.[28] As the deoxygenation step of **19a** requires the thiocarbonylimidazole derivative **30a**, we treated this compound with the (difluoroiodo)arene, even though methyl xanthates had been used before for such conversions. However, when performed under conditions suggested by Motherwell, a sole compound was isolated whose ^{1}H NMR spectrum did not conform with that of the desired fluoride but that of the interesting imidazole derivative **36** (Scheme 9).[29] This was somewhat surprising, considering the absence of such compounds in the previous cases reported. We tentatively explain this by invoking intermediate ***ii***. Perhaps the steric hindrance at C7 in ***ii*** is too pronounced for the introduction of a nucleophile even as small as the fluoride ion, therefore favoring a rearrangement with intramolecular transfer of the imidazole group, as shown in Scheme 9.

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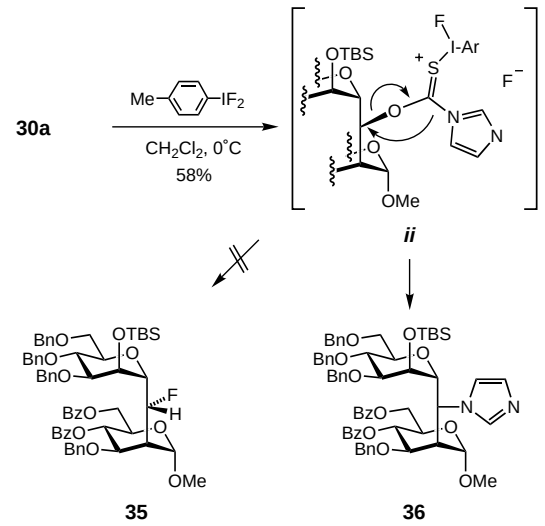
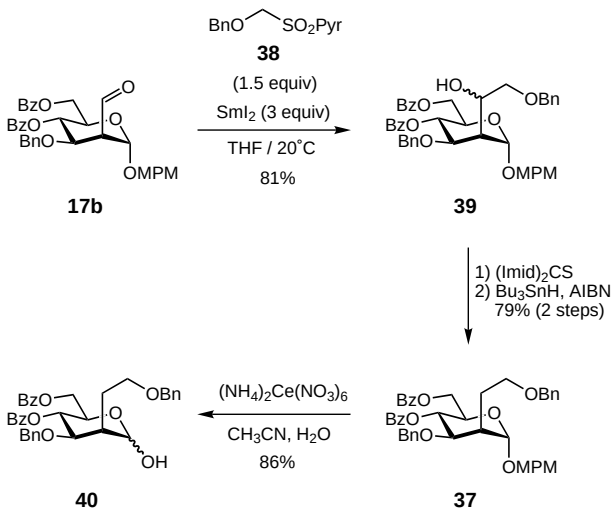


Scheme 9. Attempts to prepare fluoride **35**.



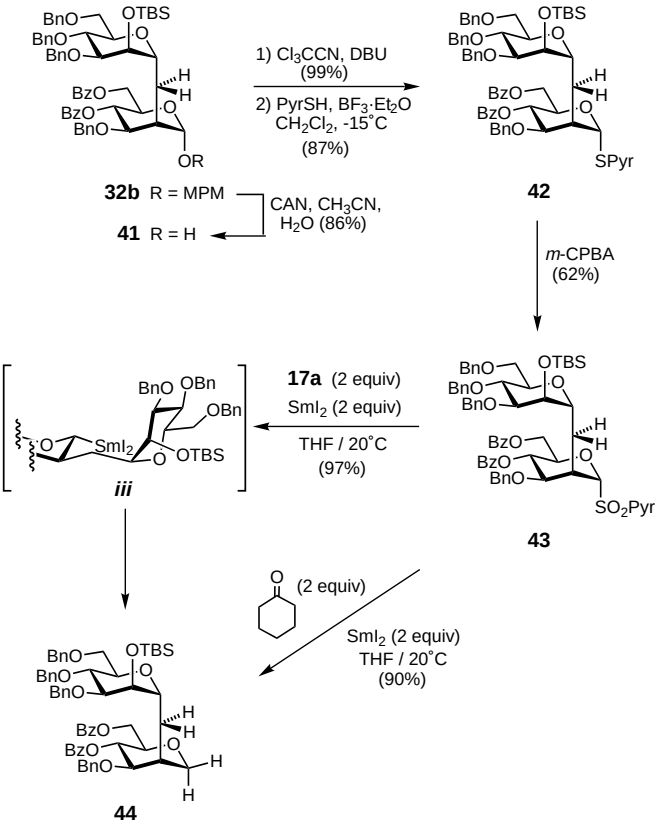
Scheme 10. Preparation of model compound **37** and its deprotection at the anomeric center.

Attempted extrapolation to the synthesis of methyl *C*-mannotrioside: With the successful construction of the *C*-mannobioside, we turned to the incorporation of a third mannosyl unit by coupling the disaccharide samarium diiodide species **5** with aldehyde **17a** (Scheme 1). This required modification of our mannobioside synthesis so that an appropriate protecting group on the anomeric hydroxy group of the reducing sugar could be incorporated, then selectively unmasked in the presence of the others. The use of *p*-methoxyphenylmethyl (MPM) ethers for the protection of anomeric centers had been used with satisfactory results and hence appeared suitable for our case.[30]

Synthesis of aldehyde **17b** was then commenced by a similar route as for **17a** (Scheme 4). Iodoglycosylation of glucal **14** with *p*-methoxybenzyl alcohol afforded iodide **15b** in good yield, followed by the ozonolysis and formyl group transfer to give the aldehyde **17b** in a combined yield of 54%. Subsequent SmI_2-promoted coupling of this unit to pyridylsulfone **18** again proved quite rewarding, efficiently generating disaccharide **19b**, which could subsequently be deoxygenated in 90% yield by our above protocol.

The efficiency of the C1 O-protecting group removal was tested by preparing the C2-branched sugar **37** in three steps from aldehyde **17b** (Scheme 10). According to our recently published method for the mild introduction of a benzyloxymethyl group, a THF solution of pyridylsulfone **38** and aldehyde **17b** was treated with SmI_2; this led to the formation of alcohol **39** in an 81% yield.[31] This compound was subsequently deoxygenated in two steps to give **37**. Modification of the previously reported conditions [10 equivalents of cerium ammonium nitrate (CAN) in an acetonitrile/water mixture for 5 min at 20 °C] permitted the removal of the MPM group to the hemiacetal **40** in 86% yield.

In a similar fashion the MPM group could be oxidatively removed from **32b** to give the hemiacetal **41** in an identical yield (Scheme 11). Conversion to the anomeric pyridylsulfide proceeded inefficiently if **41** was treated with dipyridyldisulfide in the presence of tributylphosphine, in which case substantial amounts of the *N*-glycosylated product were



Scheme 11. Synthesis of the mannobiosyl pyridylsulfone **43** and its attempted coupling with aldehyde **17a** and cyclohexanone.

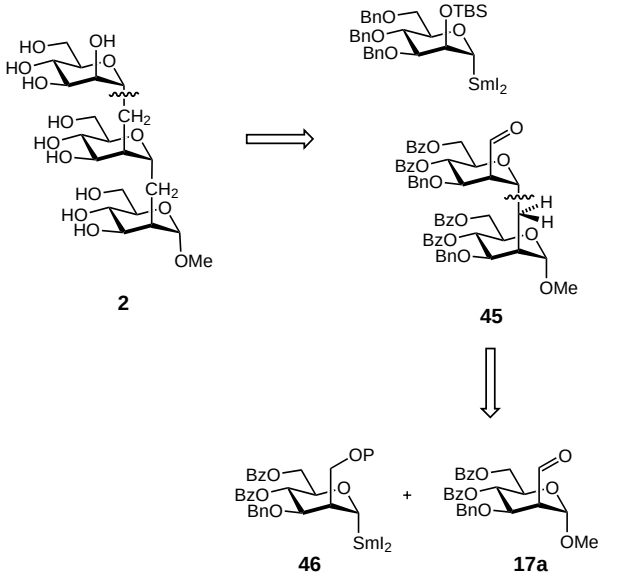
obtained. However, converting **41** to its trichloroacetimidate with trichloroacetonitrile and DBU in CH_2Cl_2, followed by treatment with thiopyridine and $BF_3 \cdot Et_2O$ (0.2 equiv) in the same solvent at -23 °C gave the pyridylsulfide **42** in 87% yield (2 steps).[15d] Further oxidation with MCPBA then led to the sulfone **43**.

Unfortunately, all attempts to couple pyridylsulfone **43** with aldehyde **17a** failed even with a substantial increase in the number of equivalents of the aldehyde used. The 1-deoxy-*C*-

disaccharide **44** was the sole product isolated from the reaction mixture. The same results were obtained with cyclohexanone. This observation was particularly surprising considering the successful Barbier reactions with the mannosyl pyridylsulfone **18**.[15a,c–e]

The inability of **43** to couple to carbonyl may be explained by the fact that although the reducing sugar in pyridylsulfone **43** adopts the normal $^4C_1$ chair conformation, in the anomeric samarium species this conformation will flip to that of an $^OS_2$ skew-boat as in ***iii*** (Scheme 11) placing the C1 and C2 substituents in pseudoequatorial positions. This orientation places the large and bulky sugar substituent at C2 in an unfavorable position, thus blocking the introduction of a carbonyl substrate to the anomeric carbanion.

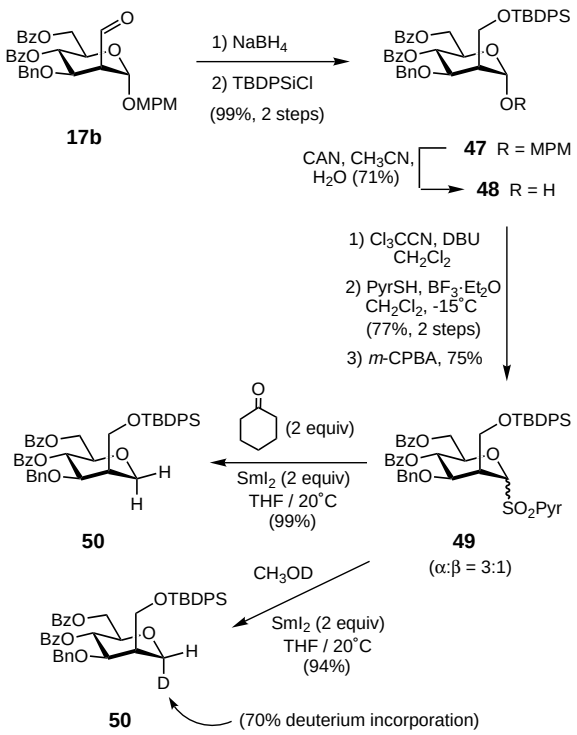
To circumvent this problem we decided to build up the *C*-mannotrioside in the reverse order as depicted in Scheme 12, where the final coupling reaction would involve the *C*-branched disaccharide **45** and the organosamarium derivative prepared from pyridylsulfone **18**. In turn, **45** could be prepared from the Barbier reaction of the anomeric organosamarium **46** with aldehyde **17a**. To prepare the precursor to



Scheme 12. An alternative synthetic approach to the *C*-trisaccharide Man(α1 $\rightarrow$2)Man(α1 $\rightarrow$2)Man (**2**).

this glycosyl samarium species we took advantage of our previous synthesis of aldehyde **17b**, which has a disposable protecting group at C1 (Scheme 13). Hence, sodium borohydride reduction of the formyl group in **17b** and subsequent protection of the primary alcohol gave the TBDPSi ether **47**. Oxidative removal of the MPM group with CAN then provided the hemiacetal **48**, which could be converted by a three-step procedure to the pyridylsulfone **49**. A similar sequence incorporating a TBS group at the primary alcohol was less rewarding and led to extensive desilylation during the cleavage of the MPM ether.

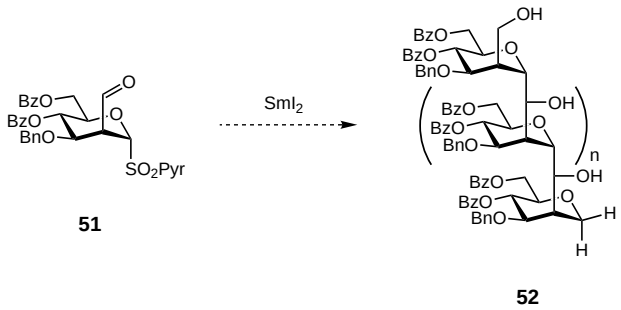
Like the *C*-disaccharide **43**, sulfone **49** proved particularly resistant to any coupling with the simple ketones such as cyclohexanone upon treatment with SmI_2. To assure that



Scheme 13. Synthesis of the C2-branched mannosyl pyridylsulfone **49** and its attempted coupling with cyclohexanone.

reduction was occurring with the formation of the C1 – Sm bond, **49** was reduced with SmI_2 in the presence of CH_3OD. Deuterium incorporation (70 %) was observed at the anomeric position and with complete stereoselectivity in favor of the α-isomer. This observation confirms that the 2-deoxy-glycosyl pyridylsulfones possessing an axially oriented C2-carbon branch show high selectivity for the formation of an α-anomeric carbanion.[32] However, the unwillingness of this organosamarium intermediate to react with cyclohexanone was somewhat surprising considering our previous successful couplings with pyridylsulfone **18**. We suggest again that steric hindrance of the metallic center by the C2 substituent is operating.

In a final attempt to prepare *C*-oligosaccharides with the Man(α1 $\rightarrow$2)Man linkage we tested whether the 2-deoxy-mannosyl pyridylsulfone **51** containing a C2-formyl group could oligomerize upon treaatment with SmI_2 (Scheme 14). The preparation of **51** required the desilylation of the glycosyl pyridylsulfone **49** and subsequent oxidation of the primary



Scheme 14. An approach to synthesis of *C*-oligosaccharides.

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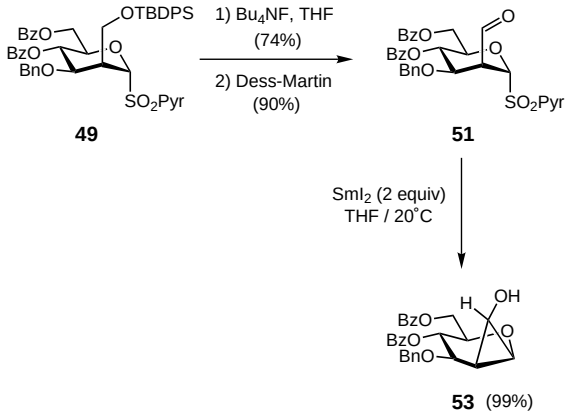
alcohol using Dess–Martin periodinane (Scheme 15).[33] Treatment of this compound with SmI_2 did not lead to any oligomerization as determined by analysis of the crude product mixture with mass spectroscopy, although a trace of the disaccharide **52** ($n = 0$) was observed. Instead a high yield



Scheme 15. Attempted oligomerization of the mannosyl pyridylsulfone **51**.

of a monosaccharide unit was isolated, whose structure was tentatively assigned as cyclopropane derivative **53** in the form of a single but undetermined stereoisomer based on its mass spectrum and ^{1}H NMR spectrum.[34] Surprisingly, complete isomerization of the original α-oriented C1–Sm bond to the β-position had been provoked by the C2 substituent, possibly by means of internal coordination.

Conclusion

The samarium diiodide induced *C*-glycosylation appears to be a viable route to *C*-disaccharides, as exemplified by our efficient and convergent synthesis of *C*-mannobioside. The interesting feature of this approach is its analogy to *O*-glycosylation with the involvement of *C*-glycosyl donors and acceptors. In addition, it provided two other *C*-mannoside derivatives possessing a hydroxy and imidazolyl group at the bridging methylene group. Interesting future studies include the investigation as to whether such compounds possess important glycosidase activity. A rigorous conformational study of the *C*-mannobioside and the hydroxy derivative is presented in the subsequent paper.[9d]

Unfortunately our attempts to extend this methodology to 1,2-trisaccharides were thwarted by the inability of the disaccharidic samarium species to undergo coupling with a mannoside acceptor. Whether this is an intrinsic property of only the C2 functionalized sugars and not of others modified at C3, C4, and C6 will be investigated in due course.

Experimental Section

General considerations: Unless otherwise stated, all reactions were carried out under argon. THF was dried and freshly distilled over sodium/benzophenone, dichloromethane over P_2O_5, and acetonitrile over CaH_2. Reactions were monitored by thin-layer chromatography (TLC). 2-*O*-*tert*-Butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl 2-pyridylsulfone (**18**) was prepared as previously described.[9d]

6-*O*-*tert*-Butyldiphenylsilyl-D-glucal (**10**): To a solution of D-glucal (1.0 g, 6.85 mmol) and imidazole (1.04 g, 15.0 mmol) in DMF (2 mL) at 0 °C was added TBDPSiCl (2.2 g, 8.2 mmol). After stirring for 16 h at 20 °C, the solution was diluted with ether and washed with water and brine. The organic phase was dried with Na_2SO_4 and evaporated to dryness. The crude product was purified by flash chromatography (pentane/EtOAc, 2:1) to give 1.93 g (73 %) of **10** as a colorless syrup. ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.72-7.68$ (m, 4H, Ph), 7.50–7.35 (m, 6H, Ph), 6.33 (dd, ^3J(H,H) = 6.0, 2.0 Hz, 1H, H1), 4.73 (dd, ^3J(H,H) = 6.0, 2.0 Hz, 1H, H2), 4.3 (dddd, ^3J(H,H) = 5.5, 2.5, 2.0, 2.0 Hz, 1H, H3), 4.03 (dd, ^3J(H,H) = 11.0, 4.0 Hz, 1H, H6b), 3.97 (dd, ^3J(H,H) = 11.0, 3.5 Hz, 1H, H6a), 3.90 (ddd, ^3J(H,H) = 9.5, 4.3, 3.0 Hz, 1H, H4), 3.82 (dt, ^3J(H,H) = 9.5, 4.0, 3.5 Hz, 1H, H5), 2.96 (d, ^3J(H,H) = 3.0 Hz, 1H, OH), 2.40 (d, ^3J(H,H) = 5.5 Hz, 1H, OH), 1.09 (s, 9H, $3CH_3$).

3-*O*-(1,3-Diphenylprop-2-en-1-yl)-6-*O*-*t*-butyldiphenylsilyl-D-glucal (**12**): Dibutyltin oxide (460 mg, 3.80 mmol) was added to a solution of diol **10** (976 mg, 2.53 mmol) in toluene (30 mL). The mixture was heated under reflux for 4 h, after which it was concentrated under reduced pressure to a third of its original volume. The mixture was cooled to 0 °C and nBu$_4$NBr (815 mg, 2.53 mmol) and 1-chloro-1,3-diphenylprop-2-ene (**11**) (1.01 g, 4.31 mmol) were added. After stirring for 15 h at 20 °C, the reaction mixture was diluted with toluene and then washed with water and brine. The organic phase was dried with Na_2SO_4 and evaporated to dryness. Purification by flash chromatograpy (pentane/EtOAc, 10:1) gave **12** as an approximately 1:1 diastereomeric mixture and as a colorless syrup (991 mg, 67 %). $[\alpha]_D^{22} = -12$ ($c = 1.0$, dichloromethane); IR (neat): $\tilde{\nu} = 3054$, 2987, 2986, 1652, 1422, 1113 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.72-7.68$ (m, 8H, $8CH_{aryl}$), 7.50–7.28 (m, 32H, 32 CH_{aryl}), 6.63 (d, ^3J(H,H) = 16.1 Hz, 1H, PhCH=C), 6.61 (d, ^3J(H,H) = 16.1 Hz, 1H, PhCH=C), 6.39–6.26 (m, 4H, 2PhC=CH, 2H1), 5.28 (d, ^3J(H,H) = 7.0 Hz, 1H, C=CCHPh), 5.24 (d, ^3J(H,H) = 7.0 Hz, 1H, C=CCHPh), 4.84 (dd, ^3J(H,H) = 6.2, 2.0 Hz, 1H, H2), 4.70 (dd, ^3J(H,H) = 6.2, 2.6 Hz, 1H, H2), 4.23–3.77 (m, 10H, 2H3, 2H4, 2H5, 2H6a, 2H6b), 2.58 (d, ^3J(H,H) = 3.5 Hz, 1H, OH), 1.06 (s, 18H, $6CH_3$), 2.37 (d, ^3J(H,H) = 3.5 Hz, 1H, OH), 1.08 (s, 18H, $6CH_3$); MS (ES): m/z 599 [M+Na]; HR-MS (ES) ($C_{37}H_{40}O_4Si$): calcd for [M+Na] 599.2616; found 599.2594.

3-*O*-(1,3-Diphenylprop-2-en-1-yl)-D-glucal (**13**): nBuN_4F (400 µL, 0.39 mmol) was added to a solution of **12** (150 mg, 0.26 mmol) in THF (3 mL) at 0 °C. After being stirred for 15 min at 20 °C, the solution was diluted with ether and washed with water and brine. The organic phase was dried with Na_2SO_4 and evaporated to dryness. The crude product was purified by flash chromatograpy (pentane/EtOAc, 3:2) to give 83 mg (94 %) of **13** as a colorless syrup. $[\alpha]_D^{22} = -58$ ($c = 1.0$, dichloromethane); IR (neat): $\tilde{\nu} = 3588$, 3054, 2987, 2306, 1646, 1495, 1421, 1072 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.46-7.21$ (m, 20H, CH_{aryl}), 6.66 (d, ^3J(H,H) = 16.1 Hz, 1H, PhCH=C), 6.62 (d, ^3J(H,H) = 16.1 Hz, 1H, PhCH=C), 6.39–6.24 (m, 4H, 2PhC=CH, 2H1), 5.21 (d, ^3J(H,H) = 7.0 Hz, 1H, C=CCHPh), 5.19 (d, ^3J(H,H) = 6.8 Hz, 1H, C=CCHPh), 4.90 (dd, ^3J(H,H) = 6.3, 2.5 Hz, 1H, H2), 4.76 (dd, ^3J(H,H) = 6.3, 2.5 Hz, 1H, H2), 4.25–3.82 (m, 10H, 2H3, 2H4, 2H5, 2H6a, 2H6b), 2.43 (d, ^3J(H,H) = 4.0 Hz, 2H, OH), 2.20 (d, ^3J(H,H) = 4.0 Hz, 2H, OH); $C_{21}H_{22}O_4$ (338.4): calcd C 74.54, H 6.55; found C 74.43, H 6.62.

4,6-Di-*O*-benzoyl-3-*O*-(1,3-diphenylprop-2-en-1-yl)-D-glucal (**14**): Benzoyl chloride (135 µL, 1.17 mmol) was added to a stirred solution of diol **13** (100 mg, 0.29 mmol) in pyridine (2 mL) at 0 °C. After stirring at this temperature for 12 h, a saturated solution of $NaHCO_3$ was added, and the reaction mixture was diluted with ether. The organic phase was washed with water and brine, dried with Na_2SO_4, and evaporated to dryness in vacuo. The crude product was purified by flash chromatograpy (pentane/EtOAc, 10:1) to give 170 mg (99 %) of **14** as a colorless syrup. $[\alpha]_D^{22} = -17$ ($c = 1.0$, dichloromethane); IR (neat): $\tilde{\nu} = 3055$, 2986, 1723, 1652, 1602, 1494, 1110 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.06-7.95$ (m, 8H, $8CH_{aryl}$), 7.59–7.17 (m, 32H, 32 CH_{aryl}), 6.65 (d, ^3J(H,H) = 15.9 Hz, 1H, PhCH=C), 6.57 (d, ^3J(H,H) = 15.9 Hz, 1H, PhCH=C), 6.52 (d, ^3J(H,H) = 6.5 Hz, 1H, H1), 6.49 (d, ^3J(H,H) = 6.5 Hz, 1H, H1), 6.25 (dd, ^3J(H,H) = 15.9, 7.0 Hz, 1H, PhC=CH), 6.16 (dd, ^3J(H,H) = 15.9, 7.0 Hz, 1H, PhC=CH), 5.67 (dd, ^3J(H,H) = 4.4, 4.4 Hz, 1H, H4), 5.28 (dd, ^3J(H,H) = 4.4, 4.4 Hz, 1H, H4), 5.27 (d, ^3J(H,H) = 6.9 Hz, 2H, 2C=CCHPh), 5.03 (dd, ^3J(H,H) = 6.5, 3.7 Hz, 1H, H2), 4.91 (dd, ^3J(H,H) = 6.5, 3.7 Hz, 1H, H2),

4.78 – 4.49 (m, 6H, 2H3, 2H6a, 2H6b), 4.20 – 4.11 (m, 2H, 2H5); $C_{35}H_{30}O_6$ (546.6): calcd C 76.91, H 5.53; found C 76.98, H 5.52.

Methyl 4,6-di-*O*-benzoyl-2-deoxy-3-*O*-(1,3-diphenylprop-2-en-1-yl)-2-iodo-α-D-mannopyranoside (**15a**): A mixture of glucal **14** (2.0 g, 3,66 mmol), methanol (741 μL, 18 mmol), and crushed molecular sieves (3 Å) in acetonitrile (40 mL) was stirred for 10 min at 20 °C. The mixture was cooled to 0 °C and *N*-iodosuccinimide (1.81 mg, 8.1 mmol) was added, after which stirring was continued overnight at 20 °C. The reaction mixture was diluted with dichloromethane and then washed consecutively with a 50% saturated solution of $Na_2S_2O_3$ and water. The organic phase was dried with Na_2SO_4 and concentrated to dryness in vacuo. Flash chromatography (cyclohexane/EtOAc, 20:1) gave **15a** (2.0 g, 78%) as a colorless syrup. $[\alpha]_D^{22} = 25$ ($c = 2.5$, chloroform); IR (neat): $\tilde{\nu} = 3061, 3031, 2960, 1725, 1602, 1584, 1451, 1265, 1110\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.15 – 7.94$ (m, 8H, $8CH_{bz}$), 7.66 – 7.02 (m, 32H, $20H_{aryl}$, $12CH_{bz}$), 6.63 (d, $^3J(H,H) = 16.0$ Hz, 1H, PhCH=C), 6.50 (d, $^3J(H,H) = 16.0$ Hz, 1H, PhCH=C), 6.32 (dd, $^3J(H,H) = 16.0$, 6.5 Hz, 1H, PhC=CH), 5.98 (dd, $^3J(H,H) = 16.0$, 7.6 Hz, 1H, PhC=CH), 5.86 (dd, $^3J(H,H) = 9.6$, 9.6 Hz, 1H, H4), 5.81 (dd, $^3J(H,H) = 9.6$, 9.6 Hz, 1H, H4), 5.18 (d, $^3J(H,H) = 9.0$ Hz, 2H, 2H1), 5.05 (d, $^3J(H,H) = 5.0$ Hz, 1H, C=CCHPh), 5.02 (d, $^3J(H,H) = 6.0$ Hz, 1H, C=CCHPh), 4.68 – 4.00 (m, 8H, 2H2, 2H5, 2H6a, 2H6b), 3.67 (dd, $^3J(H,H) = 9.0$, 4.3 Hz, 1H, H3), 3.49 (dd, $^3J(H,H) = 9.0$, 4.3 Hz, 1H, H3), 3.41 (s, 3H, MeO), 3.39 (s, 3H, MeO); $C_{36}H_{33}O_7I$ (704.6): calcd C 61.37, H 4.72; found C 61.72, H 4.66.

Methyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-formyl-α-D-mannopyranoside (**17a**): Ozone was bubbled through a solution of **15a** (150 mg, 0.21 mmol) in dichloromethane (10 mL) at −78 °C until the solution became slightly blue. Nitrogen was allowed to bubble through for 10 min, after which triphenylphosphine (140 mg, 0.53 mmol) was added. The solution was warmed to room temperature and evaporated to dryness in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc, 4:1) to give **16** (133 mg, 99%) as a colorless syrup. This iodoaldehyde (100 mg, 0.16 mmol) was dissolved in benzene (10 mL) and Bu_3SnH (72 μL, 0.27 mmol) and AIBN (5 mg, 0.022 mmol) were added. After stirring under reflux for 4 h, the solvent was removed under vacuum and the residue was purified by flash chromatography (cyclohexane/EtOAc, 6:1) affording 50 mg of **17a** as a colorless syrup (63%). The compound showed signs of decomposition and hence was immediately used in the following step. ^1H NMR (250 MHz, $CDCl_3$): $\delta = 9.98$ (d, $^3J(H,H) = 2.0$ Hz, 1H, CHO), 8.09 – 8.00 (m, 5H, Ph), 7.68 – 7.21 (m, 10H, Ph), 5.65 (dd, $^3J(H,H) = 9.5$, 8.5 Hz, 1H, H4), 5.18 (d, $^3J(H,H) = 2.5$ Hz, 1H, H1), 4.72 (d, $^2J(H,H) = 12.0$ Hz, 1H, PhCH), 4.66 (d, $^2J(H,H) = 12.0$ Hz, 1H, PhCH), 4.58 (dd, $^3J(H,H) = 12.0$, 3.5 Hz, 1H, H6b), 4.46 (dd, $^3J(H,H) = 12.0$, 5.5 Hz, 1H, H6a), 4.36 (dd, $^3J(H,H) = 8.5$, 5.5 Hz, 1H, H3), 4.27 (ddd, $^3J(H,H) = 9.5$, 5.5, 3.0 Hz, 1H, H5), 3.45 (s, 3H, MeO), 3.12 (ddd, $^3J(H,H) = 5.5$, 2.5, 2.0 Hz, 1H, H2).

Methyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylhydroxy-methyl)-α-D-mannopyranoside (**19a**): A 0.1M solution of SmI_2 in THF (8.2 mL, 0.82 mmol) was added to a stirred solution of sulfone **18** (256 mg, 0.37 mmol) and aldehyde **17a** (125 mg, 0.25 mmol) in THF (1.6 mL) under argon at 20 °C. After stirring for 10 min, saturated aqueous NH_4Cl was added to the reaction mixture, which was then extracted twice with CH_2Cl_2. The combined organic phases were washed twice with water, dried with Na_2SO_4, and evaporated to dryness. Flash chromatography (cyclohexane/EtOAc, 10:1) gave **19a** (191 mg, 73%) as a colorless syrup. $[\alpha]_D^{22} = +19.5$ ($c = 0.83$, chloroform); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.13 – 8.00$ (m, 6H, $6H_{Bz}$), 7.62 – 7.13 (m, 24H, 4Ph, $4H_{Bz}$), 5.90 (dd, $^3J(H,H) = 8.5$, 7.5 Hz, 1H, H4), 5.53 (d, $^3J(H,H) = 3.0$ Hz, 1H, H1), 4.43 (ddd, $^3J(H,H) = 8.9$, 5.0, 1.0 Hz, 1H, H7), 4.74 – 4.40 (m, 8H, 8PhCH), 4.34 (dd, $^3J(H,H) = 8.5$, 3.0 Hz, 1H, H2′), 4.32 (s, 2H, H6a, H6b), 4.17 (m, 3H, H5′, H5, H3), 3.87 (dd, $^3J(H,H) = 4.0$, 3.0 Hz, 1H, H3′), 3.80 (m, $^3J(H,H) = 8.5$, 1.0 Hz, 1H, H1′), 3.73 (dd, $^3J(H,H) = 10.0$, 7.5 Hz, 1H, H6b′), 3.61 (dd, $^3J(H,H) = 4.0$, 3.0 Hz, 1H, H4′), 3.51 (dd, $^3J(H,H) = 10.0$, 5.5 Hz, 1H, H6a′), 3.33 (s, 3H, MeO), 2.88 (d, $^3J(H,H) = 8.9$ Hz, 1H, OH), 2.44 (ddd, $^3J(H,H) = 5.0$, 5.0, 4.0 Hz, 1H, H2), 0.90 (s, 9H, Si*t*Bu), 0.20 (s, 3H, SiMe), 0.13 (s, 3H, SiMe); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 166.6$, 165.6, 138.6, 138.4, 138.2, 138.1, 133.2, 133.0, 129.9, 128.4, 127.8, 127.7, 127.5, 100.4, 78.3, 76.1, 75.2, 75.1, 74.3, 73.6, 73.0, 71.9, 69.3, 68.7, 68.6, 67.0, 65.5, 64.1, 55.1, 45.3, 27.0, 26.0, −4.2, −4.9; $C_{62}H_{72}O_{13}Si$ (1053.3): calcd C 70.70, H 6.89; found C 70.67, H 6.91.

Methyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-[2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethyl(xanthateimidazole)]-α-D-mannopyranoside (**30a**): A solution of alcohol **19a** (150 mg, 0.14 mmol) and thiocarbonyl diimidazole (507 mg, 2.85 mmol) in acetonitrile (3 mL) was refluxed overnight. The acetonitrile was distilled off leaving a dark residue, which was purified by flash chromatography (cyclohexane/EtOAc, 3:1) to afford **30a** as a colorless syrup (147 mg, 89%). This intermediate was immediately used in the following step without further characterization. ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.37$ (s, 1H, H_{imid}), 7.90 – 8.07 (m, 10H, $10H_{Bz}$), 7.63 (d, 1H, $J = 1.5$ Hz, H_{imid}), 7.14 – 7.61 (m, 20H, 4Ph), 7.00 (d, $^3J(H,H) = 1.5$ Hz, 1H, H_{imid}), 6.50 (dd, $^3J(H,H) = 7.5$, 3.0 Hz, 1H, H7), 5.45 (dd, $^3J(H,H) = 8.5$, 3.5 Hz, 1H, H4), 5.14 (d, $^3J(H,H) = 5.5$ Hz, 1H, H1), 4.83 (d, 1H, $^2J(H,H) = 12.0$ Hz, PhCH), 4.63 (d, $^2J(H,H) = 11.5$ Hz, 1H, PhCH), 4.33 – 4.53 (m, 6H, 6PhCH), 4.14 – 4.33 (m, 5H, H1′, H2′, H5, H6a, H6b), 4.10 (dd, $^3J(H,H) = 3.5$, 3.5 Hz, 1H, H3), 4.00 (ddd, $^3J(H,H) = 7.0$, 6.0, 4.5 Hz, 1H, H5′), 3.79 (dd, $^3J(H,H) = 7.0$, 7.0 Hz, 1H, H3′), 3.56 (dd, $^3J(H,H) = 10.0$, 6.0 Hz, 1H, H6b′), 3.55 (dd, $^3J(H,H) = 7.0$, 2.5 Hz, 1H, H4′), 3.43 (dd, 1H, $^3J(H,H) = 10.0$, 4.5 Hz, H6a′), 3.32 (s, 3H, $3H_{MeO}$), 2.88 (ddd, $^3J(H,H) = 7.5$, 5.5, 3.5 Hz, 1H, H2), 0.85 (s, 9H, Si*t*Bu), 0.04 (s, 3H, SiMe), 0.00 (s, 3H, SiMe).

Methyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethyl)-α-D-mannopyranoside (**32a**): To a solution of **30a** (107 mg, 0.092 mmol) in toluene (5 mL) under argon was added sequentially pentafluorophenol (34 mg, 0.184 mmol), triphenyltin hydride (84 mg, 0.24 mmol) and AIBN (2 mg). The solution was refluxed for 2 h and then concentrated in vacuo. The residue was redissolved in acetonitrile and then washed twice with hexane. Evaporation and purification by flash chromatography (cyclohexane/EtOAc, 20:1 to 10:1) gave **32a** as a colorless syrup (67 mg, 70%). $[\alpha]_D^{22} = +2.9$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 2926, 2854, 1726, 1452, 1268, 1109\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.06 – 7.98$ (m, 6H, $6H_{Bz}$), 7.64 – 7.11 (m, 24H, 4Ph, $4H_{Bz}$), 5.41 (dd, $^3J(H,H) = 9.6$, 9.6 Hz, 1H, H4), 5.09 (d, $^3J(H,H) = 1.0$ Hz, 1H, H1), 4.76 – 4.44 (m, 8H, 8PhCH), 4.56 (dd, $^3J(H,H) = 11.5$, 3.0 Hz, 1H, H6b), 4.40 (dd, $^3J(H,H) = 11.5$, 5.5 Hz, 1H, H6a), 4.14 (dd, $^3J(H,H) = 9.6$, 5.3, 1H, H3), 4.12 (ddd, $^3J(H,H) = 9.6$, 5.5, 3.0 Hz, 1H, H5), 3.96 (dd, $^3J(H,H) = 2.9$, 2.5 Hz, 1H, H2′), 3.89 (ddd, $^3J(H,H) = 11.1$, 2.9, 2.9 Hz, 1H, H1′), 3.84 (dd, $^3J(H,H) = 7.4$, 4.5 Hz, 1H, H5′), 3.80 (dd, $^3J(H,H) = 7.4$, 7.4 Hz, 1H, H4′), 3.71 (m, 2H, H6a′, H6b′), 3.64 (dd, $^3J(H,H) = 7.4$, 2.5 Hz, 1H, H3′), 3.28 (s, 3H, $3H_{MeO}$), 2.44 (dddd, $^3J(H,H) = 9.5$, 5.3, 2.4, 1.0 Hz, 1H, H2), 2.00 (ddd, $^3J(H,H) = 15.0$, 2.9, 2.4 Hz, 1H, H7b), 1.84 (ddd, $^3J(H,H) = 15.0$, 11.1, 9.5 Hz, 1H, H7a), 0.92 (s, 9H, Si*t*Bu), 0.07 (s, 6H, 2SiMe); MS (ES): *m*/*z* 1059.9 [*M*+Na]; HR-MS (ES) ($C_{62}H_{72}O_{12}Si$): calcd for [*M*+Na] 1059.4691; found 1059.4693.

Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-*C*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosylmethyl)-α-D-mannopyranoside (**33**): To a solution of **32a** (12 mg, 0.017 mmol) in THF (1 mL) under argon and at 0 °C was added a 1M THF solution of Bu_4NF (98 μL, 0.098 mmol). The solution was stirred for 24 h at 0 °C, diluted with ether and then washed twice with water and dried (Na_2SO_4). After evaporation in vacuo to dryness, the residue was redissolved in methanol (1 mL) to which was added a catalytic amount of sodium methoxide. The solution was stirred for 18 h, after which it was neutralized with amberlite IR-120. Filtration and evaporation of the solvent left a syrup which was redissolved in methanol (6 mL) and acetic acid (1 mL), to which was added 5% palladium on activated carbon (30 mg). The mixture was stirred overnight under an atmosphere of hydrogen, after which it was filtered through a pad of Celite and evaporated to dryness. The residue was redissolved in pyridine (3 mL) and Ac_2O (1 mL) with DMAP (1 mg) and left overnight. Evaporation and coevaporation with toluene afforded a syrup, which was purified by flash chromatography (cyclohexane/EtOAc, 1:1) to give **33** as a colorless syrup (6 mg, 79%). $[\alpha]_D^{22} = +10$ ($c = 0.42$, chloroform); IR (neat): $\tilde{\nu} = 3428, 1743, 1644, 1370, 1229, 1047\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.44$ (dd, $^3J(H,H) = 9.5$, 5.0 Hz, 1H, H3), 5.25 (dd, $^3J(H,H) = 8.5$, 3.5 Hz, 1H, H3′), 5.17 (dd, $^3J(H,H) = 8.5$, 8.0 Hz, 1H, H4′), 5.13 (dd, $^3J(H,H) = 3.5$, 3.0 Hz, 1H, H2′), 5.09 (dd, $^3J(H,H) = 10.0$, 9.5 Hz, 1H, H4), 4.88 (d, $^3J(H,H) = 1.5$ Hz, 1H, H1), 4.32 (dd, $^3J(H,H) = 12.0$, 6.5 Hz, 1H, H6a′), 4.20 (dd, $^3J(H,H) = 12.0$, 4.5 Hz, 1H, H6a), 4.15 (dd, $^3J(H,H) = 12.0$, 2.5 Hz, 1H, H6b), 4.13 (dd, $^3J(H,H) = 12.0$, 2.5 Hz, 1H, H6b′), 4.00 (ddd, $^3J(H,H) = 9.0$, 4.0, 3.0 Hz, 1H, H1′), 3.94 (ddd, $^3J(H,H) = 8.0$, 6.5, 2.5 Hz, 1H, H5′), 3.91 (ddd, $^3J(H,H) = 10.0$, 4.5, 2.5 Hz, 1H, H5), 3.40 (s, 3H, OMe), 2.36 (m, 1H, H2), 2.14 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.10 (s, 3H,

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CH_3), 2.07 (s, 3H, CH_3), 2.05 (s, 6H, $2CH_3$), 1.97–1.84 (m, 2H, 2H7); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.8, 170.0, 169.8, 100.7, 70.8, 70.3, 68.6, 68.1, 67.0, 66.7, 62.7, 55.3, 41.6, 29.8, 24.5, 21.1, 20.9; MS (ES): *m*/*z* 671 [*M*+Na]; HR-MS (ES) ($C_{28}H_{40}O_{17}$): calcd for [*M*+Na] 671.2163; found 671.2185.

Methyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-[2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl(1-methylimidazole)]-α-D-mannopyranoside (**36**): To a solution of the *C*-disaccharide **19a** (98 mg, 0.084 mmol) in dichloromethane (10 mL) at 0 °C was added 4-methyl(difluoroiodo)benzene (172 mg, 0.67 mmol). The solution was stirred for 4 h at 0 °C and then evaporated to dryness. The residue was purified by flash chromatography (cyclohexane/EtOAc, 2:1) to give **36** as a colorless syrup (54 mg, 58 %). $[\alpha]_D^{22} = +1.7$ (*c* = 0.83, chloroform); IR (neat): $\tilde{\nu}$ = 3063, 3032, 2928, 2855, 1827, 1725, 1452, 1725, 1452, 1265, 1108 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.20 (s, 1H, imid), 8.08–7.93 (m, 8H, 8Ph), 7.61–7.04 (m, 24H, 2imid, 22Ph), 5.82 (dd, ^3J(H,H) = 7.5, 2.3 Hz, 1H, H7), 5.53 (dd, ^3J(H,H) = 8.5, 3.5 Hz, 1H, H4), 5.13 (d, ^3J(H,H) = 6.0 Hz, 1H, H1), 4.55 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.53 (d, ^2J(H,H) = 10.0 Hz, 1H, CHPh), 4.52 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.47 (s, 2H, 2CHPh), 4.46 (dd, ^3J(H,H) = 10.0, 6.0 Hz, 1H, H6a), 4.45 (dd, ^3J(H,H) = 10.0, 4.5 Hz, 1H, H6b), 4.44 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.43 (d, ^2J(H,H) = 10.0 Hz, 1H, CHPh), 4.41 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.26 (ddd, ^3J(H,H) = 8.5, 6.0, 4.5 Hz, 1H, H5), 4.17 (dd, ^3J(H,H) = 8.0, 3.0 Hz, 1H, H6a′), 4.10 (dd, ^3J(H,H) = 4.5, 2.3 Hz, 1H, H1′), 4.06 (dd, ^3J(H,H) = 6.5, 3.5 Hz, 1H, H3′), 4.01 (t, ^3J(H,H) = 3.5, 3.5 Hz, 1H, H3), 3.80 (dd, ^3J(H,H) = 8.0, 5.0 Hz, 1H, H6b′), 3.72 (dd, ^3J(H,H) = 4.5, 3.5 Hz, 1H, H2′), 3.57 (dd, ^3J(H,H) = 9.5, 6.5 Hz, 1H, H4′), 3.40 (ddd, ^3J(H,H) = 9.5, 5.0, 3.0 Hz, 1H, H5′), 3.20 (s, 3H, OMe), 2.81 (ddd, ^3J(H,H) = 7.5, 6.0, 3.5 Hz, 1H, H2), 0.88 (s, 9H, Si*t*Bu), 0.00 (s, 3H, SiMe), −0.12 (s, 3H, SiMe); MS (ES): *m*/*z* 1148 [*M*+2Na] ($C_{65}H_{74}N_2O_{12}Si$).

***p*-Methoxyphenylmethyl 4,6-di-*O*-benzoyl-2-deoxy-3-*O*-(1,3-diphenylprop-2-en-1-yl)-2-iodo-α-D-mannopyranoside** (**15b**): The iodoglycosylation reaction was repeated as given for the preparation of **15a**, employing glucal **14** (9.77 g, 17.9 mmol), *p*-methoxyphenylmethanol (4.46 mL, 35.7 mmol) and *N*-iodosuccinimide (6.0 g, 26,7 mmol) in acetonitrile (195 mL). After work-up and flash chromatography (cyclohexane/EtOAc, 7:1), **15b** was obtained as a colorless syrup (10.7 g, 74 %). $[\alpha]_D^{22} = +27$ (*c* = 2.0, chloroform); IR (neat): $\tilde{\nu}$ = 3061, 3031, 2959, 2837, 1719, 1601, 1514, 1451, 1246 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.20–7.76 (m, 12H, $8CH_{Bz}$, $4CH_{MPM}$), 7.70–7.10 (m, 32H, $20CH_{aryl}$, $12CH_{Bz}$), 6.87 (m, 4H, $4CH_{MPM}$), 6.65 (d, ^3J(H,H) = 16.0 Hz, 1H, PhCH=C), 6.51 (d, ^3J(H,H) = 16.0 Hz, 1H, PhCH=C), 6.32 (dd, ^3J(H,H) = 16.0, 6.6 Hz, 1H, PhC=CH), 6.01 (dd, ^3J(H,H) = 16.0, 7.6 Hz, 1H, PhC=CH), 5.90 (dd, ^3J(H,H) = 9.6, 9.6 Hz, 1H, H4), 5.85 (dd, ^3J(H,H) = 9.6, 9.6 Hz, 1H, H4), 5.34 (d, ^3J(H,H) = 7.6, 6.6 Hz, 2H, 2C=CCHPh), 5.08 (d, ^3J(H,H) = 4.0 Hz, 1H, H1), 5.05 (d, ^3J(H,H) = 5.5 Hz, 1H, H1), 4.73–4.08 (m, 12H, $2CH_2$Ar, 2H2, 2H5, 2H6a, 2H6b), 3.83 (s, 6H, 2MeO), 3.73 (dd, ^3J(H,H) = 9.0, 4.0 Hz, 1H, H3), 3.58 (dd, ^3J(H,H) = 9.0, 4.0 Hz, 1H, H3); $C_{43}H_{39}O_8I$ (810.7): calcd C 63.71, H 4.85; found C 63.82, H 4.75.

***p*-Methoxyphenylmethyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-formyl-α-D-mannopyranoside** (**17b**): The ozonolysis and formyl group transfer reaction was performed exactly as given for preparation of **17a**. Purification by flash chromatography (cyclohexane/EtOAc, 6:1) gave **17b** (707 mg, 55 %) as a colorless syrup. The compound showed signs of decomposition and hence was immediately used in the following step. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.96 (d, ^3J(H,H) = 2.0 Hz, 1H, CHO), 7.69–7.20 (m, 10H, 2Ph), 8.10–8.04 (m, 5H, Ph), 6.98–6.90 (m, 4H, CH_{MPM}), 5.67 (dd, ^3J(H,H) = 9.5, 8.5 Hz, 1H, H4), 5.38 (d, ^3J(H,H) = 2.5 Hz, 1H, H1), 4.74 (d, ^2J(H,H) = 12.0 Hz, 1H, PhCH), 4.73 (d, ^2J(H,H) = 12.0 Hz, 1H, PhCH), 4.66 (d, ^2J(H,H) = 12.0 Hz, 1H, PhCH), 4.60 (dd, ^3J(H,H) = 12.0, 3.5 Hz, 1H, H6b), 4.54 (d, ^2J(H,H) = 12.0 Hz, 1H, PhCH), 4.49 (dd, ^3J(H,H) = 12.0, 5.5 Hz, 1H, H6a), 4.41 (dd, ^3J(H,H) = 8.5, 5.5 Hz, 1H, H3), 4.35 (ddd, ^3J(H,H) = 9.5, 5.5, 3.5 Hz, 1H, H5), 3.86 (s, 3H, MeO), 3.16 (ddd, ^3J(H,H) = 5.5, 2.5, 2.0 Hz, 1H, H2).

***p*-Methoxyphenylmethyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylhydroxymethyl)-α-D-mannopyranoside** (**19b**): The SmI_2-promoted coupling reaction was performed as given for the preparation of **19a**, employing aldehyde **17b** (281 mg, 0.54 mmol), pyridylsulfone **18** (490 mg, 0.71 mmol) and 0.1 M SmI_2 in THF (16 mL, 1.6 mmol). After work-up and flash chromatography (cyclohexane/EtOAc, 10:1), **19b** was obtained as a colorless syrup (525 mg, 85 %). $[\alpha]_D^{22} = +4.0$ (*c* = 0.42, chloroform); IR (neat): $\tilde{\nu}$ = 2924, 2854, 1718, 1653, 1636, 1456, 1251, 1106 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.12–7.96 (m, 6H, $6H_{Bz}$), 7.65–7.07 (m, 24H, 4Ph, $4H_{Bz}$), 6.90–6.80 (m, 4H, $4H_{MPM}$), 5.86 (dd, 1H, ^3J(H,H) = 8.5, 6.5 Hz, H4), 5.65 (d, ^3J(H,H) = 3.0 Hz, 1H, H1), 4.69–4.42 (m, 10H, 8PhCH, 2MeOPhCH), 4.40 (ddd, ^3J(H,H) = 8.5, 4.5, 1.0 Hz, 1H, H7), 4.32 (dd, ^3J(H,H) = 8.5, 3.0 Hz, 1H, H2′), 4.24 (dd, ^3J(H,H) = 8.5, 4.5 Hz, 1H, H3), 4.23 (s, 2H, H6a, H6b), 4.18 (ddd, ^3J(H,H) = 7.0, 6.0, 3.0 Hz, 1H, H5′), 4.09 (ddd, ^3J(H,H) = 6.5, 6.5, 2.5 Hz, 1H, H5), 4.06 (dd, ^3J(H,H) = 8.5, 3.0 Hz, 1H, H2′), 3.78 (dd, ^3J(H,H) = 8.5, 1.0 Hz, 1H, H1′), 3.78 (dd, ^3J(H,H) = 4.0, 3.0 Hz, 1H, H3′), 3.78 (s, 3H, MeO), 3.66 (dd, ^3J(H,H) = 4.0, 3.0 Hz, 1H, H4′), 3.55 (dd, ^3J(H,H) = 9.5, 6.0 Hz, 1H, H6b′), 3.46 (dd, ^3J(H,H) = 9.5, 7.0 Hz, 1H, H6a′), 2.92 (d, ^3J(H,H) = 8.5 Hz, 1H, OH), 2.48 (ddd, ^3J(H,H) = 4.5, 4.5, 3.0 Hz, 1H, H2), 0.88 (s, 9H, Si*t*Bu), 0.17 (s, 3H, SiMe), 0.11 (s, 3H, SiMe); MS (ES): *m*/*z* 1081.9 [*M*+Na]; HR-MS (ES) ($C_{69}H_{78}O_{14}Si$): calcd for [*M*+Na] 1181.5082; found 1181.5059.

***p*-Methoxyphenylmethyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-[2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethyl-(xanthateimidazole)]-α-D-mannopyranoside** (**30b**): The thiocarbonylation of **19b** was performed exactly as given for the preparation of **30a**. Purification by flash chromatography (cyclohexane/EtOAc, 3:1) gave **30b** (108 mg, 99 %) as a colorless syrup. This intermediate was immediately used in the following step without further characterization. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.27 (s, 1H, H_{imid}), 8.05–7.92 (m, 10H, $10H_{Bz}$), 7.65–7.07 (m, 21H, 4Ph, H_{imid}), 6.92 (d, 1H, H_{MPM}), 6.89 (d, ^3J(H,H) = 1.5 Hz, 1H, H_{imid}), 6.68 (d, 2H, H_{MPM}), 6.50 (dd, ^3J(H,H) = 7.5, 1.5 Hz, 1H, H7), 5.45 (dd, ^3J(H,H) = 8.5, 3.5 Hz, 1H, H4), 5.14 (d, ^3J(H,H) = 5.0 Hz, 1H, H1), 4.85 (d, ^3J(H,H) = 11.5 Hz, 1H, PhCH), 4.35–4.67 (m, 8H, 8PhCH), 4.35–4.04 (m, 6H, H1′, H2′, H3, H5, H6a, H6b, PhCH), 4.00 (ddd, ^3J(H,H) = 5.5, 5.5, 2.5 Hz, 1H, H5′), 3.76 (dd, ^3J(H,H) = 7.0, 7.0 Hz, 1H, H3′), 3.76 (s, 3H, $3H_{MeO}$), 3.53 (dd, ^3J(H,H) = 7.0, 2.5 Hz, 1H, H4′), 3.46 (dd, ^3J(H,H) = 10.0, 5.5 Hz, 1H, H6b′), 3.37 (dd, ^3J(H,H) = 10.0, 5.5 Hz, 1H, H6a′), 2.94 (ddd, ^3J(H,H) = 7.5, 5.0, 3.5 Hz, 1H, H2), 0.81 (s, 9H, Si*t*Bu), −0.08 (s, 3H, SiMe), −0.05 (s, 3H, SiMe).

***p*-Methoxyphenylmethyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethyl)-α-D-mannopyranoside** (**32b**): The deoxygenation reaction was performed as given for the preparation of **32a**, employing thiocarbonate **30b** (599 mg, 0.48 mmol) dissolved in toluene (32 mL), pentafluorophenol (96 mg, 0.52 mmol), triphenyltin hydride (444 mg, 1.24 mmol), and AIBN (20 mg). After work-up and flash chromatography (cyclohexane/EtOAc, 6:1), **30b** was obtained as a colorless syrup (484 mg, 90 %). $[\alpha]_D^{22} = +4.8$ (*c* = 2.5, chloroform); IR (neat): $\tilde{\nu}$ = 3064, 3030, 2959, 2928, 2857, 1725, 1515, 1453, 1267, 1098 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.07–7.98 (m, 6H, $6H_{Bz}$), 7.62–7.08 (m, 24H, 4Ph, $4H_{Bz}$), 6.90–6.82 (m, 4H, $4H_{MPM}$), 5.38 (dd, ^3J(H,H) = 9.5, 9.5 Hz, 1H, H4), 5.19 (d, ^3J(H,H) = 1.0 Hz, 1H, H1), 4.50 (dd, ^3J(H,H) = 12.0, 2.5 Hz, 1H, H6b), 4.37 (dd, ^3J(H,H) = 12.0, 5.0 Hz, 1H, H6a), 4.83–4.36 (m, 10H, 8PhCH, 2MeOPhCH), 4.15 (ddd, ^3J(H,H) = 9.5, 5.0, 2.5 Hz, 1H, H5), 4.14 (dd, ^3J(H,H) = 9.5, 5.0 Hz, 1H, H3), 3.93–3.68 (m, 4H, H1′, H2′, H4′, H5′), 3.77 (s, 3H, $3H_{MeO}$), 3.62 (dd, ^3J(H,H) = 10.7, 4.5 Hz, 1H, H6b′), 3.58 (dd, ^3J(H,H) = 6.0, 2.0 Hz, 1H, H3′), 3.52 (dd, ^3J(H,H) = 10.7, 3.5 Hz, 1H, H6a′), 2.47 (dddd, ^3J(H,H) = 9.8, 5.0, 3.0, 1.0 Hz, 1H, H2), 2.07–1.74 (m, 2H, H7a, H7b), 0.89 (s, 9H, Si*t*Bu), 0.04 (s, 3H, SiMe), 0.03 (s, 3H, SiMe); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.3, 165.7, 159.3, 138.5, 138.5, 138.3, 138.0, 133.2, 132.9, 129.8, 129.7, 129.2, 128.3, 128.2, 128.0, 127.5, 113.8, 99.5, 80.0, 78.9, 76.3, 75.0, 74.1, 73.2, 73.0, 72.7, 71.7, 71.4, 69.4, 69.2, 69.0, 68.4, 63.9, 55.2, 42.5, 25.9, 24.2, 18.1, 16.2, 15.9; MS (ES): *m*/*z* 1066 [*M*+Na]; HR-MS (ES) ($C_{69}H_{78}O_{13}Si$): calcd for [*M*+Na] 1165.5109; found 1165.5111.

4,6-Di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethyl)-α-D-mannopyranoside (**41**): Water (333 μL) and cerium ammonium nitrate (727 mg, 1.32 mmol) were added to a stirred solution of **32b** (150 mg, 0.13 mmol) in acetonitrile (3 mL) at 20 °C. After being stirred for 5 min the mixture was diluted with dichloromethane, and the organic phase was washed with a saturated solution of $NaHCO_3$, dried (Na_2SO_4), and evaporated to dryness in vacuo. Purification by flash chromatography (cyclohexane/EtOAc, 8:1) gave **41** (115 mg, 86 %) as a colorless syrup. $[\alpha]_D^{22} = +20$ (*c* = 0.7, chloroform); IR (neat): $\tilde{\nu}$ = 3063, 3032, 2927, 2856, 1725, 1452, 1271, 1111cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.02–7.93 (m, 4H, Ph), 7.48–7.09 (m, 26H, Ph), 5.54 (d, ^3J(H,H) = 2.0 Hz, 1H, H1), 5.39 (t, ^3J(H,H) = 9.0, 9.0 Hz, 1H, H4),

4.69 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.66 (d, ^2J(H,H) = 11.3 Hz, 1H, CHPh), 4.56 – 4.48 (m, 1H, H1′), 4.51 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.48 (d, ^2J(H,H) = 11.3 Hz, 1H, CHPh), 4.46 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.45 (d, ^2J(H,H) = 9.5 Hz, 1H, CHPh), 4.43 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.35 (d, ^2J(H,H) = 9.5 Hz, 1H, CHPh), 4.31 (ddd, ^3J(H,H) = 9.0, 4.5, 3.0 Hz, 1H, H5), 4.11 (dd, ^3J(H,H) = 9.0, 4.7 Hz, 1H, H3), 3.91 (dd, ^3J(H,H) = 4.0, 3.5 Hz, 1H, H2′), 3.87 (dd, ^3J(H,H) = 8.5, 3.5 Hz, 1H, H6a′), 3.84 (dd, ^3J(H,H) = 8.5, 4.5 Hz, 1H, H6b′), 3.80 (dd, ^3J(H,H) = 7.5, 3.5 Hz, 1H, H3′), 3.78 (ddd, ^3J(H,H) = 7.5, 4.5, 3.5 Hz, 1H, H5′), 3.70 (t, ^3J(H,H) = 7.5, 7.5 Hz, 1H, H4′), 3.68 (dd, ^3J(H,H) = 7.5, 4.5 Hz, 1H, H6a), 3.57 (dd, ^3J(H,H) = 7.5, 3.0 Hz, 1H, H6b), 2.49 (m, 1H, OH), 2.34 (m, 1H, H2), 2.06 – 1.70 (m, 2H, H7a, H7b), 0.87 (s, 9H, Si*t*Bu), 0.02 (s, 6H, 2SiMe); MS (ES): *m*/*z* 1046 [*M*+Na].

4,6-Di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,-4,6-tri-*O*-benzyl-*α*-D-mannopyranosylmethyl)-D-mannopyranosyl 2-pyridylsulfide (**42**): To a solution of hemiacetal **41** (275 mg, 2.72 mmol) in dichloromethane (7 mL) at 0 °C were added trichloroacetonitrile (273 μL, 2.72 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (21 μL, 0.14 mmol). After stirring for 4 h at 0 °C, the reaction mixture was evaporated to dryness and the imidate was purified by flash chromatography (cyclohexane/AcOEt, 4:1 with 1% triethylamine). The imidate was then redissolved in dichloromethane (12 mL) and cooled to − 15 °C, after which 2-mercaptopyridine (91 mg, 0.82 mmol) and $BF_3 \cdot OEt_2$ (7 μL, 0.054 mmol) were added. The solution was stirred at this temperature overnight and then evaporated to dryness in vacuo. The crude product was purified by flash chromatography (cyclohexane/EtOAc, 10:1) to give **42** (240 mg, 87%) as a colorless syrup. $[\alpha]_D^{22} = +17$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 3064$, 2924, 2854, 1726, 1600, 1261, 1108 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.36$ (m, 1H, pyr), 8.00 (m, 1H, pyr), 7.82 (m, 1H, pyr), 7.47 – 6.88 (m, 31H, pyr, 6Ph), 6.46 (d, ^3J(H,H) = 1.5 Hz, 1H, H1), 5.43 (dd, ^3J(H,H) = 9.5, 9.0 Hz, 1H, H4), 4.67 (d, ^3J(H,H) = 11.5 Hz, 1H, CHPh), 4.66 (d, ^3J(H,H) = 11.3 Hz, 1H, CHPh), 4.57 (ddd, ^3J(H,H) = 9.5, 5.0, 2.5 Hz, 1H, H5), 4.54 (s, 2H, 2CHPh), 4.52 (d, ^2J(H,H) = 11.3 Hz, 1H, CHPh), 4.47 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.42 (d, ^2J(H,H) = 12.5 Hz, 1H, CHPh), 4.33 (d, ^2J(H,H) = 12.5 Hz, 1H, CHPh), 4.08 (dd, ^3J(H,H) = 9.0, 4.6 Hz, 1H, H3), 3.92 (ddd, ^3J(H,H) = 6.5, 3.0, 2.5 Hz, 1H, H1′), 3.93 (dd, ^3J(H,H) = 7.0, 2.5 Hz, 1H, H3′), 3.91 (dd, ^3J(H,H) = 3.0, 2.5 Hz, 1H, H2′), 3.87 (d, ^3J(H,H) = 7.0, 5.0 Hz, 1H, H4′), 3.80 (dd, ^3J(H,H) = 7.0, 5.0 Hz, 1H, H6a), 3.77 (ddd, ^3J(H,H) = 5.0, 4.5, 4.5 Hz, 1H, H5′), 3.67 (d, ^3J(H,H) = 4.5 Hz, 2H, H6a′, H6b′), 3.64 (dd, ^3J(H,H) = 7.0, 2.5 Hz, 1H, H6b), 2.53 (dddd, ^3J(H,H) = 10.0, 4.6, 3.5, 1.5 Hz, 1H, H2), 2.18 – 1.95 (m, 2H, 2H7), 0.88 (s, 9H, Si*t*Bu), 0.07 (s, 3H, SiMe), 0.05 (s, 3H, SiMe); MS (ES): *m*/*z* 1139 [*M*+Na]; HR-MS (ES) ($C_{66}H_{73}NO_{11}SSi$): calcd for [*M*+Na] 1138.4574; found 1138.4571.

4,6-Di-*O*-benzoyl-3-*O*-benzyl-2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,-4,6-tri-*O*-benzyl-*α*-D-mannopyranosylmethyl)-D-mannopyranosyl 2-pyridylsulfone (**43**): To a mixture of sulfide **42** (220 mg, 0.20 mmol) and $NaHCO_3$ (118 mg, 1.40 mmol) in CH_2Cl_2 (12 mL) at 0 °C was added MCPBA of approximately 80% purity (156 mg, 0.6 mmol). The mixture was stirred for 1.5 h at 0 °C, after which it was diluted with CH_2Cl_2 and washed consecutively with a 50% saturated solution of $Na_2S_2O_3$, saturated $NaHCO_3$, and brine. The organic phase was dried with Na_2SO_4 and concentrated to dryness in vacuo. Flash chromatography (cyclohexane/EtOAc, 6:1) gave **43** (140 mg, 62%) as a colorless syrup. $[\alpha]_D^{22} = +37.2$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 3063$, 3031, 1725, 1452, 1315, 1270, 1106 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.62$ (dd, ^3J(H,H) = 5.0, 1.5 Hz, 1H, pyr), 7.98 (dd, ^3J(H,H) = 9.0, 7.5 Hz, 1H, pyr), 7.86 (d, ^3J(H,H) = 7.5 Hz, 1H, pyr), 7.61 – 7.10 (m, 31H, pyr, 6Ph), 5.40 (dd, ^3J(H,H) = 9.5, 7.0 Hz, 1H, H4), 4.88 (ddd, ^3J(H,H) = 9.5, 4.5, 3.5 Hz, 1H, H5), 4.70 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.62 (d, ^2J(H,H) = 11.5 Hz, 2H, CHPh), 4.58 (d, ^2J(H,H) = 11.5 Hz, 2H, CHPh), 4.49 (d, ^2J(H,H) = 11.5 Hz, 1H, CHPh), 4.48 (d, ^2J(H,H) = 11.5 Hz, 2H, CHPh), 4.50 (m, 1H, H1′), 4.44 (ddd, ^3J(H,H) = 4.5, 1.5, 1.5 Hz, 1H, H5′), 4.38 (dd, ^3J(H,H) = 1.5, 1.0 Hz, 1H, H2′), 4.26 (d, ^3J(H,H) = 1.2 Hz, 1H, H1), 3.88 (dd, ^3J(H,H) = 7.0, 4.2 Hz, 1H, H3), 3.86 (dd, ^3J(H,H) = 5.5, 4.5 Hz, 1H, H4′), 3.87 (dd, ^3J(H,H) = 6.0, 1.5 Hz, 1H, H6a′), 3.77 (dd, ^3J(H,H) = 6.0, 1.5 Hz, 1H, H6b′), 3.77 (dd, ^3J(H,H) = 9.5, 4.5 Hz, 1H, H6a), 3.66 (dd, ^3J(H,H) = 9.5, 3.5 Hz, 1H, H6b), 3.64 (dd, ^3J(H,H) = 5.5, 1.5 Hz, 1H, H3′), 3.20 (dddd, ^3J(H,H) = 11.5, 4.2, 4.2, 1.2 Hz, 1H, H2), 1.75 – 1.55 (m, 2H, H7a, H7b), 0.86 (s, 9H, Si*t*Bu), 0.06 (s, 3H, SiMe), 0.03 (s, 3H, SiMe); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 166.0$, 165.6, 155.9, 150.5, 138.8, 138.6, 138.3, 137.7, 133.5, 133.1, 130.1, 129.8, 129.5, 128.5, 128.4, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 123.8, 89.3, 78.9, 75.7, 74.7, 74.0, 73.2, 73.1, 72.4, 71.3, 69.1, 67.9, 63.8, 36.0, 35.6, 29.8, 26.3, 26.0, 18.1; MS (ES): *m*/*z* 1171 [*M*+Na]; HR-MS (ES) ($C_{66}H_{73}NO_{13}SSi$): calcd for [*M*+Na] 1170.4472; found 1170.4470.

4,6-Di-*O*-benzoyl-3-*O*-benzyl-1,2-deoxy-2-*C*-(2-*O*-*tert*-butyldimethylsilyl-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranosyl)-*α*-D-mannopyranoside (**44**): A 0.1M solution of SmI_2 in THF (1.4 ml, 0.14 mmol) was added to a stirred solution of sulfone **43** (70 mg, 0.062 mmol) and aldehyde **17a** (62 mg, 0.123 mmol) in THF (0.7 mL) under argon at 20 °C. After stirring for 10 min, saturated aqueous NH_4Cl was added to the reaction mixture which was then extracted twice with CH_2Cl_2. The combined organic phases were washed twice with water, dried with Na_2SO_4, and evaporated to dryness. Flash chromatography (cyclohexane/EtOAc, 10:1) gave **44** (60 mg, 97%) as a colorless syrup. $[\alpha]_D^{22} = +17.1$ ($c = 1.4$, chloroform); IR (neat): $\tilde{\nu} = 3063$, 3030, 2927, 2855, 1724, 1452, 1267, 1096 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.06 – 7.88$ (m, 4H, Ph), 7.61 – 7.09 (m, 26H, Ph), 5.34 (dd, ^3J(H,H) = 9.5, 8.5 Hz, 1H, H4), 4.68 (d, ^2J(H,H) = 12,0 Hz, 1H, CHPh), 4.67 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.56 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.54 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.52 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.46 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.44 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.44 (dd, ^3J(H,H) = 12.0, 4.5 Hz, 1H, H6a), 4.43 (d, ^2J(H,H) = 12.0 Hz, 1H, CHPh), 4.37 (dd, ^3J(H,H) = 12.0, 5.5 Hz, 1H, H6b), 4.24 (dd, ^3J(H,H) = 12.0, 3.0 Hz, 1H, H1β), 3.93 (dd, ^3J(H,H) = 5.5, 4.5 Hz, 1H, H2′), 3.86 (ddd, ^3J(H,H) = 9.5, 5.5, 4.5 Hz, 1H, H5), 3.82 (ddd, ^3J(H,H) = 5.5, 1.0, 1.0 Hz, 1H, H1′), 3.79 (dd, ^3J(H,H) = 8.5, 3.5 Hz, 1H, H3), 3.78 (ddd, ^3J(H,H) = 9.0, 6.0, 4.0 Hz, 1H, H5′), 3.73 (t, ^3J(H,H) = 9.0, 9.0 Hz, 1H, H4′), 3.70 (dd, ^3J(H,H) = 9.0, 4.5 Hz, 1H, H3′), 3.67 (dd, ^3J(H,H) = 11.0, 6.0 Hz, 1H, H6a′), 3.65 (dd, ^3J(H,H) = 11.0, 4.0 Hz, 1H, H6b′), 3.48 (dd, ^3J(H,H) = 12.0, 1.5 Hz, 1H, H1α), 3.47 (ddd, ^3J(H,H) = 9.0, 4.0, 1.0 Hz, 1H, H7a), 3.35 (ddd, ^3J(H,H) = 9.0, 9.0, 1.0 Hz, 1H, H7b), 2.26 (ddddd, ^3J(H,H) = 9.0, 4.0, 3.5, 3.0, 1.5 Hz, 1H, H2), 0.88 (s, 9H, Si*t*Bu), 0.05 (s, 3H, SiMe), 0.03 (s, 3H, SiMe); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 166.3$, 133.8, 133.6, 133.3, 133.2, 130.0, 129.9, 129.8, 129.7, 129.6, 129.0, 128.7, 128.6, 128.5, 128.0, 104.0, 102.3, 97.7, 76.7, 74.7, 72.4, 72.2, 72.0, 69.7, 69.2, 68.5, 68.3, 63.3, 63.2, 57.7, 55.4, 54.8, 38.0, 35.0, 29.7, 27.1; MS (ES): *m*/*z* 1130 [*M*+Na]; HR-MS (ES) ($C_{61}H_{70}O_{11}Si$): calcd for [*M*+Na] 1129.4587; found 1129.4585.

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