A General Approach to 1,2-*trans*-*C*-Glycosides via Glycosyl Samarium(III) Compounds

Troels Skrydstrup,* Olivier Jarreton, Daniel Mazéas, Dominique Urban and Jean-Marie Beau*

Dedicated to Professor Yoshito Kishi on the occasion of his 60th birthday

Abstract: The samarium diiodide reduction of glycosyl pyridyl sulfones with ketones or aldehydes under Barbier conditions leads to the instantaneous and stereospecific formation of 1,2-*trans*-*C*-glycosides in good to acceptable yields. Mannosyl pyridyl sulfones **5a**–**c**,**h** produce α-*C*-glycosides **7**–**10**, **12**, **13**, **15**–**17**, and **57** in yields up to 86% with minimal β elimination. In contrast, glucosyl pyridyl sulfones **19a** and **19b** lead to the corresponding β-*C*-glycosides **20**–**22** in yields up to 56% with increased β elimination. Similarly, galactosyl pyridyl sulfones **23a** and **23b** afford β-*C*-galactoside **24**. The stereochemical discrepancies between these reactions are probably based on the intermediacy of a common α-anomeric glycosyl samarium(III) compound (kinetic product) with an axially oriented C1–Sm bond after reduction of the pyridyl sulfone group. The thermodynamically more stable anomeric organosamarium with an equatorially oriented C1–Sm bond may then be obtained by a least energy pathway in the form of either a conformational ring-flip (in the manno series) or as a configurational change (in the gluco or galacto series). The tendency towards β elimination can be explained by the preference of glycosyl organosamarium compounds to undergo an unprecedented *syn*-elimination mechanism more easily achieved in the gluco and galacto series. C2-Unsubstituted 2-deoxy sugars display little or no stereoselectivity at C1 upon *C*-glycosylation.

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

Introduction

During the last decade a considerable amount of synthetic work has been devoted to the preparation of a series of *O*-glycoside mimics known as *C*-glycosides, in which the interglycosidic linkage is replaced by a methylene group.[1] The interest in such mimics was sparked by observations made by the Kishi group that in solution numerous synthesized *C*-disaccharides and *C*-trisaccharides display similar exoanomeric conformational preferences to that of the corresponding parent *O*-glycoside.[2, 3] More intensive studies recently performed by Jiménez-Barbero have shown that certain *C*-glycosides also exhibit greater flexibility and possess both exo- and nonexoanomeric conformations.[3e–g] This, along with the known chemical and enzymatic hydrolytic stability of *C*-glycosides, suggests the potential use of such carbon-analogue derivatives of significant carbohydrates (oligosaccharides) as stable biological tools or drugs.[4] Although the use of these analogues in biological systems is still in its infancy, certain reports have already described promising results in the replacement of *O*-glycosides by their *C*-congeners as ligands for carbohydrate-binding receptors.[5, 6]

Because of their great popularity, a multitude of synthetic approaches have been devised for the preparation of *C*-glycosides.[1] Despite this, there is as yet no general synthetic strategy for a facile and stereocontrolled route to a large collection of such compounds that employs a simple set of rules such as those for *O*-glycoside synthesis. In many instances access to these carbon analogues relies on synthetic strategies conceived for a particular structure, and are therefore unsuitable for the synthesis of other, though sometimes similar, *C*-glycosides. Partial solutions for a general synthetic stratagem were

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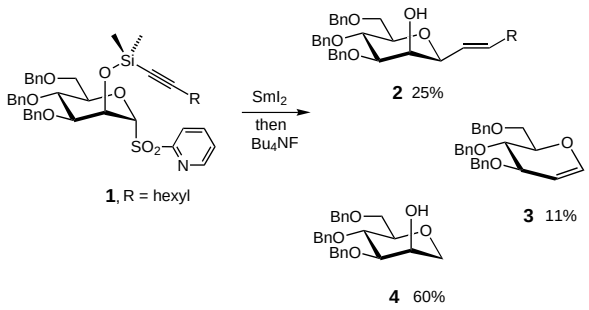
provided by several groups employing tin hydride-promoted 5-*exo* radical cyclizations with disposable tethers for the stereocontrolled synthesis of 1,2-*cis*-*C*-glycosides under mild conditions.[7, 8] We and others have since shown that the unique and polyvalent single electron reducing reagent samarium(II) diiodide (SmI_2)[9] can likewise be used for the effective generation of a glycosyl anomeric radical that may undergo intramolecular trapping to afford 1,2-*cis*-*C*-glycosides.[10]

In this paper, we report that samarium diiodide can also promote a very mild and stereospecific synthesis of 1,2-*trans*-*C*-glycosides by means of the reductive samariation of mannosyl, glucosyl, and galactosyl 2-pyridyl sulfones and the coupling of the correspondingly generated glycosyl C1-organosamarium intermediate with carbonyl substrates under Barbier conditions. The surprising finding is that β elimination of the anomeric samarium reagent leading to the formation of glycals appears to be a minor pathway that may sometimes be completely suppressed. This is in complete contrast to reports on the corresponding C1-lithium derivatives, as well as on other metals. This samariation route is an extremely mild, simple, and general approach to 1,2-*trans*-*C*-glycosides, providing a complementary strategy to the 1,2-*cis* approach.[7f, 10, 11]

Results and Discussion

Until recently, the most popular route to anomeric carbanions relied either on i) the low temperature ($-78\,^{\circ}C$) reductive lithiation of anomeric halides,[12] phenyl sulfides,[12a, 13] or phenyl sulfones,[14] ii) the transmetalation of the corresponding C1-stannyl reagents,[12d–f, 15] or iii) the direct deprotonation of the anomeric proton.[16] The use of the generated anomeric lithium species for the construction of *C*-glycosides, however, has been primarily restricted to 2-deoxy sugars[12a, b, 13e, 14, 15a–d, 16f] or glycals,[17] since β elimination of the C2-substituent is a facile process even when a stabilizing substituent is present at the anomeric carbon.[12a, 13d, 16c, d, 18, 19] Exceptions have been reported in the gluco series where the C2 hydroxyl group is lithiated before C1-lithiation, a procedure conducted at low temperatures ($\leq -78\,^{\circ}C$) to prevent elimination of Li_2O and maintain the configurational stability of the tetrahedral anionic species.[12c–f, 15e, f] Similar attempts with α-D-mannopyranosyl units have never been reported, possibly because of the *trans*-diaxial orientation of the C2-hydroxyl substituent with respect to the C1–Li bond, which should favor an easy *anti* elimination. This was the case upon reductive lithiation of a mannosyl phenyl sulfide derivative with a trimethylsilyl group at O2.[13d]

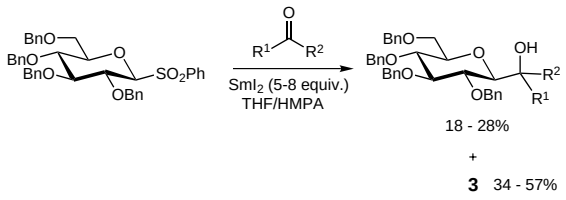
Reductive samariation of D-mannopyranosyl 2-pyridyl sulfones: Our work with anomeric organosamarium compounds began with an attempt to promote the SmI_2-induced radical cyclization of mannosyl pyridyl sulfone **1** with a nonactivated alkyne (Scheme 1).[10] At the time glycosyl pyridyl sulfones were found to be ideal candidates for C1-radical generation with samarium diiodide alone, in contrast to the more widespread phenyl sulfones, which require a cosolvent, such as hexamethylphosphoramide (HMPA), for an effective one-electron transfer from SmI_2 to the sulfone moiety.[8d, 20, 21]



Scheme 1. SmI_2 induced radical cyclization of **1**.

Whereas a low yield of the anticipated *cis*-*C*-glycoside **2** was observed after radical cyclization and desilylation of **1**, the expected side-product formed from a sequential two-electron reduction process and elimination, glucal **3**, was isolated in only 11% yield. Instead, the major product from the reaction mixture was identified as the 1-deoxymannoside derivative **4** a fact that implies that the anomeric radical had either abstracted a hydrogen atom from the ethereal solvent or undergone reduction to give a stable anomeric organosamarium intermediate. The low yield of the glycal isolated suggests that, if the latter case is correct, this organometallic species displays considerable stability towards β elimination. Since organosamarium reagents in general show a propensity to undergo efficient coupling reactions with carbonyl compounds,[9] the above results suggested the possibility of adapting this approach to *C*-glycoside synthesis.

Prior to this, Sinaÿ and co-workers reported that reductive samariation of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl phenyl sulfones by the SmI_2/HMPA system in the presence of simple carbonyl compounds provided the corresponding β-*C*-glucoside (Scheme 2), albeit in low yields (18–28%).[20c, 22]



Scheme 2. Reaction of glucosyl phenyl sulfones with SmI_2.

Contrary to our earlier observations, the major component in these condensations was the expected glucal **3** (34–57%). The same group observed that the reductive samariation of various glycosyl phenyl sulfones in the absence of a suitable carbonyl substrate provides an efficient entry to glycals.[20b] These reactions characteristically require an excess of SmI_2 (5–8 equivalents) owing to the competitive reduction of the formed phenylsulfinate ion in the presence of HMPA. It was therefore surprising that the 1-deoxymannoside **4** was the major product of the reaction in Scheme 1.

The suitability of glycosyl pyridyl sulfones for *C*-glycoside synthesis was investigated with the 3,4,6-tri-*O*-benzyl-2-*O*-trimethylsilyl-α-D-mannosyl 2-pyridyl sulfone (**5a**) which closely resembles pyridyl sulfone **1**, prepared by smooth silylation of mannoside **6** (see Scheme 3).[10] On addition of a

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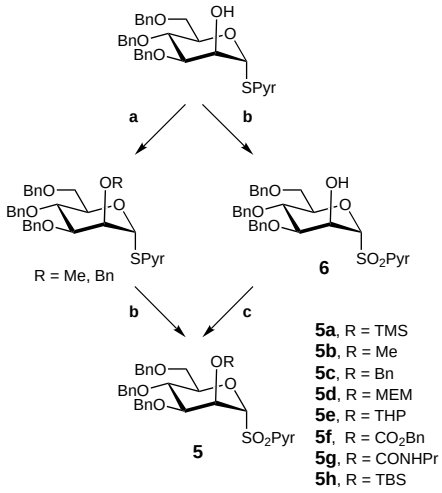
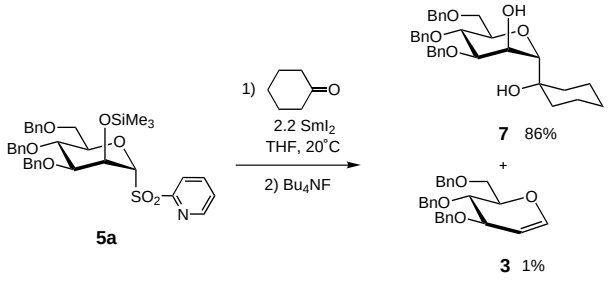


Scheme 3. Formation of mannosyl pyridyl sulfones **5a**–**5h**. Reaction conditions a) NaH, MeI, or BnBr (Bn = benzyl); b) 3-chloroperoxybenzoic acid (MCPBA); c) trimethylsilyl chloride (TMSCl) or *tert*-butyldimethylsilyltrifluoromethanesulfonate (TBSOTf) or 2-methoxyethoxymethyl chloride (MEMCl) with $ClCO_2Bn$ or pyrNCO (pyr = pyridyl) with triethylamine (TEA), 4-dimethylaminopyridine (DMAP) or 3,4-dihydro-2*H*-pyran (DHP), *p*-toluenesulfonic acid.

0.1M blue solution of samarium diiodide in THF to a 0.3M THF solution of pyridyl sulfone **5a** and cyclohexanone (1.5 equiv) at 20°C, a decoloration of the blue SmI_2 was noted until slightly more than 2 equiv of the reducing agent had been consumed. This indicated the endpoint of the reaction, as seen by the excess SmI_2. Desilylation of the crude product with tetrabutylammonium fluoride (TBAF) then led to the isolation of *C*-mannoside **7**, identified as its α anomer, in an overall yield of 86% with only 1% of the elimination product **3** and 4% of 1-deoxy derivative **4** (Scheme 4). The

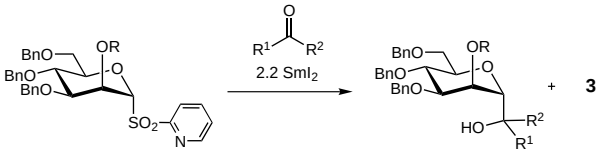


Scheme 4. Reaction of **5a** with samarium iodide and cyclohexanone.

corresponding β anomer could not be detected as we proved by its independent synthesis (see below). The reaction is general for both alkyl ketones and aldehydes, giving products **8**–**10** (Table 1, entries 1–3). With the aldehydes in entries 2 and 3, a diastereomeric mixture of *C*-glycosides is formed in approximately a 5:1 ratio at the newly created exocyclic stereocenter C7.

Whereas these results are indicative of an intermediate organosamarium compound, they are unusual in terms of efficiency and stereoselectivity. The bimolecular organosamarium carbonyl condensation is the dominant pathway instead of the elimination process, even though a *trans*-diaxial

Table 1. Anionic coupling of pyridyl sulfones **5** with carbonyl compounds.



	R		Carbonyl compound	*C*-Glycoside	Glucal **3** (isolated yields)
1	TMS	**5a**	3-pentanone	**8** 80%[a]	3%
2	TMS	**5a**	isobutyraldehyde	**9** 77% (13:2)[a]	7%
3	TMS	**5a**	octanal	**10** 82% (9:2)[a]	9%
4	TMS	**5a**	benzaldehyde	**11** 10% (2:1)[a]	32%
5	TMS	**5a**	—	**4** 91%[a]	9%
6	Me	**5b**	cyclohexanone	**12** 78%	9%
7	Bn	**5c**	cyclohexanone	**13** 82%	6%
8	MEM	**5d**	cyclohexanone	45%	25%
9	THP	**5e**	cyclohexanone	56%	21%
10	Ac[10]		cyclohexanone	0%	94%
11	CO_2Bn	**5f**	cyclohexanone	0%	62%
12	CONHPr	**5g**	cyclohexanone	0%	99%
13	H	**6**	cyclohexanone	**7** 13%	17%
				BnO, OH, O, OH, BnO, BnO **14** 19%	

[a] Yields are based on the desilylated product.

relationship between the C2–$OSiMe_3$ and the C1–Sm bonds exists. Further, α-tetrahydropyranyl anions, formed kinetically from a stepwise one-electron reduction process,[13c, f, 23] exhibit stereochemical stabilities only at low temperatures (approximately −78°C). The thermodynamically more stable β-glycosyl samarium species would be expected to dominate at room temperature, with the result of the formation of β-*C*-mannosides. The coupling reactions, which have high yields compared with previous results obtained with glucosyl phenyl sulfones,[20c] are quick and simple to execute as titrations, as a result of the immediate reaction of glycosyl pyridyl sulfones with SmI_2.

To obtain high yields of the desired α-*C*-mannoside, these C–C bond-forming reactions have to be performed under Barbier conditions. Addition of the carbonyl compound even 20 s after treatment of the glycosyl pyridyl sulfone with SmI_2 gave no coupled products. This observation is in accord with previous results demonstrating the limited stability of alkyl samarium(III) species in THF solutions; the organosamarium compound easily abstracts a proton from a metal-coordinated THF solvent molecule.[24] Only in the presence of a cosolvent,

such as HMPA, which has a strong binding affinity for the metal ion and hence provides an effective shield against THF coordination, are the alkyl samarium species sufficiently stable to partake in Grignard-type reactions.[24] In the absence of a carbonyl substrate, the reaction with pyridyl sulfone **5a** led to the formation of 1-deoxy derivative **4** in a 91% yield with only 9% of the elimination product (entry 5). Again, these results demonstrate the reluctance of the anomeric organosamarium species to undergo β elimination.

We noted a low yield of **11** in the attempted coupling between **5a** and benzaldehyde (Table 1, entry 4). Competitive reduction of benzaldehyde by SmI_2 is the most likely explanation, owing to a low-lying $\pi^*_{C=O}$ energy level; this is in line with the observation that the reaction mixture rapidly consumed approximately 4 equivalents of SmI_2. The unexpected increased formation of glucal **3** in this reaction is at present unexplained.

Evidence for the stereochemical assignment at C1 of these new *C*-glycosides is based on the following ^{1}H NMR spectral observations. Previous experiments with α-*C*-glucosides obtained by anionic condensation with aldehydes or ketones have shown that these compounds adopt conformations close to that of a $^0S_2$ skew-boat,[12c, d] which is probably the case for the corresponding α-*C*-mannosides disposing of two axially oriented substituents at C1 and C2. The vicinal coupling constants between H3–H4 and H4–H5 (e.g., for **7**: $J_{H3,H4}$ = 5.7 Hz, $J_{H4,H5}$ = 4.1 Hz) clearly deviate from the large *trans*-diaxial coupling constants normally observed for a $^4C_1$ conformation and as expected for the analogous β isomer (see below). In addition, an $^0S_2$ skew-boat conformation of α-*C*-mannosides places H1 and H6 close to each other (Figure 1), as confirmed by the strong NOE between these two hydrogens.

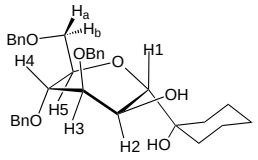


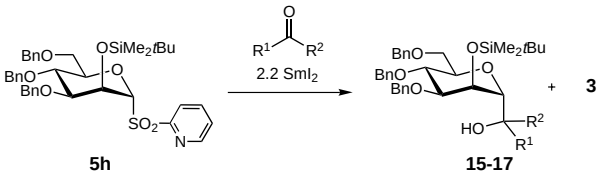
Figure 1. Conformational analysis of *C*-mannoside **7**. Coupling constants: $J_{H3,H4}$ = 5.7 Hz, $J_{H4,H5}$ = 4.1 Hz.

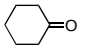
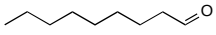
The remarkable stability displayed by the mannosyl samarium species led us to examine the influence of the O2-protecting group on the coupling efficiency and on the yields of the β-elimination product. A series of mannosyl pyridyl sulfones **5b**–**5h** were prepared from the unprotected O2-pyridyl sulfone **6** by means of standard protocols (Scheme 3). Direct alkylation of the C2-hydroxy group in **6** was, however, not rewarding owing to competitive deprotonation of the acidic anomeric hydrogen of **6** upon treatment with strong bases. Instead, initial alkylation of the corresponding pyridyl sulfide and subsequent oxidation with MCPBA led to the desired compounds **5b** and **5c**.[25] Each mannosyl pyridyl sulfone was then treated with 2 equivalents of SmI_2 in the presence of cyclohexanone (1.5 equiv) employing the standard procedure. Incorporation of a C2-alkoxy group in **5** did not lower condensation yields (Table 1, entries 6 and 7), and only the α-*C*-mannosides **12** and **13** were obtained, allowing for an extension of this *C*-mannosylation technique to even simpler mannosyl pyridyl sulfones as the tetrabenzyl derivative **5c**. On the other hand, in the examples bearing acetal linkages to the C2-hydroxyl group, such as the MEM and THP protecting groups (entries 8 and 9), β elimination increased. Even worse were the C2-acetoxy,[10] C2-benzylcarbonate, and C2-*N*-propylcarbamate derivatives (entries 10–12), which possess a sufficiently low-lying σ^*_{C2-O2} orbital to make elimination the more energetically favored pathway.

The coupling of **6**, unprotected at 2-OH, to cyclohexanone gave another unexpected result (Table 1, entry 13). A 2:3 mixture of α- and β-*C*-glycosides **7** and **14**, albeit in low yields, was obtained as well as the major product, the 1-deoxy sugar **4**. The stereochemical assignment of this new C1 isomer indicated that **14** occupies a normal $^4C_1$ chair conformation shown by the large *trans*-diaxial coupling constants between H3 and H4, and H4 and H5 ($J_{H3,H4}$ = 9.0 Hz, $J_{H4,H5}$ = 9.0 Hz) in the ^{1}H NMR spectrum.

We also examined the importance of a sterically more hindered protecting group at C2 such as the *tert*-butyldimethylsilyl (TBS) group in **5h** (Table 2). Condensation with

Table 2. Anionic coupling of pyridyl sulfone **5h** with carbonyl compounds.



	Carbonyl compound	*C*-Glycoside (isolated yields)	Glucal **3**
1		**15** 80%	0%
2		**16** 84% (4:1)	0%
3		**17** 71% (5:1)	0%

cyclohexanone was equally efficient, although in contrast to the other reactions, no tribenzylglucal could be detected in the reaction mixture (entry 1). Examples of coupling with alkyl aldehydes gave high yields of α-*C*-mannosides as approximately 5:1 diastereomeric mixtures at C7 also with no β elimination (entries 2 and 3).

For the relative stereochemical assignment of the two diastereomeric *C*-mannosides at C7 obtained from coupling reactions with aldehydes, we resorted to a simple and reliable protocol devised by Rychnovsky for the determination of the stereochemistry of 1,3-diols.[27] According to Rychnovsky, the *syn*-1,3-diol acetonides occupy a single chair conformation; this results in two distinguishable methyl groups upon analysis of their ^{13}C NMR spectra. An axial methyl group is typically observed at $\delta \approx 19$, whereas an equatorial methyl group shows a peak at $\delta \approx 30$. In contrast, *anti*-1,3-diol acetonides adopt a skew-boat conformation because of an unfavorable 1,3-diaxial interaction in the chair, and both methyl groups appear at $\delta \approx 25$.

The chromatographically separable *C*-mannosides **17** (Table 2, entry 3) were desilylated and converted to their corresponding acetonides **18a** and **18b** (Scheme 5). ^{13}C NMR analysis of the acetonide derivative **18a** of the major

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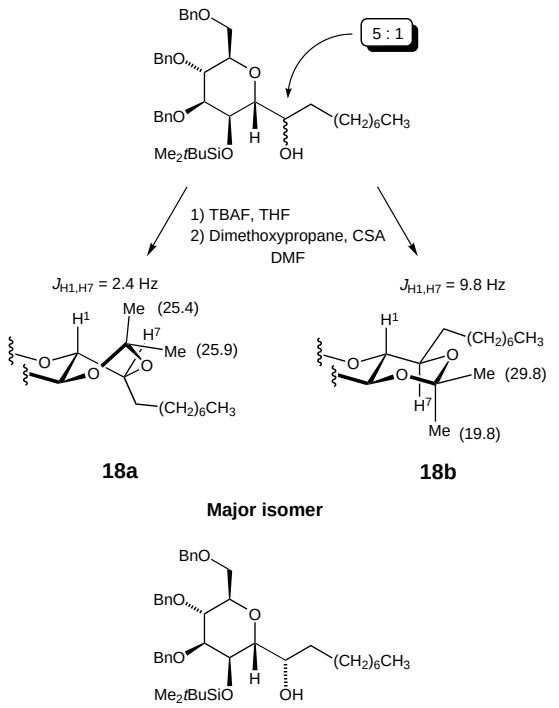
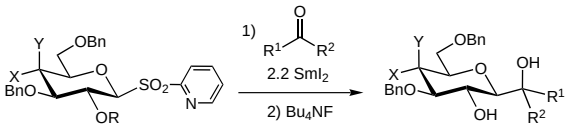


Scheme 5. Formation of the acetonides **18a** and **18b**. The chemical shifts of the protons (δ) are given in brackets.

C-glycoside revealed methyl resonances at 25.4 and $\delta = 25.9$, whereas corresponding resonances for the minor isomer **18b** were observed at $\delta = 29.8$, 19.8. This suggests that the dioxolane ring of the minor isomer occupies a chair conformation, a conclusion also supported by the large *trans*-diaxial coupling constant between H1 and H7 ($J_{H1,H7} =$ 9.8 Hz), a situation which can only occur if the minor isomer possesses the *R* configuration at C7. The almost identical ^{13}C chemical shifts for the two acetonide methyl groups of the major isomer in turn correlate well with an *anti* relationship between the C2 and C7 hydroxyl groups. Extrapolation of these results to all other coupling reactions between mannosyl pyridyl sulfones and alkyl aldehydes suggests that the major diastereomer formed is the *S* isomer at C7.

Reductive samariation of D-gluco and D-galactopyranosyl 2-pyridyl sulfones: Having examined the successful Barbier condensation with mannosyl pyridyl sulfones, we next turned to exploring similar reactions in the corresponding gluco series. As with **5a**, the glucosyl pyridyl sulfone **19a** afforded a single *C*-glycoside upon coupling with cyclohexanone, but in this case the expected β anomer was the preferred product (Table 3, entry 1), parelleling the earlier reports by Sinaÿ.[20c] Quite extraordinary, though, was the almost twofold reduction in yields of the *C*-glucoside formed compared with **7**, which was compensated by an increase in glucal production. A similar result was noted in the condensation with heptanal to afford a 7:2 diasteromeric mixture at C7 (entry 2). Also in contrast to previous results with **5a**, **19a** showed a preference for β elimination rather than proton abstraction upon treatment with divalent samarium in the absence of a carbonyl substrate (entry 3). Hence, β elimination appears to be an energetically more favored pathway for the gluco series than for the analogous

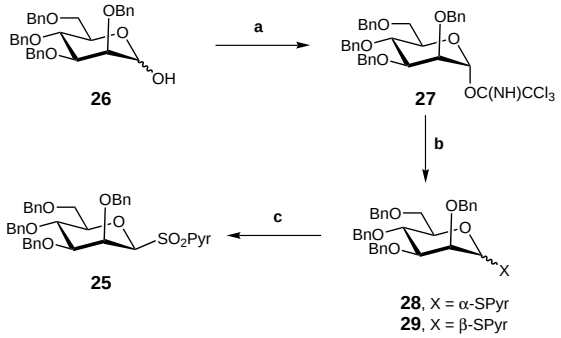
Table 3. Anionic coupling of pyridyl sulfone **19** and **23** with carbonyl compounds.



	R	Carbonyl compound	*C*-glycoside isolated yields	Glycal
1	$SiMe_3$, **19a**	cyclohexanone	**20**, 44 %	37 %
2	$SiMe_3$, **19a**	heptanal	**21**, 43 % (7:2)	36 %
3	$SiMe_3$, **19a**	–	(1-deoxy), 23 %	60 %
4	$SiMe_2t$Bu, **19b**	cyclohexanone	**20**, 57 %	21 %
5	$SiMe_2t$Bu, **19b**	isobutyraldehyde	**22**, 55 % (3:2)	22 %
6	$SiMe_3$, **23a**	cyclohexanone	**24**, 25 %	35 %
7	$SiMe_2t$Bu, **23b**	cyclohexanone	**24**, 22 %	32 %

manno series, a fact that is quite remarkable considering that only with the latter is a more favorable *trans*-diaxial arrangement between the C2–O2 and C1–Sm bonds obtained upon reduction of the common anomeric radical intermediates. The unwanted β elimination could be partly suppressed by substituting the TMS protecting group of O2 with the more bulky TBS group as in **19b**, leading to more acceptable yields of β-*C*-glucosides (entries 4 and 5). The low diastereoselectivity observed at the newly created exocyclic stereocenter parallels previous results noted in low-temperature coupling reactions with anomeric lithium reagents and shows that the major isomer has C7-(*R*)-configuration.[12c, d] A similar result was obtained with the galactosyl pyridyl sulfones **23a** and **23b**, which produced only β-*C*-galactoside **24** (Table 3, entries 6 and 7), albeit in low yields even with a TBS group at O2.

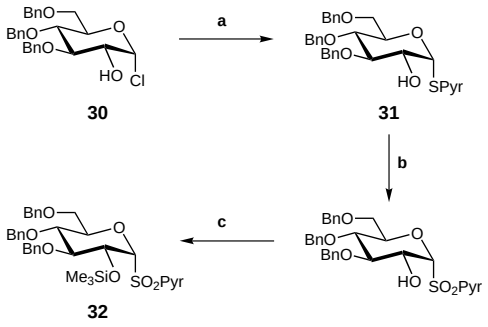
Influence of the anomeric configuration of the glycosyl pyridyl sulfones: The starting glycosyl pyridyl sulfones had identical anomeric compositions as did their *C*-glycosides. To provide more mechanistic insight into these reactions and to investigate whether stereochemical transmission was only a consequence of the starting glycoside's C1-configuration, we prepared β-mannosyl and α-glucosyl pyridyl sulfones and studied their SmI_2-promoted reaction with carbonyl compounds. For the manno series, we chose the β-pyridyl sulfone **25**, the preparation of which is outlined in Scheme 6. The



Scheme 6. Synthesis of β-pyridyl sulfone **25**. Reagents: a) NaH, Cl_3CCN; b) pyrSH, BF_3:Et_2O (cat.); c) chromatographic separation then MCPBA.

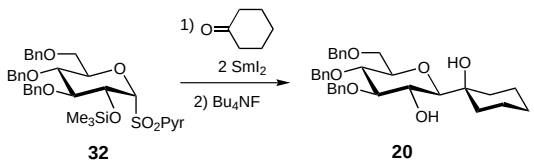
readily accessible tetrabenzylmannopyranose **26**[28] was converted to the α-trichloroacetimidate **27**, followed by the introduction of a pyridylsulfide unit by treatment of the latter with mercaptopyridine and catalytic amounts of BF_3:Et_2O. This afforded a chromatographically separable mixture of α and β anomers **28** and **29**. Finally, the β-pyridyl sulfide **29** was oxidized to the corresponding β-sulfone **25**. The structure of the β anomer was confirmed by the following spectral observation. It was earlier noted that in the ^{1}H NMR spectrum of all α-pyridyl sulfones, the axially oriented C5 hydrogen is strongly shifted downfield (ca. 4.2 ppm) as a result of an anisotropic effect with the proximal sulfone oxygens. For β-sulfone **25**, as well as for the glucosyl pyridyl sulfones **19a** and **19b** this effect is absent, and a normal chemical shift of $\delta = 3.5$ was found for the C5 hydrogens.

For the synthesis of an α-glucosyl pyridyl sulfone we chose a somewhat unorthodox synthetic route, illustrated in Scheme 7, which was justified by the lack of literature



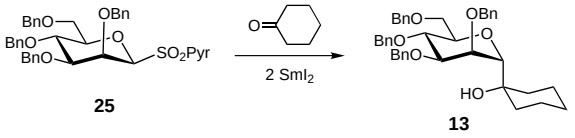
Scheme 7. Synthesis of α-glucosyl pyrdiyl sulfone (**32**). Reagents: a) i) BuLi, $-78\,^\circ$C, ii) LN, $-95\,^\circ$C, iii) pyrSSpyr; b) MCPBA; c) TMSCl, TEA.

precedent for their effective preparation. Hence, the easily accessible glucosyl chloride **30** was converted to its dilithium dianion according to the procedure developed by Wittmann and Kessler.[12c] Subsequent treatment with dipyridyl disulfide led to the exclusive formation of the α-sulfide **31**, which upon oxidation with MCPBA and trimethylsilylation afforded sulfone **32**. Subjecting **32** to the standard coupling conditions with cyclohexanone again led to the generation of a single *C*-glycoside (Scheme 8) in an unoptimized yield (single trial),



Scheme 8. Reaction of **32** with samarium iodide and cyclohexanone.

which was identified as the β anomer **20**. In a similar manner (Scheme 9), the β-mannosyl pyridyl sulfone **25** gave the previously synthesized α-*C*-mannoside **13** (Table 1, entry 7). Hence as expected, the anomeric configuration of the starting glycosyl sulfone has no influence on the outcome of the *C*-glycoside structure formed.



Scheme 9. Reaction of **25** with samarium iodide and cyclohexanone.

A mechanistic proposal: In Scheme 10, we provide a mechanistic rationale for the above observations on these highly stereoselective *C*-glycosylation reactions. One-electron transfer from SmI_2 to the aryl sulfone LUMO of either glycosyl pyridyl sulfone leads to homolytic C1–S bond cleavage and concomitant formation of the thermodynamically more stable α-radical owing to favorable overlap between the singly occupied p_{C1} and n_{O5} orbitals.[13c, 23, 29] This electron-reduction step should therefore be independent of the anomeric configuration of the starting sulfones, as is observed. The formation of only β-*C*-glycosides in the gluco and galacto series (in the following, the discussion concerning the gluco series also includes the galacto series) confirms that the *C*-glycosides formed in the manno series were not, at this stage, merely products of an intermolecular radical coupling process affording the α-*C*-anomer. A second reduction step then leads to a kinetic α-oriented organosamarium **33** or **34** in analogy to previous reports on the low-temperature reductive lithiation studies on similar compounds. In order to relieve the energetically unfavored interaction between the occupied σ_{C1-Sm} and n_{O5} orbitals, intermediates **33** and **34** have two ways to place these two bonds in an orthogonal arrangement.[13c, 23] Either a conformational ring flip to give **35** and **36** as either a boat or skew-boat conformer or a configurational change affording anomers **37** and **38** may be envisaged, positioning the C1- and C2-substituents in an energetically and sterically more favored diequatorial arrangement. For the manno compounds the former is apparently the preferred pathway, helped by the *trans*-diaxial orientation at C1 and C2 of **33**, and hence leads to the α-*C*-mannosides. In the gluco series, the equatorially oriented C2–O2 bond must move through an eclipsed conformer with the C1–Sm bond, making this a higher energy process. Hence configurational change to the β-organosamarium **38** is the dominant pathway.[30]

To explain the surprisingly greater facility for β elimination in the latter series, we suggest that in heteroatom-substituted organosamarium compounds a hitherto unknown *syn*-elimination mechanism is operating which is energetically preferred over the *anti* process.[31] The reduced yields of tribenzylglucal upon reaction with the more bulky C2-protected sulfones **5h** and **19b** (TBS compared with TMS) lends support to this hypothesis. The high 1,2-*trans* selectivity observed in the two series may therefore be the direct result of a facile β elimination of the 1,2-*cis* samarium(III) species **37** in the manno series, and **34** and/or **36** in the gluco series. As reduction of the glucosyl C1-radical leads directly to the 1,2-*cis* spatial arrangement in **34**, elimination is expected to be faster in this series. This behavior contrasts with that of the corresponding lithium reagents, which at $-78\,^\circ$C undergo fast β elimination in the manno series or 1,3-O2-to-C1 silyl migration in the gluco case.[13d]

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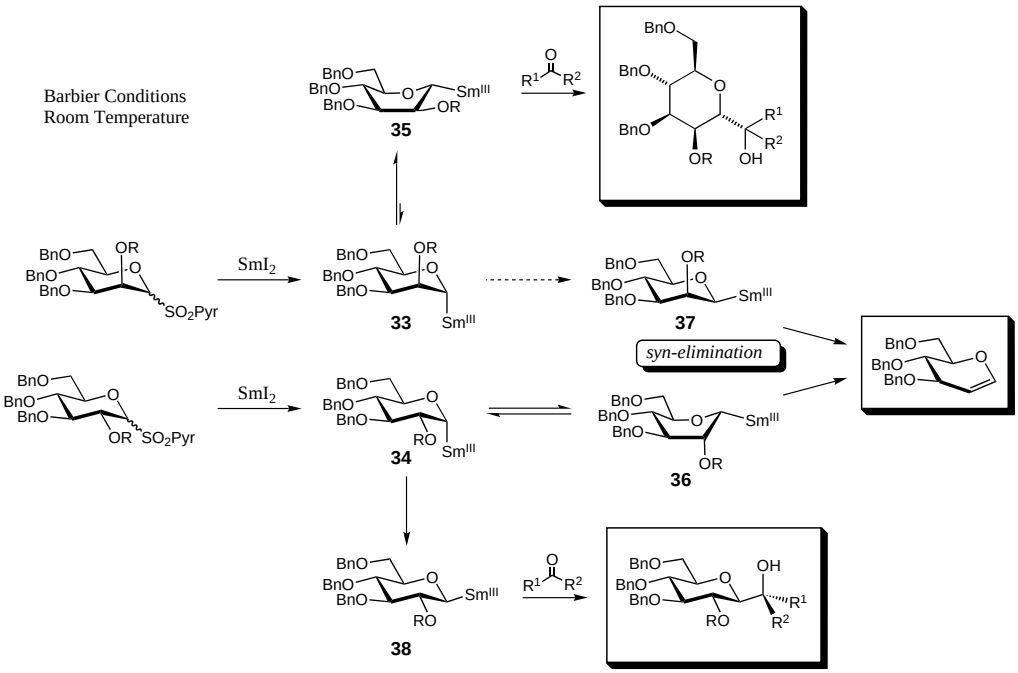
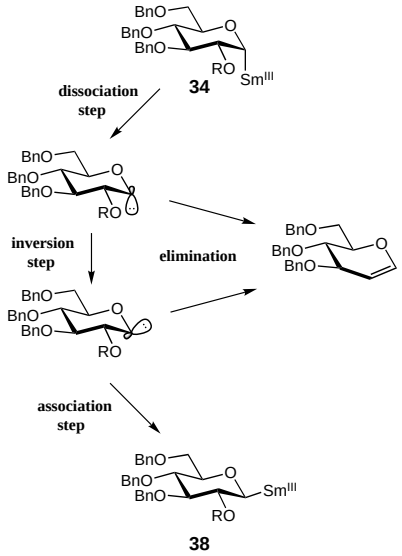


Scheme 10. Mechanistic rationale for the highly stereoselective *C*-glycosylation reactions.

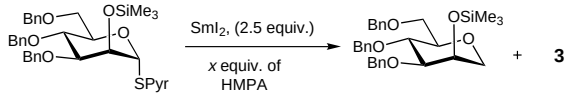
The higher elimination yields in the gluco series could likewise be the coincidental result of the anomerization process itself. Assuming that first-order kinetics hold in the configurational change between **34** and **38**, then the intervention of two naked anomeric anions must be considered as depicted in Scheme 11. Either one of these highly reactive



Scheme 11. Configurational change between **34** and **38**.

intermediates[32] may undergo competitive β elimination before recombination with the metal cation to the more stable β anomer. We are of course assuming that the σ_{C1-Sm} bond itself is of sufficiently low energy such that any overlap with the σ^*_{C2-O2} bond is negligible. The almost exclusive production of glycal upon treatment of glycosyl phenyl sulfones with the SmI_2/HMPA combination[20b, c] (compare this result with those of Table 3) provides some basis for this hypothesis. The good metal-complexing ability of HMPA allows for more anionic character at the anomeric center and hence greater ease in elimination. Increased elimination was also noted in the manno case upon reductive samariation in the presence of HMPA (see Table 4). Further work will be

Table 4. Influence of HMPA on the reductive samariation of pyridyl sulfones **43**.



43 **44**

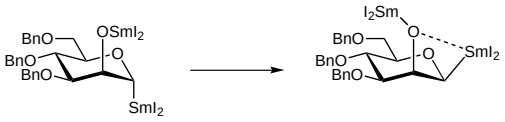
	x equiv of HMPA	1-Deoxy **44** Isolated yields	Glucal **3** Isolated yields
1	0	71%	5%
2	2	13%	65%
3	4	9%	73%

necessary to determine whether this mechanism or the one involving *syn* elimination is operating.

An unexpected feature of the glucosyl and galactosyl pyridyl sulfones was the poor *C*-glycosylation efficiency in the latter series. This is again surprising considering that the only difference between the two series is the stereochemistry of the distal chiral center in the sugar rings (C4). In addition, no difference in coupling or elimination yields was noted between substrates possessing a C2-OTMS or -OTBS substituent (Table 3). Apparently, the subtle differences in the stereochemistry of the sugar ring-carbons greatly influence the efficiency of the resulting *C*-glycosides. It is possible that in the galacto series the association step considered in

Scheme 11 is slowed for steric reasons (axially oriented C4-substituent), thus favoring elimination. These preliminary studies in this series clearly show the need for additional work in order to make these reactions of synthetic use for the preparation *C*-galactosides. If optimized, the reductive samariation approach will provide a rapid and easy approach to β-*C*-galactosides.

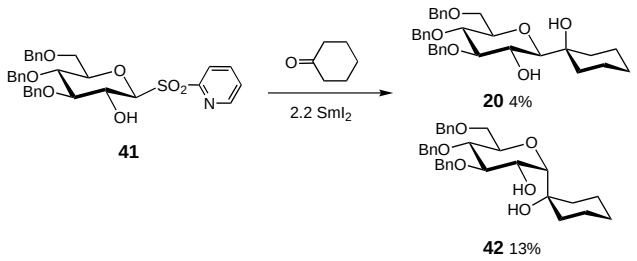
One result which did not conform to the above stereochemical trends was the nonselective *C*-glycosylation (α:β ca. 2:3) noted for the mannosyl pyridyl sulfone **6** with a free C2-hydroxyl group. The yields were nonetheless low and production of the 1-deoxy derivative was likewise increased. Hence partial intermolecular self-protonation is the most likely explanation for the inefficiency of the glycosylation process itself. It is therefore conceivable that the samarium C2-alkoxide species **39** is formed under these reaction conditions in which, because of the formation of a stable 4-membered cyclic intermediate involving a β-oriented C1–Sm bond, a configurational change to form **40** becomes energetically favored (Scheme 12). This result was confirmed by



39 **40**

Scheme 12. Formation of the stable 4-membered cyclic intermediate.

repeating the reaction with the analogous gluco derivative **41**, furnishing a 3:1 mixture of α- and β-*C*-glucosides **42** and **20** in 17% yield (Scheme 13). The conformation of **42** deviates



41

20 4%

42 13%

Scheme 13. Formation of α- and β-*C*-glucosides **42** and **20**.

from the normal $^4C_1$ chair conformation as observed for the β-*C*-glucosides and instead resembles that of $^0S_2$ skew-boat as seen from comparison of its proton coupling constants with those of other α-*C*-glucosides.[10, 12c] Again, the intervention of a 4-membered-ring organosamarium intermediate may account for the observed anomeric stereoselective deviation with respect to **19a** and **19b**. The isolation of 1,2-*cis*-*C*-glycosides in these two examples is also in agreement with the previously suggested *syn* elimination mechanism as now 1,2-*cis*-glycosyl samarium reagents are formed that are less prone to elimination of $O(SmI_2)_2$.

At this point, we were curious to examine the influence of the addition of HMPA on these *C*-glycosylation reactions. Whereas it is well known that HMPA increases the reducing potential of SmI_2 by means of its complexation to the divalent metal and subsequent raising of the HOMO energy level,[33–35] it has also been demonstrated that alkyl organosamarium reagents prepared in the presence of HMPA display increased stability towards protonation from solvent.[24] Subsequently, these reagents have been exploited in Grignard-type reactions. The greater complexing ability of HMPA with the trivalent metal cation compared with THF prevents complexation of the ethereal solvent and hence the ensuing deprotonation. Would it therefore be possible to perform the SmI_2-promoted glycosylations under Grignard conditions? The previous observations by Sinaÿ and co-workers in comparison with ours suggest not,[20c] but under these highly reducing conditions excess divalent samarium was mandatory owing to the competitive reduction of the generated sulfinate ion. We have previously observed that glycosyl pyridyl sulfides are also reduced by SmI_2, albeit slower (approx. 1 h) than their corresponding sulfones.[36] The addition of HMPA should therefore increase their reduction rate whilst addition of excess SmI_2 would be superfluous.

To test the behavior of glycosyl pyridyl sulfides to the SmI_2/HMPA combination, sulfide **43** was subjected to 2.5 equivalents of SmI_2 with varying amounts of HMPA (Table 4). Without HMPA, the reduction of the aryl sulfide moiety by SmI_2 required 1.5 hours, and afforded the 1-deoxy derivative **44** and glucal **3** in a ratio of 13:1, paralleling previous results seen with sulfone **5a**. However, addition of 2–4 equivalents of HMPA resulted in an immediate decoloration of the reaction mixture indicating the rapid consumption of SmI_2 by the pyridyl sulfide moiety. Analysis of the product mixture after work-up revealed a new proportion of **44** and **3** that was a complete reversal of the above ratio. β elimination appears now to be the preferred pathway with increasing addition of HMPA, whereas protonation proves less important. The greater complexation of HMPA to Sm^{III} and subsequent increased ionic character of the C1–Sm bond is the most likely explanation for the increased formation of glucal. These observations explain the lower coupling yields and increased β elimination reported by Sinaÿ and co-workers compared with our results. For the success of these coupling reactions it is therefore necessary that an aryl sulfone entity possessing a sufficiently low-lying LUMO energy level be employed for their effective reduction by divalent samarium in the absence of cosolvents, such as HMPA.[10, 21a, 37] Under these conditions, the anomeric organosamarium reagents display adequate stability to undergo coupling with carbonyl compounds, though under Barbier conditions.

Reductive samariation of 2-deoxyglycopyranosyl 2-pyridyl sulfones: The range of samarium-diiodide-promoted *C*-glycosylations was extended to another class of glycosyl pyridyl sulfones, the 2-deoxy sugars **45**–**48**. As with the mannosyl pyridyl sulfones, we predicted that these particular pyridyl sulfones would produce the corresponding α-*C*-glycosides (Scheme 14). Reduction of the pyridyl sulfone moiety would lead to the axially oriented C1–Sm bond. In the absence of a C2 substituent, we expected a conformational change to be facile, placing the C1–Sm bond in an equatorial orientation. This assumption was supported by previous results,[20c] where 2-deoxytribenzylglucosyl chloride gave predominately the α-

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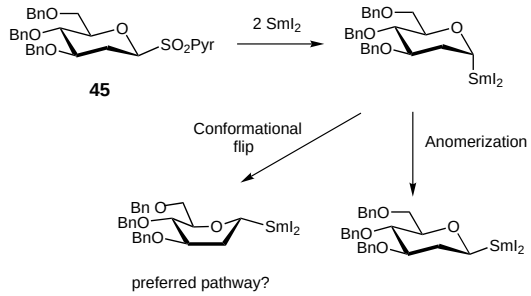


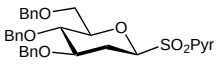
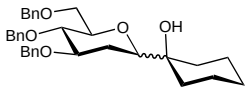
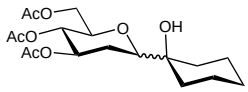
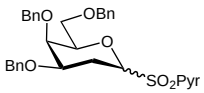
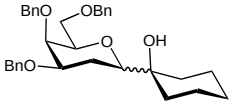
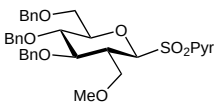
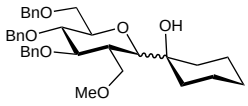
Scheme 14. Possible pathways for *C*-glycosylation of **45**.

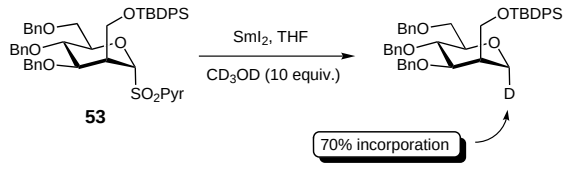
C-glycosides upon the sequential addition of SmI_2/HMPA and a carbonyl substrate.[20c]

A THF solution of pyridyl sulfones **45**–**48** and cyclohexanone subjected to 2 equivalents of SmI_2 gave good coupling yields of *C*-glycosides **49**–**52** (Table 5). Even with acetyl protecting groups as **46**, the Barbier-type condensation was efficient (88% yield). However, these *C*-glycosylation reactions did not display any stereochemical preferences at the anomeric center! The selectivity could be regenerated by the placement of a noneliminating group (CH_2OR) at C2 as with **48**[38] (mimic of a *gluco* configuration) or **53** (mimic of a *manno* configuration). The reductive samariation of **48** in the presence of cyclohexanone yielded *C*-glycosides **52** with a β-selectivity (α:β, 1:4) analogous to the one noted in the gluco series.[39] Whereas C–C bond formation was not possible with the samarium reagent derived from **53**, possibly owing to the steric shielding of the TBDPSiO group in the anomeric organosamarium intermediate, deuteriation experiments with CD_3OD provided only the α-deuteriated product (Scheme 15, α:β > 95:5), an α selectivity in line with *C*-mannosylation results. Again these results validate the hypothesis delineated in Scheme 10.

The lack of stereoselectivity in the 2-deoxy series is puzzling and contradicts previous reports in the same series. It is possible that the configurational and conformational changes of the kinetically formed anomeric organosamarium species lie close in energy resulting in no stereochemical discrepancy upon trapping with a carbonyl substrate. On the other hand, a slow configurational change at the anomeric center could compete with the coupling reaction. The fact that a 1:1 ratio of α and β anomers was obtained in all three examples without a C2-substituent (**45**–**47**) favors the first explanation. HMPA has an important effect on the stereoselectivities of these coupling reactions where elimination cannot take place. Complexation with the more bulky HMPA ligands than THF around the metal ion could favor a rapid conformational change and hence conservation of the α stereochemistry upon coupling with aldehydes and ketones. In the absence of HMPA, this stereochemical preservation is lost.

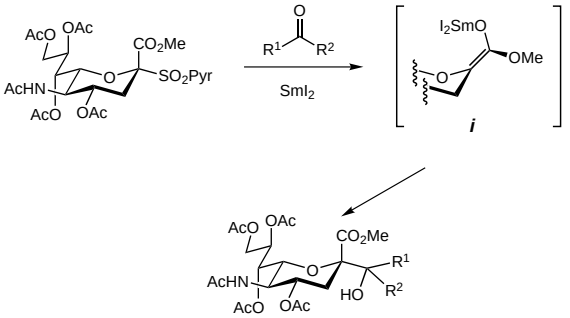
Table 5. Anionic coupling of pyridyl sulfones **45**–**48** with carbonyl compounds.

Sulfone	Carbonyl compound	*C*-Glycoside	Isolated yield (selectivity)
 **45**		 **49**	82% (α:β, 1:1)
 **46**		 **50**	88% (α:β, 1:1)
 **47**		 **51**	86% (α:β, 1:1)
 **48**		 **52**	73% (α:β, 1:4)



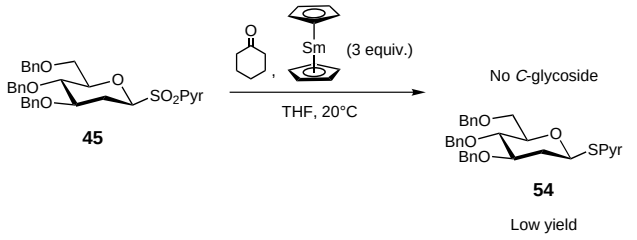
Scheme 15. Formation of the α-deuterated product of **53**.

In this context, it is interesting to note the recent work of Linhardt and collaborators, who have employed our pyridyl sulfone chemistry for the stereocontrolled synthesis of *C*-glycosides of *N*-acetylneuraminic acid (Scheme 16).[40] Whereas this reaction resembles those of the 2-deoxy series, the coupling to carbonyl substrates involves a samarium enolate intermediate (***i***) and not an anomeric organosamarium species as in the above examples. The high stereoselectivity observed, favoring introduction of an equatorial substituent, has precedence with other exocyclic enolates of conformationally biased 6-membered rings where, apparently, steric factors control the direction of the attack by the electrophile.[14d, 41]



Scheme 16. Stereocontrolled synthesis of *C*-glycosides of *N*-acetylneuraminic acid.

To improve the anomeric selectivity in the 2-deoxy series, we also attempted the reductive samariation of pyridyl sulfone **45** with the previously described dicyclopentadienylsamarium(II)[42] supposing that the bulky anomeric Sm^{III} species would prefer a conformational change over anomerization. A solution of **45** and cyclohexanone added to a THF suspension of brown Cp_2Sm at 20 °C gave a complex mixture of products none of which were the *C*-glycosides **49**. One of the products, obtained in low yield, corresponded to pyridyl sulfide **54**, presumably formed by the deoxygenation of sulfone **45** (Scheme 17). Although further studies with Cp_2Sm were abandoned as no coupling products were furnished, this surprising result clearly indicates the importance of the electron source for the chemical pathway chosen.

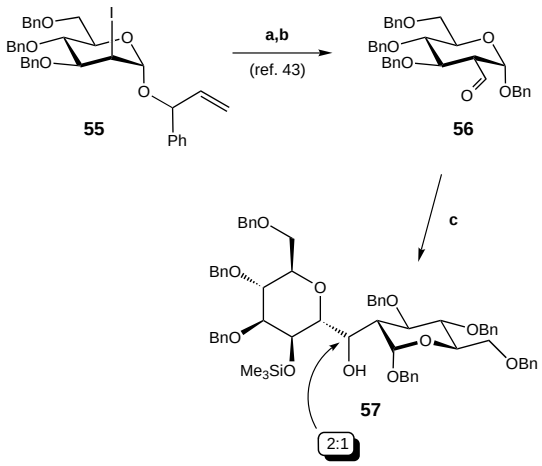


Scheme 17. Deoxygenation of **45**.

Synthesis of a *C*-disaccharide: Finally, we extended this procedure to the synthesis of a carbon-linked disaccharide, α-D-mannopyranosyl(1→2)-D-glucopyranoside. Aldehyde **56** was prepared following the stereospecific formyl-group transfer procedure developed by Jung and Choe.[43] Ozonolysis and 5-*exo* radical cyclization of iodide **55** followed by fragmentation afforded the crystalline aldehyde **56**. Reductive samariation of sulfone **5a** in the presence of **56** (1.5 equiv) rapidly afforded a 2:1 mixture of *C*-disaccharides **57** in 75% yield (Scheme 18).[44]

Conclusion

Glycosyl pyridyl sulfones appear to be suitable reagents for the preparation of *C*-glycosides by means of their reductive samariation with samarium diiodide in the presence of alkyl aldehydes or ketones. These mild and simple reactions provide a viable and stereoselective approach to 1,2-*trans*-*C*-glycosides of biologically relevant neutral hexopyranoses. The very high 1,2-*trans*-selectivity results from a fortunate situation in which only the 1,2-*trans* glycosyl samarium reagents lead to a productive carbon–carbon bond formation under Barbier conditions. This procedure complements our SmI_2-induced 1,2-*cis*-*C*-glycoside method,[10] and does not require low temperature techniques.[45]



Scheme 18. Synthesis of **57**. Reagents: a) O_3, PPh_3; b) Bu_3SnH, azobisisobutyronitrile (AIBN); c) **5a**, 2.2 SmI_2.

Experimental Section

General considerations: Unless otherwise stated, all reactions were carried out under argon. THF was dried and freshly distilled over sodium/benzophenone. Dichloromethane was freshly distilled over P_2O_5. Acetonitrile was distilled over CaH_2. Reactions were monitored by thin-layer chromatography (TLC) analysis. The following compounds were prepared as previously published:[10] 2-pyridyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside, 3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl 2-pyridyl sulfone (**6**), 2-pyridyl 3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside and 3,4,6-tri-β-D-glucopyranosyl 2-pyridyl sulfone (**41**). Samarium diiodide was prepared according to the method reported by Kagan et al.[46]

3,4,6-Tri-*O*-benzyl-2-*O*-trimethylsilyl-α-D-mannopyranosyl 2-pyridyl sulfone (5a): Chlorotrimethylsilane (258 μL, 2.04 mmol) was added to a stirred solution of sulfone **6** (586 mg, 1.02 mmol), triethylamine (568 μL, 4.07 mmol), and DMAP (2 mg) in CH_2Cl_2 (25 mL) at 0 °C after which the solution was warmed to 20 °C. The solution was stirred for 10 min, after which it was diluted with CH_2Cl_2, washed with ice-cold water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (heptane/EtOAc, 3:1) to give 622 mg (94%) of **5a** as a colorless syrup. As compound **5a** showed signs of facile hydrolysis of the O–Si bond, it was immediately used in the subsequent coupling step. $[\alpha]_D^{22} = +83$ ($c = 2.0$, chloroform); IR (neat): $\tilde{\nu} = 3054, 2986, 2958, 2305, 1453, 1428, 1315, 1250, 1103\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.73$ (br d, $^3J(H,H) = 4.6$ Hz, 1H; pyr), 8.06 (br d, $^3J(H,H) = 8.0$ Hz, 1H; pyr), 7.68 (dt, $^3J(H,H) = 8.0, 1.8$ Hz, 1H; pyr), 7.45–7.17 (m, 16H; 3Ph, pyr), 5.37 (d, $^3J(H,H) = 2.2$ Hz, 1H; H1), 5.02 (dd, $^3J(H,H) = 2.9, 2.2$ Hz, 1H; H2), 4.83 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.83 (d, $^2J(H,H) = 11.4$ Hz, 1H; CHPh), 4.77 (d, $^2J(H,H) = 11.4$ Hz, 1H; CHPh), 4.50 (ddd, $^3J(H,H) = 9.7, 4.0, 4.0$ Hz, 1H; H5), 4.50 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.48 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.29 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.23 (dd, $^3J(H,H) = 8.5, 2.9$ Hz, 1H; H3), 3.93 (dd, $^3J(H,H) = 9.7, 8.5$ Hz, 1H; H4), 3.62–3.53 (m, 2H; H6a, H6b), 0.22 (s, 9H; $SiMe_3$).

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-1-cyclohexanol (7). General procedure for *C*-glycosylation and desilylation: A 0.1M solution of SmI_2 in THF (2.7 mL, 0.27 mmol) was added to a stirred solution of sulfone **5a** (85 mg, 0.13 mmol) and cyclohexanone (20 μL, 0.19 mmol) in THF (0.5 mL) at 20 °C. The solution was stirred for 10 min, after which saturated aq. NH_4Cl was added to the reaction mixture and was then extracted twice with CH_2Cl_2. The combined organic phases were washed twice with water, dried (Na_2SO_4), and evaporated to dryness. The residue was redissolved in THF (5 mL), cooled to 0 °C, and Bu_4NF in THF (1.0M, 135 μL, 0.135 mmol) was added. The solution was stirred for 5 min, after which water and CH_2Cl_2 were added, the organic phase was washed twice with water, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography (heptane/EtOAc, 7:1 to 3:1) gave first tribenzyl-D-glucal **3** (0.4 mg, 1%) and then **7** (60.5 mg, 86%). $[\alpha]_D^{22} = +8.3$ ($c = 1.0$, chloroform); IR (neat): $\tilde{\nu} = 3434, 2930, 1454, 1100\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.38–7.22$ (m, 15H; 3Ph), 4.61 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.60 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.56 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.49 (s, 2H; CH_2Ph), 4.16 (ddd, $^3J(H,H) = 7.7, 5.2, 3.9$ Hz, 1H; H2), 4.11 (ddd, $^3J(H,H) = 5.9, 5.0, 4.1$ Hz, 1H; H5), 3.87 (dd, $^3J(H,H) = 5.7, 3.9$ Hz, 1H; H3), 3.72 (dd, $^3J(H,H) = 5.7, 4.1$ Hz, 1H; H4), 3.71 (dd, $^3J(H,H) = 10.2, 5.9$ Hz, 1H; H6a), 3.62 (dd, $^3J(H,H) = 10.2, 5.0$ Hz, 1H; H6b), 3.48 (d, $^3J(H,H) = 7.7$ Hz, 1H; H1), 2.73 (d, $^3J(H,H) = 5.2$, 1H; OH), 2.50 (s, 1H; OH), 1.71–1.47 (m, 10H; $5CH_2$); MS (CI, isobutene): *m/*

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$z = 515$ [$M+1-H_2O$], 497 [$M+1-2H_2O$], 425 [$M+1-$BnOH], 407 [$M+1-$BnOH$-H_2O$], 389 [$M+1-$BnOH$-2H_2O$]; HR-MS (CI, isobutene) $C_{33}H_{39}O_5$: calcd for [$M+1-H_2O$] 515.2799, found 515.2790.

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-3-pentanol (**8**): The *C*-mannoside **8** was prepared according to the general procedure outlined for **7**, to give **8** as a colorless syrup (33 mg, 80%) and glucal **3** (1 mg, 3%) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). $[\alpha]_D^{22} = +7.7$ ($c = 1.2$, chloroform); IR (neat): $\tilde{\nu} = 3446, 2928, 1454, 1094\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37-7.23$ (m, 15H; 3Ph), 4.60 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.58 (s, 2H; CH_2Ph), 4.56 (d, $^2J(H,H) = 12.3$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 12.3$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.19 (ddd, $^3J(H,H) = 7.6, 5.9, 3.8$ Hz, 1H; H2), 4.12 (ddd, $^3J(H,H) = 6.9, 5.6, 3.8$ Hz, 1H; H5), 3.88 (dd, $^3J(H,H) = 5.7, 3.8$ Hz, 1H; H3), 3.75 (dd, $^3J(H,H) = 10.0, 6.9$ Hz, 1H; H6a), 3.74 (dd, $^3J(H,H) = 5.7, 3.8$, 1H; H4), 3.67 (d, $^3J(H,H) = 7.6$ Hz, 1H; H1), 3.67 (dd, $^3J(H,H) = 10.0, 5.6$ Hz, 1H; H6b), 2.72 (d, $^3J(H,H) = 5.9$ Hz, 1H; OH), 2.40 (s, 1H; OH), 1.79–1.46 (m, 10H; $2CH_2$), 0.91 (t, $^3J(H,H) = 7.2$ Hz, 3H; Me), 0.90 (t, $^3J(H,H) = 7.2$ Hz, 3H; Me); MS (CI, isobutene): $m/z = 503$ [$M+1-H_2O$], 485 [$M+1-2H_2O$], 413 [$M+1-$BnOH], 395 [$M+1-$BnOH$-H_2O$], 377 [$M+1-$BnOH$-2H_2O$]; HR-MS (CI, isobutene) $C_{32}H_{39}O_5$: calcd for [$M+1-H_2O$] 503.2799, found 515.2807.

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-2-methyl-1-propanol (**9**): The *C*-mannoside **9** was prepared according to the general procedure outlined for **7** affording first glucal **3** (2.4 mg, 7%) and then **9** as an inseparable 13:2 epimeric mixture (31.4 mg, 77%) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). The isomeric *C*-glycosides were then subjected to standard *O*-acetylation conditions (Ac_2O/pyridine) allowing for their separation after flash chromatography (CH_2Cl_2). *Major isomer*: $[\alpha]_D^{22} = +20.2$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 2966, 2873, 1739, 1372, 1243\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34-7.21$ (m, 15H; 3Ph), 5.20 (dd, $^3J(H,H) = 5.2, 2.8$ Hz, 1H; H2), 4.95 (dd, $^3J(H,H) = 6.8, 6.1$ Hz, 1H; H7), 4.69 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.56 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.53 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.48 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.45 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.06 (dd, $^3J(H,H) = 5.6, 5.6$ Hz, 1H; H3), 4.03 (ddd, $^3J(H,H) = 5.6, 5.6, 4.1$ Hz, 1H; H5), 3.83–3.74 (m, 3H; H1, H4, H6a), 3.62 (dd, $^3J(H,H) = 10.4, 4.1$ Hz, 1H; H6b), 2.08 (s, 3H; OAc), 2.00 (s, 3H; OAc), 1.87 (m, 1H; $CHMe_2$), 0.90 (d, $^3J(H,H) = 5.6$ Hz, 3H; Me), 0.88 (d, $^3J(H,H) = 6.4$ Hz, 3H; Me); MS (CI, isobutene): $m/z = 591$ [$M+1$], 531 [$M+1-$AcOH], 433 [$M+1-$BnOH]; HR-MS (CI, isobutene) $C_{35}H_{43}O_8$: calcd for [$M+1$] 591.2959, found 591.2941.

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-1-heptanol (**10**): The *C*-manoside **10** was prepared according to the general procedure outlined for **7** affording first glucal **3** (3 mg, 9%) and then **10** as an inseparable 9:2 epimeric mixture (35.4 mg, 82%) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). The isomeric *C*-glycosides were then subjected to standard *O*-acetylation conditions (Ac_2O/pyridine) allowing for their separation after flash chromatography (CH_2Cl_2).
Major isomer: $[\alpha]_D^{22} = +19.6$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 2928, 2860, 1739, 1454, 1372, 1241\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34-7.19$ (m, 15H; 3Ph), 5.24 (dd, $^3J(H,H) = 5.2, 2.6$ Hz, 1H; H2), 5.13 (ddd, $^3J(H,H) = 8.5, 5.4, 5.4$ Hz, 1H; H7), 4.72 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.58 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.52 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.49 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.01 (ddd, $^3J(H,H) = 6.6, 5.4, 4.0$ Hz, 1H; H5), 3.93 (dd, $^3J(H,H) = 5.4, 5.4$ Hz, 1H; H3), 3.80 (dd, $^3J(H,H) = 6.6, 5.4$ Hz, 1H; H4), 3.79 (dd, $^3J(H,H) = 5.4, 2.6$ Hz, 1H; H1), 3.77 (dd, $^3J(H,H) = 10.5, 5.4$ Hz, 1H; H6a), 3.64 (dd, $^3J(H,H) = 10.5, 4.0$ Hz, 1H; H6b), 2.08 (s, 3H; OAc), 1.97 (s, 3H; OAc), 1.64–1.45 (m, 2H; CH_2), 1.33–1.18 (m, 8H; $4CH_2$), 0.86 (t, $^3J(H,H) = 6.7$ Hz, 3H; Me); MS (ES): $m/z = 655$ [$M+$Na]; HR-MS (ES) $C_{38}H_{48}NaO_8$: calcd for [$M+$Na] 655.3247, found 655.3253.

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosylphenylmethanol (**11**): The *C*-mannoside **11** was prepared according to the general procedure outlined for **7**, to give **11** as a colorless syrup (5 mg, 10%) and glucal **3** (11 mg, 32%) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). IR (neat): $\tilde{\nu} = 3419, 2925, 2817, 1496, 1454\ cm^{-1}$.
Major isomer: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37-7.20$ (m, 20H; 4Ph), 4.81 (d, $^3J(H,H) = 7.8$ Hz, 1H; H7), 4.71 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.62 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.56 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.53 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.48 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 3.95 (ddd, $^3J(H,H) = 7.2, 5.0, 3.9$ Hz, 1H; H5), 3.89 (dd, $^3J(H,H) = 7.8, 3.7$ Hz, 1H; H1), 3.87–3.78 (m, 3H; H2, H3, H4), 3.73–3.67 (m, 2H; H6a, H6b), 3.07 (brs, 1H; OH), 2.36 (d, $^3J(H,H) = 4.0$ Hz, 1H; OH).
Minor isomer: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.42-7.18$ (m, 20H; 4Ph), 4.93 (d, $^3J(H,H) = 6.5$ Hz, 1H; H7), 4.61 (d, $^2J(H,H) = 11.7$ Hz, 1H; CHPh), 4.61 (d, $^2J(H,H) = 11.7$ Hz, 1H; CHPh), 4.54 (d, $^2J(H,H) = 11.7$ Hz, 1H; CHPh), 4.53 (d, $^2J(H,H) = 11.7$ Hz, 1H; CHPh), 4.37 (s, 2H; CHPh), 4.11 (ddd, $^3J(H,H) = 6.3, 5.3, 3.8$ Hz, 1H; H5), 4.06 (ddd, $^3J(H,H) = 6.7, 6.3, 5.3$ Hz, 1H; H2), 3.94 (dd, $^3J(H,H) = 6.7, 6.5$ Hz, 1H; H1), 3.91 (dd, $^3J(H,H) = 5.3, 3.8$ Hz, 1H; H4), 3.75 (dd, $^3J(H,H) = 5.3, 5.3$ Hz, 1H; H3), 3.65 (dd, $^3J(H,H) = 10.4, 6.3$ Hz, 1H; H6a), 3.60 (dd, $^3J(H,H) = 10.4, 5.3$ Hz, 1H; H6b), 2.89 (brs, 1H; OH), 2.58 (d, $^3J(H,H) = 6.3$ Hz, 1H; OH); MS (CI, isobutene): $m/z = 523$ [$M+1-H_2O$], 505 [$M+1-2H_2O$], 433 [$M+1-$BnOH], 415 [$M+1-$BnOH$-H_2O$], 397 [$M+1-$BnOH$-2H_2O$]; HR-MS (CI, isobutene) $C_{34}H_{35}O_5$: calcd for [$M+1-H_2O$] 523.2486, found 523.2493.

3,4,6-Tri-*O*-benzyl-2-*O*-methyl-α-D-mannopyranosyl 2-pyridyl sulfone (**5b**): 50% NaH in parafin (10 mg, 0.42 mmol) was added to a stirred solution of 2-pyridyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (150 mg, 0.28 mmol) in DMF (5 mL) at 0°C. After 20 min, MeI (34 μL, 0.56 mmol) was added, and the reaction mixture was warmed to 20°C and stirred for 1 h. A few drops of methanol were added and the solution was diluted with ether. Water was added, and the organic phase was washed three times with water and then with brine, after which it was dried (Na_2SO_4) and concentrated to dryness in vacuo. The crude product was redissolved in CH_2Cl_2 (5 mL) and cooled to 0°C. To this solution was first added $NaHCO_3$ (165 mg, 1.96 mmol) and then MCPBA of approximately 80% purity (220 mg, 0.84 mmol). The mixture was warmed to 20°C, stirred for 1.5 h, 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, 2:1) gave **5b** (139 mg, 84%) as a colorless solid. $[\alpha]_D^{22} = +104.4$ ($c = 1.0$, chloroform); IR (neat): $\tilde{\nu} = 3031, 2930, 2865, 1454, 1428, 1316\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.77$ (d, $^3J(H,H) = 4.3$ Hz, 1H; pyr), 8.06 (d, $^3J(H,H) = 7.5$ Hz, 1H; pyr), 7.73 (dt, $^3J(H,H) = 7.5, 1.5$ Hz, 1H; pyr), 7.52–7.16 (m, 16H; 3Ph, pyr), 5.50 (d, $^3J(H,H) = 2.0$ Hz, 1H; H1), 4.89 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.80 (s, 2H; 2CHPh), 4.48 (ddd, $^3J(H,H) = 9.0, 4.0, 4.0$ Hz, 1H; H5), 4.47 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.38 (dd, $^3J(H,H) = 4.0, 2.0$ Hz, 1H; H2), 4.30 (dd, $^3J(H,H) = 9.0, 4.0$ Hz, 1H; H3), 4.27 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 3.90 (dd, $^3J(H,H) = 9.0, 9.0$ Hz, 1H; H4), 3.58–3.50 (m, 2H; H6a, H6b), 3.51 (s, 3H; OMe); MS (ES): $m/z = 590$ [$M+1$]; HR-MS (CI, isobutene) $C_{33}H_{36}NO_7S$: calcd for [$M+1$] 590.2213, found 590.2166.

2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl 2-pyridyl sulfone (**5c**): MCPBA of approximately 80% purity (399 mg, 1.52 mmol) was added to a mixture of 2-pyridyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-mannopyranoside (**28**) (322 mg, 0.51 mmol) and $NaHCO_3$ (299 mg, 3.56 mmol) in CH_2Cl_2 (12 mL) at 0°C. The mixture was warmed to 20°C, stirred for 1.5 h, 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, 2:1) gave **5c** (287 mg, 85%) as a colorless solid. $[\alpha]_D^{22} = +60$ ($c = 1.0$, chloroform); IR (neat): $\tilde{\nu} = 3085, 2987, 2305, 1104\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.76$ (d, $^3J(H,H) = 4.3$ Hz, 1H; pyr), 8.05 (d, $^3J(H,H) = 7.5$ Hz, 1H; pyr), 7.71 (dt, $^3J(H,H) = 7.5, 1.5$ Hz, 1H; pyr), 7.51–7.16 (m, 21H; 4Ph, pyr), 5.54 (d, $^3J(H,H) = 2.3$ Hz, 1H; H1), 4.85 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.78 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.68 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.68 (dd, $^3J(H,H) = 4.0, 2.3$ Hz, 1H; H2), 4.63 (2d, $^2J(H,H) = 12.0$ Hz, 2H; CHPh), 4.49 (ddd, $^3J(H,H) = 9.0, 4.0, 4.0$ Hz, 1H; H5), 4.47 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.29 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.26 (dd, $^3J(H,H) = 9.0, 4.0$ Hz, 1H; H3), 3.96 (dd, $^3J(H,H) = 9.0, 9.0$ Hz, 1H; H4), 3.64–3.53 (m, 2H; H6a, H6b); $C_{39}H_{39}NO_7S$ (605.8): calcd C 70.35, H 5.90; found C 70.14, H 6.18.

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl 2-pyridyl sulfone (**5h**): TBSOTf (600 μL, 2.63 mmol) was added to a stirred solution of sulfone **6** (500 mg, 0.88 mmol), triethylamine (550 μL, 3.95 mmol), and DMAP (20 mg) in CH_2Cl_2 (10 mL) at 0°C, and the solution was left overnight at 4°C. The solution was stirred for 20 min, after

which it was diluted with CH_2Cl_2, washed with ice-cold water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (cyclohexane/EtOAc, 3:1) to afford 469 mg (78%) of **5h** as a colorless syrup. $[\alpha]_D^{22} = +69$ ($c = 0.92$, chloroform); IR (neat): $\tilde{\nu} =$ 3031, 2928, 2857, 1395 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.73$ (dd, $^3J(H,H) = 4.7$, 2.0 Hz, 1H; pyr), 8.03 (br d, $^3J(H,H) = 7.8$ Hz, 1H; pyr), 7.68 (dt, $^3J(H,H) = 7.8$, 2.0 Hz, 1H; pyr), 7.45 (dd, $^3J(H,H) = 7.8$, 4.7 Hz, 1H; pyr), 7.49–7.12 (m, 15H; 3Ph), 5.24 (d, $^3J(H,H) = 2.1$ Hz, 1H; H1), 4.94 (dd, $^3J(H,H) = 2.6$, 2.1 Hz, 1H; H2), 4.82 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.81 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.72 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.46 (m, 1H; H5), 4.44 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.27 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.29 (dd, $^3J(H,H) = 9.0$, 2.6 Hz, 1H; H3), 3.94 (dd, $^3J(H,H) = 9.7$, 9.0 Hz, 1H; H4), 3.55 (m, 2H; H6a, H6b), 0.90 (s, 9H; *t*Bu), 0.20 (s, 3H; SiMe), 0.10 (s, 3H; SiMe); $C_{38}H_{47}NO_7SSi$ (690.0): calcd C 66.15, H 6.87; found C 65.79, H 6.81.

3,4,6-Tri-*O*-benzyl-2-*O*-methyl-α-D-mannopyranosyl-1-cyclohexanol (12): The *C*-mannoside **12** was prepared according to the general procedure outlined for **7**, to give **12** as a colorless syrup (37 mg, 78%) and glucal **3** (3 mg, 9%) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). $[\alpha]_D^{22} = +20.4$ ($c = 0.83$, chloroform); IR (neat): $\tilde{\nu} = 3476$, 2932, 2861, 1453 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.36-7.22$ (m, 15H; 3Ph), 4.60 (d, $^2J(H,H) = 12.5$ Hz, 1H; CHPh), 4.58 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.57 (d, $^2J(H,H) = 12.5$ Hz, 1H; CHPh), 4.52 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.47 (d, $^2J(H,H) =$ 12.2 Hz, 1H; CHPh), 4.13 (ddd, $^3J(H,H) = 7.1$, 5.7, 3.2 Hz, 1H; H5), 3.93 (dd, $^3J(H,H) = 5.3$, 3.1 Hz, 1H; H3), 3.75 (dd, $^3J(H,H) = 10.2$, 7.1 Hz, 1H; H6a), 3.70 (dd, $^3J(H,H) = 7.4$, 3.1, 1H; H2), 3.69 (dd, $^3J(H,H) = 5.3$, 3.2 Hz, 1H; H4), 3.64 (dd, $^3J(H,H) = 10.2$, 5.7 Hz, 1H; H6b), 3.60 (d, $^3J(H,H) =$ 7.4 Hz, 1H; H1), 3.37 (s, 3H; OMe), 2.81 (s, 1H; OH), 1.72–1.43 (m, 10H; $5CH_2$); MS (ES): $m/z = 569$ [M+Na]; HR-MS (CI, isobutene) $C_{34}H_{42}NaO_8$: calcd for [M+Na] 569.2879, found 569.2882.

2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl-1-cyclohexanol (13): The *C*-mannoside **13** was prepared according to the general procedure outlined for **7**, to give **13** as a colorless syrup (72 mg, 82%) and glucal **3** (4 mg, 6%) after flash chromatography (cyclohexane/EtOAc, 8:1). $[\alpha]_D^{22} = +20.5$ ($c =$ 1.24, chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.38-7.22$ (m, 20H; 4Ph), 4.60 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.56–4.44 (m, 6H; 6CHPh), 4.39 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.15 (ddd, $^3J(H,H) = 7.1$, 5.6, 3.1 Hz, 1H; H5), 3.98 (dd, $^3J(H,H) = 7.4$, 3.1 Hz, 1H; H2), 3.95 (dd, $^3J(H,H) = 5.3$, 3.1 Hz, 1H; H3), 3.80 (dd, $^3J(H,H) = 10.2$, 7.1 Hz, 1H; H6a), 3.74 (dd, $^3J(H,H) = 5.3$, 3.1 Hz, 1H; H4), 3.68 (d, $^3J(H,H) = 7.4$ Hz, 1H; H1), 3.66 (dd, $^3J(H,H) = 10.2$, 5.6 Hz, 1H; H6b), 2.93 (s, 1H; OH), 1.68–1.43 (m, 10H; $5CH_2$); $C_{40}H_{47}O_6$ (623.8): calcd C 77.02, H 7.59; found C 77.21, H 7.45.

3,4,6-Tri-*O*-benzyl-β-D-mannopyranosyl-1-cyclohexanol (14): The *C*-mannosides **7** and **14** were prepared according to the general procedure outlined for **7**, to give first glucal **3** (22 mg, 17%) and then α-*C*-mannoside **7** (22 mg, 13%) and β-*C*-mannoside **14** (32 mg, 19%) after flash chromatography (cyclohexane/EtOAc, 6:1 to 3:1). **14**: $[\alpha]_D^{22} = -1$ ($c = 1.0$, chloroform); IR (neat): $\tilde{\nu} = 3550$, 3456, 3053, 2963, 2862, 2304, 1454, 1265, 1102 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.55-7.18$ (m, 15H; 3Ph), 4.95 (d, $^2J(H,H) = 10.7$ Hz, 1H; CHPh), 4.82 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.69 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.62 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 10.7$ Hz, 1H; CHPh), 4.54 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.34 (dd, $^3J(H,H) = 3.0$, 0.5 Hz, 1H; H2), 3.95 (d, $^3J(H,H) =$ 0.5 Hz, 1H; H1), 3.94 (dd, $^3J(H,H) = 9.6$, 9.2 Hz, 1H; H4), 3.79 (dd, $^3J(H,H) = 10.5$, 2.2 Hz, 1H; H6a), 3.74 (dd, $^3J(H,H) = 10.5$, 4.0 Hz, 1H; H6b), 3.49 (dd, $^3J(H,H) = 9.2$, 3.0 Hz, 1H; H3), 3.43 (ddd, $^3J(H,H) = 9.6$, 4.0, 2.2 Hz, 1H; H5), 3.04 (s, 1H; OH), 2.83 (s, 1H; OH), 2.06–1.19 (m, 10H; 5 CH_2); MS (CI, isobutene): $m/z = 533$ [M+1], 515 [M+1 − H_2O], 497 [M+1 − 2H_2O], 425 [M+1 − BnOH], 407 [M+1 − BnOH − H_2O], 389 [M+1 − BnOH − 2H_2O]; HR-MS (CI, isobutene) $C_{33}H_{41}O_6$: calcd for [M+1] 533.2904, found 533.2904.

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl-1-cyclohexanol (15): The *C*-mannoside **15** was prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **15** as a colorless syrup (45 mg, 80%) after flash chromatography (cyclohexane/EtOAc, 8:1). $[\alpha]_D^{22} = +9$ ($c = 0.5$, chloroform); IR (neat): $\tilde{\nu} =$ 3450, 3053, 2931, 2858, 2305, 1454, 1265, 1091 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.36-7.22$ (m, 15H; 3Ph), 4.63 (s, 4H; 4CHPh), 4.51 (s, 2H; 2CHPh), 4.30 (dd, $^3J(H,H) = 5.4$, 2.5 Hz, 1H; H2), 4.20 (ddd, $^3J(H,H) = 8.0$, 5.4, 3.0 Hz, 1H; H5), 3.82 (dd, $^3J(H,H) = 10.0$, 8.0 Hz, 1H; H6a), 3.81 (dd, $^3J(H,H) = 6.7$, 2.5 Hz, 1H; H3), 3.74 (dd, $^3J(H,H) = 6.7$, 3.0 Hz, 1H; H4), 3.62 (d, $^3J(H,H) = 5.5$ Hz, 1H; H1), 3.59 (dd, $^3J(H,H) = 10.0$, 5.4 Hz, 1H; H6b), 1.80–1.50 (m, 10H; $5CH_2$), 0.90 (s, 9H; *t*Bu), 0.20 (s, 3H; SiMe), 0.10 (s, 3H; SiMe); $C_{39}H_{54}O_6Si$ (646.9): calcd C 72.41, H 8.41; found C 72.52, H 8.47.

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl-1-cyclohexylmethanol (16): The *C*-mannoside **16** was prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give first the minor isomer (49 mg, 17%) and then the major isomer (193 mg, 67%) after flash chromatography (CH_2Cl_2:acetone, 200:1 to 150:1).

Major isomer: $[\alpha]_D^{22} = +6.5$ ($c = 0.7$, chloroform); IR (neat): $\tilde{\nu} = 3450$, 2927, 2854, 1453, 1098 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.40-7.20$ (m, 15H; 3Ph), 4.69 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.52 (s, 2H; 2CHPh), 4.48 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.44 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.12 (dd, $^3J(H,H) = 7.8$, 3.0 Hz, 1H; H2), 4.08 (ddd, $^3J(H,H) = 7.4$, 4.5, 2.9 Hz, 1H; H5), 3.83 (dd, $^3J(H,H) = 10.0$, 7.4 Hz, 1H; H6a), 3.84 (dd, $^3J(H,H) = 7.8$, 2.5 Hz, 1H; H1), 3.69 (dd, $^3J(H,H) = 4.5$, 3.0 Hz, 1H; H3), 3.65 (dd, $^3J(H,H) = 4.5$, 4.5 Hz, 1H; H4), 3.58 (dd, $^3J(H,H) = 10.5$, 4.5 Hz, 1H; H6b), 3.42 (m, 1H; H7), 2.10–1.89 (m, 2H; CH_2), 1.80–1.16 (m, 9H; CH, 4CH_2), 0.92 (s, 9H; *t*Bu), 0.13 (s, 3H; SiMe), 0.08 (s, 3H; SiMe); $C_{40}H_{56}O_6Si$ (661.0): calcd C 72.69, H 8.54; found C 72.86, H 8.55.

Minor isomer: $[\alpha]_D^{22} = +2.5$ ($c = 0.6$, chloroform); IR (neat): $\tilde{\nu} = 3450$, 2926, 2854, 1496, 1453, 1252, 1096 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.35-$ 7.10 (m, 15H; 3Ph), 4.65 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.64 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.52 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.50 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.49 (s, 2H; 2CHPh), 4.25 (dd, $^3J(H,H) = 5.0$, 2.5 Hz, 1H; H2), 3.89 (ddd, $^3J(H,H) = 6.0$, 4.0, 3.7 Hz, 1H; H5), 3.82 (dd, $^3J(H,H) = 6.7$, 4.0 Hz, 1H; H4), 3.80 (dd, $^3J(H,H) = 10.0$, 6.0 Hz, 1H; H6a), 3.74 (dd, $^3J(H,H) = 6.7$, 2.5 Hz, 1H; H3), 3.73 (dd, $^3J(H,H) = 6.7$, 4.0 Hz, 1H; H4), 3.65 (dd, $^3J(H,H) = 10.0$, 3.7 Hz, 1H; H6b), 3.40 (dd, $^3J(H,H) = 6.0$, 1.5 Hz, 1H; H7), 1.76–1.15 (m, 11H; CH, 5CH_2), 0.88 (s, 9H; *t*Bu), 0.08 (s, 3H; SiMe), 0.05 (s, 3H; SiMe); $C_{40}H_{56}O_6Si$ (661.0): calcd C 72.69, H 8.54; found C 72.78, H 8.49.

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl-1-nonanol (17): The *C*-mannoside **17** was prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give first the minor isomer (23 mg, 13%) and then the major isomer (105 mg, 58%) after flash chromatography (CH_2Cl_2:acetone, 200:1).

Major isomer: $[\alpha]_D^{22} = +5.0$ ($c = 1.3$, chloroform); IR (neat): $\tilde{\nu} = 3450$, 3054, 2936, 2929, 2856, 2305, 1454, 1422, 1265, 1094 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.45-7.25$ (m, 15H; 3Ph), 4.73 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.58 (4d, $^2J(H,H) = 11.5$ Hz, 4H; CHPh), 4.55 (d, $^2J(H,H) =$ 11.8 Hz, 1H; CHPh), 4.18 (dd, $^3J(H,H) = 7.5$, 2.3 Hz, 1H; H2), 4.10 (ddd, $^3J(H,H) = 7.2$, 5.2, 4.9 Hz, 1H; H5), 3.84 (dd, $^3J(H,H) = 10.3$, 7.2 Hz, 1H; H6a), 3.74 (dd, $^3J(H,H) = 7.5$, 5.0 Hz, 1H; H1), 3.70 (dd, $^3J(H,H) = 4.9$, 4.9 Hz, 1H; H4), 3.67 (dd, $^3J(H,H) = 10.3$, 5.2 Hz, 1H; H6b), 3.66 (dd, $^3J(H,H) = 4.9$, 2.3 Hz, 1H; H3), 3.42 (m, 1H; H7), 1.80–1.30 (m, 14H; 7CH_2), 0.95 (s, 9H; *t*Bu), 0.86 (t, $^3J(H,H) = 6.7$ Hz, 3H; Me), 0.17 (s, 3H; SiMe), 0.12 (s, 3H; SiMe); $C_{42}H_{62}O_6Si$ (691.0): calcd C 73.00, H 9.04; found C 73.09, H 8.81.

Minor isomer: $[\alpha]_D^{22} = +8.0$ ($c = 0.4$, chloroform); IR (neat): $\tilde{\nu} = 3450$, 3053, 2931, 2858, 2305, 1454, 1265, 1091 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta =$ 7.40–7.25 (m, 15H; 3Ph), 4.71 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.68 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.59 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.57 (d, $^2J(H,H) = 11.5$ Hz, 1H; CHPh), 4.55 (s, 2H; 2CHPh), 4.29 (dd, $^3J(H,H) = 5.8$, 2.5 Hz, 1H; H2), 3.95 (ddd, $^3J(H,H) = 6.5$, 4.5, 4.5 Hz, 1H; H5), 3.82 (dd, $^3J(H,H) = 6.0$, 4.5 Hz, 1H; H4), 3.81 (dd, $^3J(H,H) = 10.5$, 6.5 Hz, 1H; H6a), 3.75 (dd, $^3J(H,H) = 6.0$, 2.5 Hz, 1H; H3), 3.74 (dd, $^3J(H,H) = 6.5$, 5.8 Hz, 1H; H4), 3.68 (dd, $^3J(H,H) = 10.5$, 4.5 Hz, 1H; H6b), 3.40 (dd, $^3J(H,H) = 6.0$, 1.5 Hz, 1H; H7), 1.40–1.28 (m, 14H; 7CH_2), 0.95 (s, 9H; *t*Bu), 0.86 (t, $^3J(H,H) = 6.7$ Hz, 3H; Me), 0.14 (s, 3H; SiMe), 0.12 (s, 3H; SiMe); $C_{42}H_{62}O_6Si$ (691.0): calcd C 73.00, H 9.04; found C 72.81, H 8.91.

3,4,6-Tri-*O*-benzyl-α-D-manno-pyranosyl-1-nonanol, isopropylidene derivatives (18a) and (18b): 1.0 M Bu_4NF in THF (0.16 mL, 0.16 mmol) was added to a stirred solution of silyl ether **17** (major isomer, 27 mg, 0.039 mmol) dissolved in THF (1 mL) at 0 °C. The solution was stirred

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for 2 h at 0 °C and 1 h at 20 °C, ether was added, and the organic phase was washed with water and brine, dried (Na_2SO_4), and evaporated to dryness. The residue was redissolved in DMF (0.3 mL) and dimethoxypropane (0.2 mL) and camphorsulfonic acid (CSA, 1.5 mg) was added. The solution was stirred for 5 h at 20 °C, ether was added, and the organic phase was washed with water (4 times) and brine, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography (cyclohexane/EtOAc, 15:1) gave the corresponding isopropylidene derivative **18a** (15 mg, 71 %) as a colorless oil. In a similar manner, the minor isomer was converted to **18b** in a 55 % overall yield.

18a: $[\alpha]_D^{22} = -8.7$ ($c = 0.7$, chloroform); IR (neat): $\tilde{\nu} = 2924, 2855, 1453, 1222, 1095, 1074\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.44-7.18$ (m, 15H; 3Ph), 4.76 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.60 (d, $^2J(H,H) = 12.4$ Hz, 1H; CHPh), 4.50 (d, $^2J(H,H) = 12.4$ Hz, 1H; CHPh), 4.50 (s, 2H; 2CHPh), 4.49 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.20 (dd, $^3J(H,H) = 7.0, 7.0$ Hz, 1H; H5), 4.09 (dd, $^3J(H,H) = 5.5, 2.9$ Hz, 1H; H1), 4.09 (d, $^3J(H,H) = 5.5$ Hz, 1H; H2), 3.99 (ddd, $^3J(H,H) = 10.3, 5.6, 2.9$ Hz, 1H; H7), 3.92 (d, $^3J(H,H) = 3.9$ Hz, 1H; H3), 3.83 (dd, $^3J(H,H) = 9.9, 7.0$ Hz, 1H; H6a), 3.69 (dd, $^3J(H,H) = 9.9, 7.0$ Hz, 1H; H6b), 3.66 (d, $^3J(H,H) = 3.9$ Hz, 1H; H4), 1.89–1.61 (m, 2H; CH_2), 1.57–1.26 (m, 12H; $6CH_2$), 1.45 (s, 3H; Me), 1.38 (s, 3H; Me), 0.90 (t, $^3J(H,H) = 6.7$ Hz, 3H; Me); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 138.8, 138.4, 138.1, 128.4, 128.3, 127.8, 127.7, 127.5, 127.4, 100.9, 75.9, 75.6, 75.4, 73.1, 73.0, 71.6, 71.3, 67.9, 67.1, 66.5, 32.0, 29.7, 29.4, 28.6, 26.3, 25.9, 25.4, 22.8, 14.3$; $C_{39}H_{52}O_6Si$ (644.9): calcd C 75.94, H 8.50; found C 76.21, H 8.57.

18b: $[\alpha]_D^{22} = +3.0$ ($c = 0.4$, chloroform); IR (neat): $\tilde{\nu} = 2924, 2856, 1454, 1380, 1259, 1201, 1072\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.40-7.24$ (m, 15H; 3Ph), 4.81 (d, $^2J(H,H) = 12.3$ Hz, 1H; CHPh), 4.58 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.53 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 12.3$ Hz, 1H; CHPh), 4.50 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.48 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.19 (dd, $^3J(H,H) = 7.2, 6.8$ Hz, 1H; H5), 4.10 (dd, $^3J(H,H) = 9.8, 2.8$ Hz, 1H, H2), 3.90 (dd, $^3J(H,H) = 10.0, 6.8$ Hz, 1H; H6a), 3.83 (dd, $^3J(H,H) = 2.8, 2.8$ Hz, 1H; H3), 3.77 (ddd, $^3J(H,H) = 10.3, 5.6, 2.9$ Hz, 1H; H7), 3.72 (dd, $^3J(H,H) = 10.0, 7.2$ Hz, 1H; H6b), 3.66 (d, $^3J(H,H) = 2.8$ Hz, 1H; H4), 3.55 (dd, $^3J(H,H) = 9.8, 9.8$ Hz, 1H; H1), 1.84 (m, 2H; CH_2), 1.52–1.27 (m, 12H; $6CH_2$), 1.54 (s, 3H; Me), 1.45 (s, 3H; Me), 0.90 (t, $^3J(H,H) = 6.7$ Hz, 3H; Me); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 138.9, 128.5, 128.4, 127.9, 127.7, 127.5, 99.5, 75.7, 75.4, 74.4, 73.5, 73.3, 72.3, 71.7, 70.2, 68.1, 66.7, 32.1, 32.0, 29.8, 29.5, 25.2, 22.8, 19.8, 15.4, 14.3$; $C_{39}H_{52}O_6Si$ (644.9): calcd C 75.94, H 8.50; found C 76.22, H 8.19.

3,4,6-Tri-*O*-benzyl-2-*O*-trimethylsilyl-β-D-glucopyranosyl 2-pyridyl sulfone (**19a**): Chlorotrimethysilane (220 μL, 1.74 mmol) was added to a stirred solution of sulfone **41** (500 mg, 0.87 mmol), triethylamine (485 μL, 3.47 mmol), and DMAP (2 mg) in CH_2Cl_2 (22 mL) at 0 °C, after which the solution was warmed to 20 °C. The solution was stirred for 20 min, diluted with CH_2Cl_2, washed with ice-cold water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (cyclohexane/EtOAc, 3:1) to give 562 mg (99 %) **19a** as a colorless syrup. As compound **19a** showed signs of facile hydrolysis of the O–Si bond, it was used immediately in the subsequent coupling step. $[\alpha]_D^{22} = -54.5$ ($c = 1.5$, chloroform); IR (neat): $\tilde{\nu} = 2953, 2904, 1453, 1428, 1366, 1336, 1250\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.70$ (br d, $^3J(H,H) = 4.7$ Hz, 1H; pyr), 8.03 (br d, $^3J(H,H) = 7.6$ Hz, 1H; pyr), 7.80 (dt, $^3J(H,H) = 7.6, 1.8$ Hz, 1H; pyr), 7.39–7.04 (m, 16H; 3Ph, pyr), 4.98 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.89 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.83 (d, $^3J(H,H) = 9.1$ Hz, 1H; H1), 4.67 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.50 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.37 (dd, $^3J(H,H) = 9.1, 8.5$ Hz, 1H; H2), 4.21 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.12 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 3.63 (dd, $^3J(H,H) = 8.9, 5.5$ Hz, 1H; H3), 3.56 (dd, $^3J(H,H) = 9.0, 8.9$ Hz, 1H; H4), 3.49–3.32 (m, 3H; H5, H6a, H6b), 0.24 (s, 9H; $SiMe_3$).

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl 2-pyridyl sulfone (**19b**): TBSOTf (120 μL, 0.52 mmol) was added to a stirred solution of sulfone **41** (202 mg, 0.35 mmol), triethylamine (98 μL, 0.72 mmol), and DMAP (2 mg) in CH_2Cl_2 (4 mL) at 0 °C, after which the solution was left overnight at 4 °C. The solution was stirred for 20 min, diluted with CH_2Cl_2, washed with ice-cold water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (heptane/EtOAc, 4:1) to afford 195 mg (81 %) of **19b** as a colorless syrup. $[\alpha]_D^{22} = -48.8$ ($c = 1.5$, chloroform); IR (neat): $\tilde{\nu} = 2927, 2885, 2857, 1453, 1428, 1337, 1252\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 8.70 (br d, $^3J(H,H) = 4.7$ Hz, 1H; pyr), 8.02 (br d, $^3J(H,H) = 7.6$ Hz, 1H; pyr), 7.78 (dt, $^3J(H,H) = 7.6, 1.8$ Hz, 1H; pyr), 7.37–7.02 (m, 16H; 3Ph, pyr), 4.94 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.90 (d, $^3J(H,H) = 8.1$ Hz, 1H; H1), 4.85 (d, $^2J(H,H) = 11.9$ Hz, 1H; CHPh), 4.62 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.46 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.42 (dd, $^3J(H,H) = 8.1, 7.7$ Hz, 1H; H2), 4.20 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.12 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 3.64 (dd, $^3J(H,H) = 7.7, 7.7$ Hz, 1H; H3), 3.60 (dd, $^3J(H,H) = 8.5, 7.7$ Hz, 1H; H4), 3.49–3.27 (m, 3H; H5, H6a, H6b), 0.94 (s, 3H; *t*Bu), 0.30 (s, 3H; SiMe), 0.07 (s, 3H; SiMe); MS (ES): $m/z = 690$ [M+1]; HR-MS (ES) $C_{38}H_{48}NO_7SSi$: calcd for [M+1] 690.2921, found 690.2872.

3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyl-1-cyclohexanol (**20**): The *C*-glucoside **20** was prepared according to the general procedure outlined for **7**, to give **20** as a colorless syrup (28 mg, 57 %) and glucal **3** (8 mg, 21 %) after flash chromatography (heptane/EtOAc, 7:1 to 1:1). $[\alpha]_D^{22} = +22.7$ ($c = 2.0$, chloroform); IR (neat): $\tilde{\nu} = 3426, 2928, 2858, 1453, 1095\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37-7.20$ (m, 15H; 3Ph), 4.93 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.81 (d, $^2J(H,H) = 10.8$ Hz, 1H; CHPh), 4.80 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.62 (d, $^2J(H,H) = 10.8$ Hz, 1H; CHPh), 4.60 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 3.77 (dd, $^3J(H,H) = 9.1, 9.1$ Hz, 1H; H2), 3.70 (s, 1H; H6a), 3.69 (s, 1H; H6b), 3.62–3.52 (m, 2H; H3, H4), 3.43 (ddd, $^3J(H,H) = 9.6, 3.2, 3.2$ Hz, 1H; H5), 3.11 (br s, 1H; OH), 3.02 (d, $^3J(H,H) = 9.6$ Hz, 1H; H1), 2.73 (br s, 1H; OH), 1.87–1.44 (m, 10H; $5CH_2$); MS (ES): $m/z = 555$ [M+Na]; HR-MS (ES) $C_{33}H_{40}NaO_6$: calcd for [M+Na] 555.2723, found 555.2716.

3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyl-1-heptanol (**21**): The *C*-glucoside **21** was prepared according to the general procedure outlined for **7**, to give the **21** as an inseparable 7:2 epimeric mixture and as a colorless syrup (22 mg, 43 %) and glucal **3** (13 mg, 36 %) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). The isomeric *C*-glycosides were then subjected to standard *O*-acetylation conditions (Ac_2O/pyridine) allowing for their separation after flash chromatography (CH_2Cl_2).

Major isomer: $[\alpha]_D^{22} = +37.8$ ($c = 0.58$, chloroform); IR (neat): $\tilde{\nu} = 2927, 2859, 1744, 1370, 1242\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37-7.17$ (m, 15H; 3Ph), 5.07 (dd, $^3J(H,H) = 9.7, 9.7$ Hz, 1H; H2), 4.93 (ddd, $^3J(H,H) = 7.0, 7.0, 2.2$ Hz, 1H; H7), 4.79 (d, $^2J(H,H) = 11.3$ Hz, 1H; CHPh), 4.78 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.62 (d, $^2J(H,H) = 11.3$ Hz, 1H; CHPh), 4.61 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.57 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 3.75 (dd, $^3J(H,H) = 11.3, 2.2$ Hz, 1H; H6a), 3.69 (dd, $^3J(H,H) = 11.3, 4.7$ Hz, 1H; H6b), 3.69–3.59 (m, 2H; H3, H4), 3.43 (ddd, $^3J(H,H) = 8.3, 4.7, 2.2$ Hz, 1H; H5), 3.39 (dd, $^3J(H,H) = 9.7, 2.2$ Hz, 1H; H1), 2.05 (s, 3H; OAc), 1.89 (s, 3H; OAc), 1.77–1.60 (m, 2H; CH_2), 1.30–1.19 (m, 8H; $4CH_2$), 0.85 (t, $^3J(H,H) = 6.8$ Hz, 3H; Me); MS (ES): $m/z = 655$ [M+Na]; HR-MS (ES) $C_{38}H_{48}NaO_8$: calcd for [M+Na] 655.3247, found 655.3244.

Minor isomer: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.36-7.16$ (m, 15H; 3Ph), 4.96 (dd, $^3J(H,H) = 10.2, 9.2$ Hz, 1H; H2), 4.83 (ddd, $^3J(H,H) = 9.8, 9.8, 2.0$ Hz, 1H; H7), 4.80 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.76 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.64 (d, $^2J(H,H) = 11.6$ Hz, 1H; CHPh), 4.61 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.58 (d, $^2J(H,H) = 11.0$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 3.75 (dd, $^3J(H,H) = 11.3, 2.5$ Hz, 1H; H6a), 3.70 (dd, $^3J(H,H) = 11.3, 3.6$ Hz, 1H; H6b), 3.67–3.58 (m, 2H; H3, H4), 3.46 (dd, $^3J(H,H) = 10.2, 2.0$ Hz, 1H; H1), 3.40 (ddd, $^3J(H,H) = 9.8, 3.6, 2.5$ Hz, 1H; H5), 2.05 (s, 3H; OAc), 1.96 (s, 3H; OAc), 1.76–1.60 (m, 2H; CH_2), 1.31–1.19 (m, 8H; $4CH_2$), 0.85 (t, $^3J(H,H) = 7.0$ Hz, 3H; Me); MS (ES): $m/z = 655$ [M+Na]; HR-MS (ES) $C_{38}H_{48}NaO_8$: calcd for [M+Na] 655.3247, found 655.3234.

3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyl-2-methylpropanol (**22**): The *C*-glucoside **22** was prepared according to the general procedure outlined for **7**, to give **22** as an inseparable 3:2 epimeric mixture and as a colorless syrup (23 mg, 55 %) and glucal **3** (7.5 mg, 22 %) after flash chromatography (heptane/EtOAc, 6:1 to 1:1). The known isomeric *C*-glycosides[12d] were then subjected to standard *O*-acetylation conditions (Ac_2O/pyridine) allowing for their separation after flash chromatography (CH_2Cl_2/acetone, 40:1 to 10:1).

Major isomer: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.37-7.19$ (m, 15H; 3Ph), 4.95 (d, $^3J(H,H) = 11.8$ Hz, 1H; CHPh), 4.82 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.79 (d, $^2J(H,H) = 11.8$ Hz, 1H; CHPh), 4.59 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.56 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.51 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 3.77 (dd, $^3J(H,H) = 9.4, 9.3$ Hz, 1H; H2), 3.70 (s, 1H;

H6a), 3.69 (s, 1H; H6b), 3.58 (dd, ^3J(H,H) = 9.3, 8.9 Hz, 1H; H3), 3.53 (dd, ^3J(H,H) = 9.3, 8.9 Hz, 1H; H4), 3.45 (ddd, ^3J(H,H) = 9.3, 3.2, 3.2 Hz, 1H; H5), 3.40 (d, ^3J(H,H) = 8.2 Hz, 1H; H7), 3.28 (dd, ^3J(H,H) = 9.4, 1.9 Hz, 1H; H1), 2.42 (brs, 1H; OH), 1.87 (m, 1H; $CHMe_2$), 1.03 (d, ^3J(H,H) = 6.6 Hz, 3H; Me), 0.90 (d, ^3J(H,H) = 6.6 Hz, 3H; Me).

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.18 (m, 15H; 3Ph), 4.92 (d, ^2J(H,H) = 11.3 Hz, 1H; CHPh), 4.82 (d, ^2J(H,H) = 11.3 Hz, 1H; CHPh), 4.81 (d, ^2J(H,H) = 11.1 Hz, 1H; CHPh), 4.59 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 4.58 (d, ^2J(H,H) = 11.1 Hz, 1H; CHPh), 4.52 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 3.74–3.63 (m, 4H; H2, H6a, H6b, H7), 3.61 (dd, ^3J(H,H) = 9.0, 9.0 Hz, 1H; H3), 3.56 (dd, ^3J(H,H) = 9.2, 9.0 Hz, 1H; H4), 3.42 (ddd, ^3J(H,H) = 9.2, 3.2, 3.2 Hz, 1H; H5), 3.19 (dd, ^3J(H,H) = 9.3, 7.5 Hz, 1H; H1), 3.16 (brs, 1H; OH), 2.72 (brs, 1H; OH), 2.10 (m, 1H; $CHMe_2$), 0.99 (d, ^3J(H,H) = 7.0 Hz, 3H; Me), 0.91 (d, ^3J(H,H) = 7.0 Hz, 3H; Me).

3,4,6-Tri-*O*-benzyl-2-*O*-trimethylsilyl-β-D-galactopyranosyl 2-pyridyl sulfone (23a): TMSCl (40 µL, 0.29 mmol) was added to a stirred solution of 3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl 2-pyridyl sulfone (110 mg, 0.19 mmol),[10] triethylamine (55 µL, 0.38 mmol), and DMAP (2 mg) in CH_2Cl_2 (3 mL) at 0 °C, after which the solution was warmed to 20 °C. The solution was stirred for 20 min, diluted with CH_2Cl_2, washed with ice-cold water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (cyclohexane/EtOAc, 2:1) to give 119 mg (97%) of **23a** as a colorless syrup. As compound **23a** showed signs of facile hydrolysis of the O–Si bond, it was used immediately in the subsequent coupling step. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67 (brd, ^3J(H,H) = 4.8 Hz, 1H; pyr), 8.07 (brd, ^3J(H,H) = 7.5 Hz, 1H; pyr), 7.82 (dt, ^3J(H,H) = 7.5, 1.8 Hz, 1H; pyr), 7.43–7.11 (m, 16H; 3Ph, pyr), 4.92–4.68 (m, 5H; H1, H2, 3CHPh), 4.48 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.17 (s, 2H; 2CHPh), 3.87 (d, ^3J(H,H) = 3.1 Hz, 1H; H4), 3.60 (dd, ^3J(H,H) = 5.8, 5.8 Hz, 1H; H5), 3.55 (dd, ^3J(H,H) = 8.1, 3.1 Hz, 1H; H3), 3.39 (dd, ^3J(H,H) = 10.1, 5.8 Hz, 1H; H6a), 3.29 (dd, ^3J(H,H) = 10.1, 5.8 Hz, 1H; H6b), 0.28 (s, 9H; 3SiMe); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 155.9, 149.8, 138.3, 137.6, 137.2, 128.3, 128.2, 127.6, 127.5, 127.4, 127.2, 126.8, 123.7, 90.6, 83.9, 78.2, 74.2, 73.0, 72.6, 72.2, 68.4, 67.1, 53.4, 0.5.

3,4,6-Tri-*O*-benzyl-2-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyl 2-pyridyl sulfone (23b): TBSCl (180 mg, 1.20 mmol) was added to a stirred solution of 3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl 2-pyridyl sulfone (86 mg, 0.15 mmol),[10] and imidazole (20 mg, 0.30 mmol) in DMF (0.2 mL) after which the solution was left overnight at 55 °C. The solution was diluted with CH_2Cl_2, washed 4 times with water, dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by flash chromatography (cyclohexane/EtOAc, 6:1 to 3:1) to afford 93 mg (90%) of **19b** as a colorless syrup. $[\alpha]_D^{22} = -58.9$ (c = 1.9, chloroform); IR (neat): $\tilde{\nu}$ = 3054, 2987, 1422, 1266 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.70 (brd, ^3J(H,H) = 4.7 Hz, 1H; pyr), 8.02 (brd, ^3J(H,H) = 7.6 Hz, 1H; pyr), 7.78 (dt, ^3J(H,H) = 7.6, 1.8 Hz, 1H; pyr), 7.37–7.02 (m, 16H; 3Ph, pyr), 4.94 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.84 (d, ^3J(H,H) = 8.1 Hz, 1H; H1), 4.77 (d, ^2J(H,H) = 12.5 Hz, 1H; CHPh), 4.76 (dd, ^3J(H,H) = 8.1, 8.1 Hz, 1H; H2), 4.67 (d, ^2J(H,H) = 12.5 Hz, 1H; CHPh), 4.48 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.11 (s, 2H; 2CHPh), 3.86 (d, ^3J(H,H) = 3.2 Hz, 1H; H4), 3.56 (dd, ^3J(H,H) = 6.0, 6.0 Hz, 1H; H5), 3.53 (dd, ^3J(H,H) = 8.1, 3.2 Hz, 1H; H3), 3.36 (dd, ^3J(H,H) = 10.1, 6.0 Hz, 1H; H6a), 3.32 (dd, ^3J(H,H) = 10.1, 6.0 Hz, 1H; H6b), 0.97 (s, 3H; *t*Bu), 0.33 (s, 3H; SiMe), 0.13 (s, 3H; SiMe); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.4, 149.7, 138.3, 137.6, 137.5, 137.2, 128.3, 128.2, 128.1, 127.6, 127.5, 127.4, 126.8, 123.7, 90.6, 84.3, 78.3, 74.3, 73.0, 72.7, 72.1, 68.6, 67.0, 26.0, 18.2, −3.6, −4.2; $C_{38}H_{47}NO_7SSi$ (690.0): calcd C 66.15, H 6.87; found C 66.24, H 6.77.

3,4,6-Tri-*O*-benzyl-β-D-galactopyranosyl-1-cyclohexanol (24): The *C*-galactoside **24** was prepared from pyridyl sulfone **23a** according to the general procedure outlined for **7**, to give **20** as a colorless syrup (19 mg, 25%) and tribenzylgalactal (21 mg, 35%) after flash chromatography (cyclohexane/EtOAc, 7:1 to 1:1). $[\alpha]_D^{22} = +27.1$ (c = 1.5, chloroform); IR (neat): $\tilde{\nu}$ = 3426, 2928, 2858, 1453, 1095 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 15H; 3Ph), 4.87 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.76 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.60 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.53 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.50 (s, 2H; 2CHPh), 4.22 (dd, ^3J(H,H) = 9.3, 9.3 Hz, 1H; H2), 4.10 (d, ^3J(H,H) = 3.0 Hz, 1H; H4), 3.66–3.57 (m, 3H; H5, H6a, H6b), 3.48 (dd, ^3J(H,H) = 9.3, 3.0 Hz, 1H; H3), 3.05 (d, ^3J(H,H) = 9.3 Hz, 1H; H1), 3.00 (brs, 1H; OH), 1.88–1.40 (m, 10H; $5CH_2$); MS (CI, NH_3) m/z = 550 [M+18], 515 [M+1 − H_2O]; MS (ES): m/z = 555 [M+Na]: HR-MS (ES) $C_{33}H_{41}O_6$: calcd for [M+1] 533.2904, found 533.2859.

2,3,4,6-Tetra-*O*-benzyl-β-D-mannopyranosyl 2-pyridyl sulfone (25): BF_3/Et_2O (12 µL, 0.094 mmol) was added to a solution of trichloroimidate **27** (323 mg, 0.47 mmol) and 2-mercaptopyridine (157 mg, 1.41 mmol) in CH_2Cl_2 (20 mL) at −15 °C. The solution was stirred for 2 h at −15 °C, evaporated to dryness, and the crude product was purified by flash chromatography (cyclohexane/EtOAc, 8:1 to 5:1) to give first the α-sulfide **28** (130 mg, 43%) and then the β-sulfide **29** (161 mg, 54%). Product **29** was redissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. To this solution was first added $NaHCO_3$ (149 mg, 1.78 mmol) and then MCPBA of approximately 80% purity (133 mg, 5.08 mmol). The mixture was warmed to 20 °C, and then stirred for 4 h, 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 (Na_2SO_4) and concentrated to dryness in vacuo. Flash chromatography (cyclohexane/EtOAc, 2:1) gave **25** (54 mg, 32%) as a colorless syrup. $[\alpha]_D^{22} = -84.2$ (c = 1.5, chloroform); IR (neat): $\tilde{\nu}$ = 3061, 3030, 2909, 2868, 1458, 1362, 1330 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.57 (d, ^3J(H,H) = 4.5 Hz, 1H; pyr), 8.03 (d, ^3J(H,H) = 7.5 Hz, 1H; pyr), 7.67 (dt, ^3J(H,H) = 7.5, 1.5 Hz, 1H; pyr), 7.48–7.09 (m, 21H, 4Ph; pyr), 5.03 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.97 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.97 (d, ^3J(H,H) = 1.0 Hz, 1H; H1), 4.89 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.79 (dd, ^3J(H,H) = 2.5, 1.0 Hz, 1H; H2), 4.73 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.62 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.59 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.42 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.30 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.02 (dd, ^3J(H,H) = 9.0, 9.0 Hz, 1H; H4), 3.72 (s, 2H; H6a, H6b), 3.67 (dd, ^3J(H,H) = 9.0, 2.5 Hz, 1H; H3), 3.48 (ddd, ^3J(H,H) = 9.0, 3.8, 3.8 Hz, 1H; H5); MS (ES): m/z = 666 [M+1]; HR-MS (ES) $C_{39}H_{40}NO_7S$: calcd for [M+1] 666.2525, found 666.2481.

2-Deoxy-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl 2-pyridyl sulfone (45): Tributylphosphine (430 µL, 1.73 mmol) was added to a stirred solution of 2-deoxy-3,4,6-tri-*O*-benzyl-D-glucopyranose (625 mg, 1.44 mmol)[47] and 2,2′-dipyridyl disulfide (348 mg, 1.58 mmol) in CH_2Cl_2. The yellow solution was stirred for 1 h at 20 °C, after which it was evaporated to dryness. Purification of the crude product by flash chromatography (heptane/EtOAc, 4:1) afforded first the β-glucosyl pyridylsufide (489 mg) and then the corresponding α anomer (80 mg). The β-sulfide was then redissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C. To this solution was first added $NaHCO_3$ (539 mg, 6.44 mmol) and then MCPBA of approximately 80% purity (606 mg, 2.86 mmol). The mixture was stirred for 4 h at 0 °C and then for 1 h at 20 °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 (heptane/EtOAc, 3:2) gave **45** (453 mg, 87%) as a colorless solid. Recrystallization from heptane/EtOAc afforded colorless needles. M.p.: 99–101 °C; $[\alpha]_D^{22} = +16.9$ (c = 1.5, chloroform); IR (neat): $\tilde{\nu}$ = 2867, 1497, 1453, 1321, 1105 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.73 (dd, ^3J(H,H) = 4.7, 2.2 Hz, 1H; pyr), 8.11 (brd, ^3J(H,H) = 7.8 Hz, 1H; pyr), 7.84 (dt, ^3J(H,H) = 7.8, 2.2 Hz, 1H; pyr), 7.46 (brdd, ^3J(H,H) = 7.8, 4.7 Hz, 1H; pyr), 7.37–7.10 (m, 15H; 3Ph), 4.91 (dd, ^3J(H,H) = 12.3, 2.2 Hz, 1H; H1), 4.90 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.77 (d, ^2J(H,H) = 11.7 Hz, 1H; CHPh), 4.62 (d, ^2J(H,H) = 11.7 Hz, 1H; CHPh), 4.57 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.32 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.24 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 3.76 (ddd, ^3J(H,H) = 11.3, 8.5, 5.1 Hz, 1H; H3), 3.58 (s, 1H; H6a), 3.57 (s, 1H; H6b), 3.49 (dd, ^3J(H,H) = 9.6, 8.5 Hz, 1H; H4), 3.41 (ddd, ^3J(H,H) = 9.6, 3.3, 3.3 Hz, 1H; H5), 2.80 (ddd, ^3J(H,H) = 12.6, 5.1, 2.2 Hz, 1H; H2eq), 2.05 (ddd, ^3J(H,H) = 12.6, 11.3, 11.2 Hz, 1H; H2ax); $C_{32}H_{33}NO_6S$ (559.7): calcd C 68.67, H 5.94, N 2.50; found C 68.54, H 6.01, N 2.55.

2-Deoxy-3,4,6-tri-*O*-acetyl-D-glucopyranosyl 2-pyridyl sulfone (46): Gaseous HCl was bubbled through a solution of triacetylglucal (1.32 g, 3.17 mmol) in toluene (10 mL) for 20 min at 0 °C and then left to stir for another 30 min. Argon was bubbled through the solution for 45 min at 0 °C, after which the solution was concentrated under vacuum to half volume. Then CH_2Cl_2 (5 mL) was added followed by diisopropylethylamine (0.83 mL, 4.76 mmol) and 2-mercaptopyridine (528 mg, 4.76 mmol), and the solution was left to stir overnight. Further addition of CH_2Cl_2, washing with water, drying (Na_2SO_4), and evaporation under vacuum afforded the crude pyridylsulfide which was purified by flash chromatography (heptane/EtOAc, 3:2) giving 1.57 g (84%) of a colorless syrup. The pyridylsulfide

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was then oxidized according to the general procedure outlined for **45**, to give **46** as a colorless syrup (α:β, 2:3) in 72% yield (427 mg) after flash chromatography (heptane/EtOAc, 2:1).

β anomer: $[\alpha]_D^{22} = +29.4$ ($c = 1.5$, chloroform); IR (neat): $\tilde{\nu} = 2960$, 2885, 1745, 1429, 1368, 1325, 1230 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.79$ (br d, $^3J(H,H) = 4.7$ Hz, 1H; pyr), 8.11 (br d, $^3J(H,H) = 7.9$ Hz, 1H; pyr), 7.99 (dt, $^3J(H,H) = 7.9$, 1.8 Hz, 1H; pyr), 7.59 (ddd, $^3J(H,H) = 7.9$, 4.7, 1.2 Hz, 1H; pyr), 5.11 (ddd, $^3J(H,H) = 11.6$, 9.6, 5.2 Hz, 1H; H3), 5.04 (dd, $^3J(H,H) = 12.1$, 2.3 Hz, 1H; H1), 4.98 (dd, $^3J(H,H) = 9.6$, 9.6 Hz, 1H; H4), 4.08 (dd, $^3J(H,H) = 12.4$, 5.8 Hz, 1H; H6a), 3.96 (dd, $^3J(H,H) = 12.4$, 2.5 Hz, 1H; H6b), 3.60 (ddd, $^3J(H,H) = 9.6$, 5.2, 2.5 Hz, 1H; H5), 2.70 (ddd, $^3J(H,H) = 12.7$, 5.2, 2.3 Hz, 1H; H2eq), 2.18 (ddd, $^3J(H,H) = 12.7$, 12.1, 11.6 Hz, 1H; H2ax), 2.06, 2.05, 2.02, 1.96, 1.91, (5s, 15H; OAc). Characterisic peaks for the α anomer were found at $\delta = 8.81$ (br d, $^3J(H,H) = 4.7$ Hz, 1H; pyr), 8.15 (br d, $^3J(H,H) = 7.9$ Hz, 1H; pyr), 8.00 (dt, $^3J(H,H) = 7.9$, 1.8 Hz, 1H; pyr), 7.60 (ddd, $^3J(H,H) = 7.9$, 4.7, 1.2 Hz, 1H; pyr), 5.57 (ddd, $^3J(H,H) = 10.0$, 8.0, 5.2 Hz, 1H; H3), 5.49 (dd, $^3J(H,H) = 7.1$, 3.2 Hz, 1H; H1), 4.99 (dd, $^3J(H,H) = 9.6$, 8.0 Hz, 1H; H4), 4.66 (ddd, $^3J(H,H) = 9.6$, 5.0, 2.5 Hz, 1H; H5), 4.18 (dd, $^3J(H,H) = 12.5$, 5.5 Hz, 1H; H6a), 3.89 (dd, $^3J(H,H) = 12.5$, 2.5 Hz, 1H; H6b), 3.00 (ddd, $^3J(H,H) = 15.0$, 5.2, 3.2 Hz, 1H; H2eq), 2.27 (ddd, $^3J(H,H) = 15.0$, 8.0, 7.1 Hz, 1H; H2ax); MS (ES): $m/z = 416$ [M+1].

2-Deoxy-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl 2-pyridyl sulfone (**47**): Sulfone **47** was prepared in an analogous fashion to **45**. Recrystallization from heptane/EtOAc afforded the β-sulfone as colorless needles. M.p.: 131–132 °C; $[\alpha]_D^{22} = -43.9$ ($c = 1.1$, chloroform); IR (neat): $\tilde{\nu} = 3054$, 2987, 1422, 1266 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.72$ (dd, $^3J(H,H) = 4.7$, 2.2 Hz, 1H; pyr), 8.13 (d, $^3J(H,H) = 7.8$ Hz, 1H; pyr), 7.87 (dt, $^3J(H,H) = 7.8$, 2.2 Hz, 1H; pyr), 7.47 (dd, $^3J(H,H) = 7.8$, 4.7 Hz, 1H; pyr), 7.38–7.10 (m, 15H; 3Ph), 4.95 (m, 1H; H1), 4.94 (d, $^2J(H,H) = 11.3$ Hz, 1H; CHPh), 4.71 (d, $^2J(H,H) = 12.5$ Hz, 1H; CHPh), 4.58 (d, $^2J(H,H) = 11.3$ Hz, 1H; CHPh), 4.57 (d, $^2J(H,H) = 12.5$ Hz, 1H; CHPh), 4.24 (s, 2H; CHPh), 3.82 (dd, $^3J(H,H) = 2.7$ Hz, 1H; H4), 3.67 (ddd, $^3J(H,H) = 11.0$, 5.0, 2.7 Hz, 1H; H3), 3.57–3.40 (m, 3H; H5, H6a, H6b), 2.56–2.02 (m, 2H; H2ax, H2eq); $C_{32}H_{33}NO_6S$ (559.7): calcd C 68.67, H 5.94; found C 68.63, H 5.97.

2-Deoxy-3,4,6-tri-*O*-benzyl-D-glucopyranosyl-1-cyclohexanol (**49**): The 2-deoxy-*C*-glucosides **49** were prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **49** as an inseparable 1:1 mixture of α and β anomers as a colorless syrup (38 mg, 82%) after flash chromatography (heptane/EtOAc, 7:1 to 2:1). IR (neat): $\tilde{\nu} = 3419$, 2932, 2859, 1453, 1364, 1268 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.20 (m, 30H; 3Ph), 4.91 (d, $^2J(H,H) = 12.0$ Hz, 1H; β-CHPh), 4.71 (d, $^2J(H,H) = 11.6$ Hz, 1H; β-CHPh), 4.62 (d, $^2J(H,H) = 11.6$ Hz, 1H; β-CHPh), 4.59 (d, $^2J(H,H) = 11.1$ Hz, 1H; β-CHPh), 4.58 (d, $^2J(H,H) = 12.3$ Hz, 1H; α- or β-CHPh), 4.55 (s, 2H; α- or β-CH_2Ph), 4.53 (d, $^2J(H,H) = 12.3$ Hz, 1H; α- or β-CHPh), 4.50 (s, 2H; CH_2Ph), 4.49 (d, $^2J(H,H) = 12.0$ Hz, 1H; α-CHPh), 4.44 (d, $^2J(H,H) = 12.0$ Hz, 1H; α-CHPh), 4.22 (ddd, $^3J(H,H) = 7.0$, 6.3, 3.0 Hz, 1H; α-H5), 3.83 (dd, $^3J(H,H) = 10.3$, 7.0 Hz, 1H; α-H6a), 3.83 (m, 1H; α-H3), 3.73, 3.71 (2s, 2H; β-H6a, β-H6b), 3.67 (dd, $^3J(H,H) = 10.3$, 6.3 Hz, 1H; α-H6b), 3.66 (ddd, $^3J(H,H) = 11.6$, 8.2, 5.1 Hz, 1H; β-H3), 3.64 (dd, $^3J(H,H) = 11.4$, 3.3 Hz, 1H; α-H1), 3.49 (dd, $^3J(H,H) = 3.0$, 2.8, 1H; α-H4), 3.47 (dd, $^3J(H,H) = 9.8$, 8.2, 1H; β-H4), 3.40 (ddd, $^3J(H,H) = 9.8$, 3.2, 3.2 Hz, 1H; β-H5), 3.16 (dd, $^3J(H,H) = 12.0$, 2.1 Hz, 1H; β-H1), 2.18 (ddd, $^3J(H,H) = 12.8$, 5.1, 2.1 Hz, 1H; β-H2eq), 2.07 (ddd, $^3J(H,H) = 14.0$, 11.5, 3.4 Hz, 1H; α-H2eq), 1.73 (ddd, $^3J(H,H) = 14.0$, 3.3, 3.3 Hz, 1H; α-H2ax), 1.61 (ddd, $^3J(H,H) = 12.8$, 12.0, 11.6 Hz, 1H; β-H2ax), 1.79–1.19 (m, 22H; $10CH_2$, 2OH); MS (EI) $m/z = 516$ [M]; HR-MS (EI) $C_{33}H_{40}O_5$: calcd for [M] 516.2877, found 516.2915.

2-Deoxy-3,4,6-tri-*O*-acetyl-D-glucopyranosyl-1-cyclohexanol (**50**): The *C*-glucosides **50** were prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **50** as an inseparable 1:1 mixture of α and β anomers as a colorless syrup (30.2 mg, 88%) after flash chromatography (heptane/EtOAc, 4:1 to 3:1). IR (neat): $\tilde{\nu} = 3522$, 2936, 2859, 1743, 1368, 1232 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.12$ (ddd, $^3J(H,H) = 4.0$, 4.0, 4.0 Hz, 1H; α-H3), 4.99 (ddd, $^3J(H,H) = 11.3$, 9.3, 5.2 Hz, 1H; β-H3), 4.89 (dd, $^3J(H,H) = 9.3$, 9.3 Hz, 1H; β-H4), 4.71 (dd, $^3J(H,H) = 4.0$, 2.9 Hz, 1H; α-H4), 4.61 (dd, $^3J(H,H) = 11.7$, 8.3 Hz, 1H; α-H6a), 4.20 (dd, $^3J(H,H) = 12.3$, 5.1 Hz, 1H; β-H6a), 4.18 (m, 1H; α-H5), 4.07 (dd, $^3J(H,H) = 12.3$, 2.4 Hz, 1H; β-H6b), 4.06 (dd, $^3J(H,H) = 11.7$, 4.5 Hz, 1H; α-H6b), 3.61 (dd, $^3J(H,H) = 10.3$, 3.2 Hz, 1H; α-H1), 3.56 (ddd, $^3J(H,H) = 9.3$, 5.1, 2.4 Hz, 1H; β-H5), 3.27 (dd, $^3J(H,H) = 11.7$, 2.2 Hz, 1H; β-H1), 2.12–1.98 (m, 2H; α-H2eq, β-H2eq), 2.07, 2.06, 2.05, 2.04, 2.01, 2.00 (6s, 18H; 6OAc), 1.75–1.16 (m, 24H; $10CH_2$, α-H2ax, β-H2ax, 2OH); MS (EI) $m/z = 372$ [M]; HR-MS (EI) $C_{18}H_{28}O_8$: calcd for [M] 372.1784, found 372.1797.

2-Deoxy-3,4,6-tri-*O*-benzyl-D-galactopyranosyl-1-cyclohexanol (**51**): The 2-deoxy-*C*-galactosides **51** were prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **51** as an inseparable 1:1 mixture of α and β anomers as a colorless syrup (32 mg, 86%) after flash chromatography (cyclohexane/EtOAc, 3:1). IR (neat): $\tilde{\nu} = 3420$, 2932, 2859, 1453, 1364 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.43$–7.24 (m, 30H; 3Ph), 5.00 (d, $^2J(H,H) = 11.6$ Hz, 1H; β-CHPh), 4.73 (d, $^2J(H,H) = 11.8$ Hz, 1H; α-CHPh), 4.64–4.44 (m, 10H; 10CHPh), 4.22 (ddd, $^3J(H,H) = 9.2$, 5.9, 2.2 Hz, 1H; α-H5), 4.18 (dd, $^3J(H,H) = 10.3$, 7.0 Hz, 1H; α-H6a), 3.96 (m, 1H; α-H4), 3.82 (d, $^3J(H,H) = 2.5$ Hz, 1H; β-H4), 3.82 (dd, $^3J(H,H) = 11.5$, 2.3 Hz, 1H; α-H1), 3.73–3.57 (m, 4H; β-H3, β-H5, β-H6a, β-H6b), 3.66 (dd, $^3J(H,H) = 11.3$, 2.2 Hz, 1H; α-H6b), 3.62 (m, 1H; α-H3), 3.24 (dd, $^3J(H,H) = 11.5$, 2.3 Hz, 1H; β-H1), 2.08 (dd, $^3J(H,H) = 11.8$, 11.8 Hz, 1H; β-H2ax), 1.86 (ddd, $^3J(H,H) = 13.8$, 4.3, 2.6 Hz, 1H; α-H2ax), 1.83–1.17 (m, 24H; α-H2eq, β-H2eq, $10CH_2$, 2OH); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 132.1$, 132.0, 131.8, 131.5, 131.2, 131.1, 131.0, 85.6, 82.9, 81.4, 81.1, 80.8, 80.1, 79.0, 76.9, 76.3, 75.8, 74.8, 73.8, 73.7, 73.2, 70.4, 38.6, 38.1, 36.2, 36.0, 32.3, 29.7, 25.3; MS (CI, NH_3) $m/z = 534$ [M+18], 517 [M+1], 499 [M+1 − H_2O]; MS (ES): $m/z = 539$ [M+Na]; HR-MS (ES) $C_{33}H_{41}O_5$: calcd for [M+1] 517.2955, found 517.2909.

2-Deoxy-2-methoxymethyl-3,4,6-tri-*O*-benzyl-D-glucopyranosyl-1-cyclohexanol (**52**): The 2-deoxy-*C*-glucosides **52** were prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **52** as an inseparable 4:1 mixture of α and β anomers (8 mg, 73%) after flash chromatography (heptane/EtOAc, 4:1 to 3:1). IR (neat): $\tilde{\nu} = 3419$, 2928, 2859, 1744, 1428, 1270 cm^{-1}; MS (ES): $m/z = 583$ [M+Na]; HR-MS (ES) $C_{35}H_{44}NaO_6$: calcd for [M+Na] 583.3036, found 583.3043.

β anomer: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.22 (m, 15H; 3Ph), 4.92 (d, $^2J(H,H) = 11.4$ Hz, 1H; CHPh), 4.78 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.64 (d, $^2J(H,H) = 12.4$ Hz, 1H; CHPh), 4.63 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.59 (d, $^2J(H,H) = 11.4$ Hz, 1H; CHPh), 4.57 (d, $^2J(H,H) = 12.4$ Hz, 1H; CHPh), 3.81 (br s, 1H; OH), 3.73 (dd, $^3J(H,H) = 11.2$, 3.9 Hz, 1H; H6a), 3.69 (dd, $^3J(H,H) = 11.2$, 2.6 Hz, 1H; H6b), 3.66 (dd, $^3J(H,H) = 9.8$, 2.5 Hz, 1H; H2′a), 3.61 (dd, $^3J(H,H) = 9.6$, 8.4 Hz, 1H; H4), 3.59 (dd, $^3J(H,H) = 9.8$, 6.2 Hz, 1H; H2′b), 3.43 (dd, $^3J(H,H) = 10.3$, 8.4 Hz, 1H; H3), 3.36 (ddd, $^3J(H,H) = 9.6$, 3.9, 2.6 Hz, 1H; H5), 3.26 (s, 3H; OMe), 3.06 (d, $^3J(H,H) = 9.6$ Hz, 1H; H1), 2.05 (dddd, $^3J(H,H) = 10.3$, 9.6, 6.2, 2.5 Hz, 1H; H2), 1.89–1.37 (m, 10H; $5CH_2$).

α anomer: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.26$–7.22 (m, 15H; 3Ph), 4.55 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.55 (s, 2H; CH_2Ph), 4.50 (s, 2H; CH_2Ph), 4.47 (d, $^2J(H,H) = 12.0$ Hz, 1H; CHPh), 4.27 (ddd, $^3J(H,H) = 6.3$, 6.3, 2.6 Hz, 1H; H5), 4.09 (dd, $^3J(H,H) = 10.2$, 7.3 Hz, 1H; H2′a), 3.93 (dd, $^3J(H,H) = 3.2$, 2.6 Hz, 1H; H4), 3.80 (dd, $^3J(H,H) = 9.9$, 6.3 Hz, 1H; H6a), 3.76 (d, $^3J(H,H) = 2.5$ Hz, 1H; H1), 3.70 (dd, $^3J(H,H) = 9.9$, 6.3 Hz, 1H; H6b), 3.53 (dd, $^3J(H,H) = 3.2$, 2.6 Hz, 1H; H3), 3.45 (dd, $^3J(H,H) = 10.2$, 6.0 Hz, 1H; H2′b), 3.30 (s, 3H; OMe), 3.17 (s, 1H; OH), 2.26 (dddd, $^3J(H,H) = 7.3$, 6.0, 3.2, 2.5 Hz, 1H; H2), 1.90–1.19 (m, 10H; $5CH_2$).

Benzyl 2-deoxy-2-formyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (**56**)**:** The procedure described by Jung and Choe[43] was employed to give aldehyde **56** as colorless crystals after recrystallization from EtOAc/heptane. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.52$ (d, $^3J(H,H) = 2.8$ Hz, 1H; CHO), 7.40–7.17 (m, 20H; 4Ph), 5.20 (d, $^3J(H,H) = 3.9$ Hz, 1H; H1), 4.89 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.83 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.77 (d, $^2J(H,H) = 11.2$ Hz, 1H; CHPh), 4.67 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.66 (d, $^2J(H,H) = 12.1$ Hz, 1H; CHPh), 4.59 (d, $^2J(H,H) = 10.9$ Hz, 1H; CHPh), 4.55 (d, $^2J(H,H) = 12.1$ Hz, 1H; CHPh), 4.48 (d, $^2J(H,H) = 12.2$ Hz, 1H; CHPh), 4.41 (dd, $^3J(H,H) = 11.2$, 9.1 Hz, 1H; H3), 3.91 (ddd, $^3J(H,H) = 10.1$, 3.7, 2.2 Hz, 1H; H5), 3.81 (dd, $^3J(H,H) = 10.2$, 3.7 Hz, 1H; H6a), 3.77 (dd, $^3J(H,H) = 10.1$, 9.1 Hz, 1H; H4), 3.67 (dd, $^3J(H,H) = 10.2$, 2.2 Hz, 1H; H6b), 3.59 (ddd, $^3J(H,H) = 11.2$, 3.9, 2.8 Hz, 1H; H2).

***C*-Disaccharide** (**57**): The *C*-mannosides **57** were prepared according to the general procedure outlined for **7** with the exception of the desilylation step, to give **57** as a 2:1 mixture of diastereomers and as a colorless syrup (63 mg, 74%) after flash chromatography (CH_2Cl_2 to CH_2Cl_2/EtOAc, 25:1).

Major isomer: $[\alpha]_D^{22} = +52.6$ ($c = 1.0$, chloroform); IR (neat): $\tilde{\nu} = 3500$, 2926, 2856, 1454, 1360, 1253 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.38$-

7.13 (m, 35H; 7Ph), 5.43 (d, ^3J(H,H) = 3.6 Hz, 1H; H1), 4.88 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.81 (d, ^2J(H,H) = 10.9 Hz, 1H; CHPh), 4.74 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.73 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.66 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.64 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 4.62 (d, ^2J(H,H) = 11.7 Hz, 1H; CHPh), 4.58 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.55 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 4.55 (d, ^2J(H,H) = 11.7 Hz, 1H; CHPh), 4.54 (d, ^2J(H,H) = 11.6 Hz, 1H; CHPh), 4.50 (d, ^2J(H,H) = 11.2 Hz, 1H; CHPh), 4.46 (d, ^2J(H,H) = 11.6 Hz, 1H; CHPh), 4.45 (d, ^2J(H,H) = 10.9 Hz, 1H; CHPh), 4.43 (dd, ^3J(H,H) = 8.0, 3.1 Hz, 1H; H2′), 4.32 (d, ^2J(H,H) = 12.1 Hz, 1H; CHPh), 4.14 (ddd, ^3J(H,H) = 10.5, 10.5, 3.2 Hz, 1H; H5′), 4.10 (dd, ^3J(H,H) = 11.2, 9.0 Hz, 1H; H3), 3.93 (dd, ^3J(H,H) = 8.5, 8.5 Hz; 1H), 3.87 (ddd, ^3J(H,H) = 10.0, 4.5, 2.2 Hz, 1H; H5), 3.78–3.55 (m, 8H; H1′, H3′, H4, H4′, H6a, H6b, H6′a, H7), 3.47 (dd, ^3J(H,H) = 11.0, 3.2 Hz, 1H; H6′b), 2.25 (ddd, ^3J(H,H) = 11.2, 3.6, 3.6 Hz, 1H; H2), 0.12 (s, 3H; $SiMe_3$); MS (CI, NH_3): m/z = 1076 [M+18], 968 [M+18 − BnOH], 859 [M+18 − 2BnOH], 843 [M+1 − 2BnOH].

Minor isomer: IR (neat): $\tilde{\nu}$ = 3450, 2928, 2856, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.12 (m, 35H; 7Ph), 5.15 (d, ^3J(H,H) = 3.3 Hz, 1H; H1), 4.99 (d, ^2J(H,H) = 10.7 Hz, 1H; CHPh), 4.70 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.72 (d, ^2J(H,H) = 10.7 Hz, 1H; CHPh), 4.66 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 4.64 (d, ^2J(H,H) = 12.1 Hz, 1H; CHPh), 4.57 (d, ^2J(H,H) = 11.0 Hz, 1H; CHPh), 4.55 (d, ^2J(H,H) = 12.3 Hz, 1H; CHPh), 4.51 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.51 (d, ^2J(H,H) = 11.5 Hz, 1H; CHPh), 4.45 (d, ^2J(H,H) = 12.0 Hz, 1H; CHPh), 4.41 (s, 2H, CH_2Ph), 4.37 (dd, ^3J(H,H) = 8.5, 2.9 Hz, 1H; H2′), 4.32 (d, ^2J(H,H) = 12.1 Hz, 1H; CHPh), 4.18 (ddd, ^3J(H,H) = 6.4, 6.4, 3.3 Hz, 1H; H5′), 4.15 (dd, ^3J(H,H) = 11.2, 9.0 Hz, 1H; H3), 4.09 (ddd, ^3J(H,H) = 8.8, 1.6, 1.6 Hz, 1H; H7), 3.90 (br d, ^3J(H,H) = 5.2 Hz, 1H; H1′), 3.86 (ddd, ^3J(H,H) = 10.0, 4.3, 2.2 Hz, 1H; H5), 3.79–3.64 (m, 6H; H3′, H4, H4′, H6a, H6b, H6′a), 3.60 (dd, ^3J(H,H) = 10.3, 6.4 Hz, 1H; H6′b), 2.46 (ddd, ^3J(H,H) = 11.2, 8.8, 3.3 Hz, 1H; H2), 0.14 (s, 3H; $SiMe_3$); MS (CI, NH_3): m/z = 1076 [M+18], 968 [M+18 − BnOH], 951 [M+1 − BnOH], 859 [M+18 − 2BnOH], 843 [M+1 − 2BnOH].

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