Stereoselective Synthesis of *carba*- and *C*-Glycosyl Analogs of Fucopyranosides

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Dedicated to Professor Pierre Sinaÿ on the ocassion of his 62nd birthday

Keywords: Carbocycles / Carbohydrates

Fucopyranoside analogs with methylene groups instead of *endo*- or *exo*-anomeric oxygens, *carba*- and *C*-fucopyranosides, respectively, were synthesized. For the synthesis of 5a-*carba*-L-fucose (**1**) two approaches were studied, which shared a common cyclitol building block (**8**), obtained from a SmI_2-promoted carbocyclization of a D-mannitol derivative. The first route made use of a Stork radical cyclization onto a conduritol derivative **13** as the key step, which failed to give the silyl ether ring. The second route furnished the target **1**, and involved regioselective elimination of a cyclic sulfate **9**, and stereoselective hydrogenation of a double bond, controlled by substitution on the substrate. For the synthesis of 1-*C*-fucopyranosides (**37**, **38**, and **42**) a new method based on the use of fucosyl phenyl sulfoxides (**35** and **41**) was employed. An anomeric carbanion is generated through phenylsulfinyl-lithium exchange, which reacted with electrophiles with retention of configuration at the anomeric center. The required fucosyl sulfoxides were prepared from L-fucose by highly stereoselective thioglycosylation reactions.

Introduction

Research on carbohydrates has grown considerably over the last years and promises to be a major focus led by drug discovery.[1] Oligosaccharides on the cell-surface membranes play an important role in processes such as fertilization, immune defense, parasitic infection, cell growth, cell–cell adhesion, and inflammation.[2] However, the use of oligosaccharides as new drug candidates is hampered by their susceptibility to hydrolysis by glycosidases, enzymes that are ubiquitous in tissue. This limitation has stimulated the synthesis of more stable oligosaccharide analogs and mimetics.[3] In this context, 5a-carbapyranoses, also named pseudosugars, and 1-*C*-glycopyranosides, analogs in which the *endo*- and the *exo*-anomeric oxygen, respectively, are replaced by a methylene group, have attracted considerable interest owing to their inherent stability to the hydrolytic activity of glycosidases. Inhibitors of glycosidases and glycosyltransferases, enzymes involved in oligosaccharide-chain biosynthesis, have been prepared on the basis of these structures,[4] thus expanding their potential applications. Apart from that, little has been done with regard to studying the conformation around the glycosidic linkage in the 5a-carba- and 1-*C*-glycosides, and comparing it with the parent glycosides; this may shed light on the influence of the *exo*-anomeric effect.

Within a project[5,6] on the synthesis of Lewis^X trisaccharide analogs,[7] we were interested in the preparation of 5a-carba-L-fucose and 1-*C*-fucosyl glycosides. Several syntheses of 5a-carba-L-fucose have been published.[8] Two of them[8a][8b] make use of a cyclization of acyclic carbohydrate derivatives; other approaches employ cyclitols as starting materials, and a recent report,[8f] describes the desymmetrization of a dienylsilane. In the present work, we explored new routes to synthesize 5a-carba-L-fucose from a readily available D-mannitol derivative, through an SmI_2-promoted carbocyclization and further functional group manipulation. Our approaches make use of symmetry elements;[6a] this significantly simplifies the synthesis.

The synthesis of *C*-glycosides has been an active field of research over the last years. Several approaches have been published, including ones via anomeric carbocations and radicals.[9] For the synthesis of 1-*C*-fucosyl glycosides, we employed a strategy based on the reaction of an anomeric carbanion with a carbon electrophile. We recently communicated[6b] a new method to generate anomeric carbanions from easily accessible glycosyl sulfoxides, and their stereoselective reaction with electrophiles with retention of configuration at the anomeric center. Full details of the application of this method for the stereoselective synthesis of *C*-fucosides is now described.

Results and Discussion

Synthesis of 5a-Carba-α-L-fucopyranose

Two routes, depicted in Scheme 1, were designed for the preparation of 5a-carba-α-L-fucopyranose (**1**) from D-mannitol derivative **VIII** through a common intermediate cyclitol **VII** obtained by a SmI_2-promoted carbocyclization. To introduce the methyl group into the cyclitol ring, we first tried to apply the Stork radical cyclization on a conduritol derivative **V** (route 1, Scheme 1). A second approach involved the generation of a ketone **VI** by regioselective elimination of the cyclic sulfate derived from cyclitol **VII**; this was followed by a Wittig reaction and stereoselective hydro-

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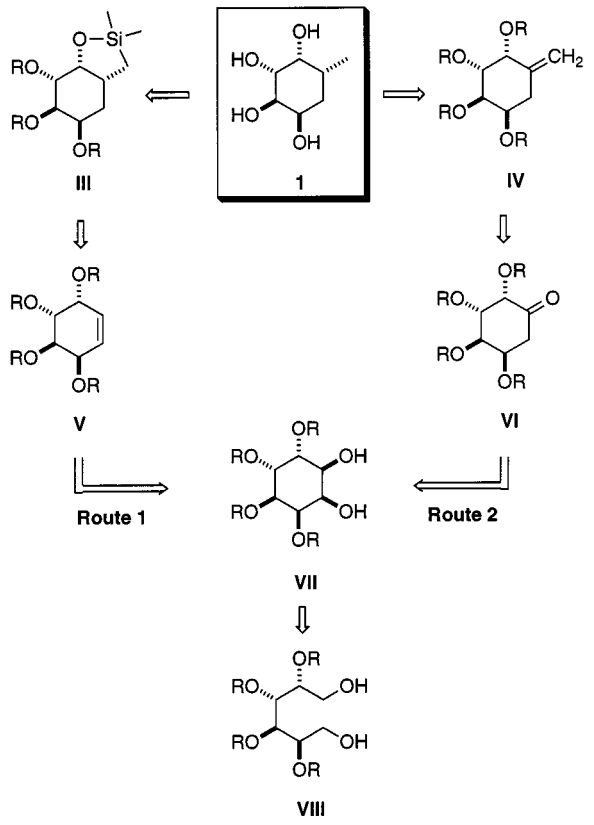


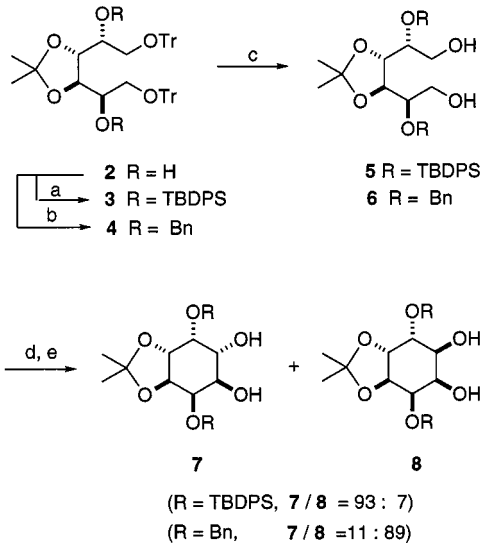
Scheme 1. Retrosynthetic analysis of the two routes to **1**

genation of the *exo*-methylene double bond in **IV** (route 2, Scheme 1).

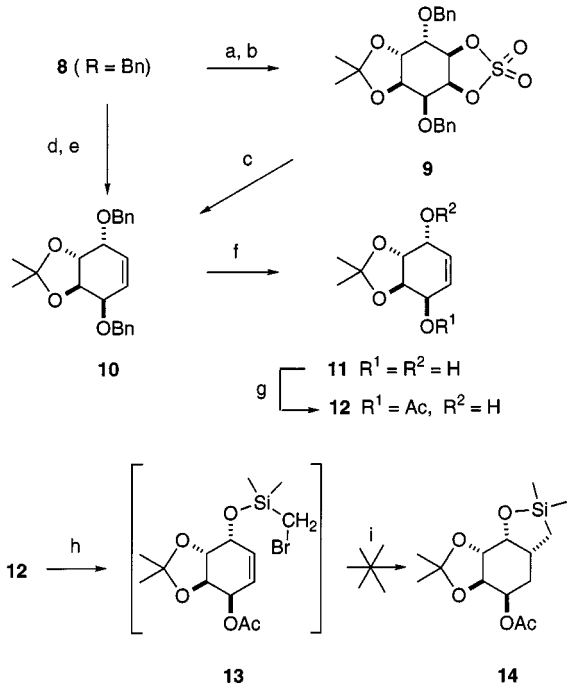
The carbocyclization key step was carried out with the use of the sequence of oxidation and samarium diiodide-promoted pinacol coupling[10] on two differently substituted diols **5** and **6** prepared from 1,6-di-*O*-trityl-3,4-*O*-isopropylidene-D-mannitol (**2**, Scheme 2). The diastereoselectivity of the cyclization was found[6a] to be dependent on the protecting group R at the vicinal position of the primary alcohol.

Once the cyclitol was formed, its transformation into the target 5a-carba-α-L-fucopyranose was first tried by route 1 depicted in Scheme 1. Conversion of *trans*-diol **7** (R = TBS) into the corresponding conduritol by dihydroxy elimination turned out to be difficult due to both the diequatorial configuration of the diol system and the lability of the silyl protecting groups. We then focused our attention on *cis*-diol **8** (R = Bn), which could be converted into protected conduritol **10** by the Corey–Winter method[11] or, more conveniently, by treatment of its cyclic sulfate **9** with sodium hydrogen telluride (Scheme 3). Debenzylation of **10** by the Birch reduction furnished conduritol **11** which was partially acetylated to give **12** by a lipase-catalyzed transesterification with vinyl acetate in an organic solvent.[12] Of the different organic solvents tested (THF, acetonitrile, and toluene), dichloromethane gave the highest ratio of mono/diacetyl derivatives.

The regio- and stereoselective hydromethylation of the double bond of **12** was tried with the Stork procedure,[13]



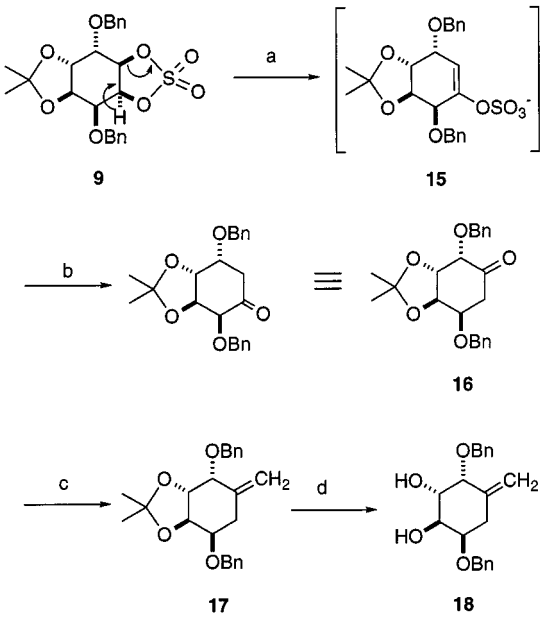
Scheme 2. Reagents and conditions: (a) TBDPSCl, ImH, DMAP, DMF, 66%; (b) BnBr, NaH, DMF, 95%; (c) H_2, Pd/C, EtOAc, 61% (R = TBDPS), or *p*TsOH, EtOAc/MeOH, 84% (R = Bn); (d) Swern oxidn.; (e) SmI_2, *t*BuOH, THF, –60 °C, 91% (R = TBDPS), or 82% (R = Bn)



Scheme 3. Reagents and conditions: (a) $SOCl_2$, Et_3N, CH_2Cl_2; (b) $NaIO_4$, $RuCl_3$, MeCN, CCl_4, H_2O, 86% (2 steps); (c) NaTeH, DMF, 95%; (d) $Im_2C(S)$, PhMe, 77%; (e) $P(OEt)_3$, 165 °C, 76%; (f) Na, NH_3, –78 °C, 56%; (g) vinyl acetate, CH_2Cl_2, PS lipase, 66%; (h) Me_2SiCH_2BrCl, CH_2Cl_2, Et_3N; (i) Bu_3SnH, AIBN, PhMe

that is, bromomethyldimethylsilylation of the free hydroxyl group and radical cyclization, followed by protodesilylation. Although the silyl ether derivative **13** was cleanly formed,[14] several attempts to perform the cyclization, even with different protecting groups on the cyclitol ring, by treatment with Bu_3SnH, were unfruitful, leading to complex mixtures of by-products.

We then began to explore the second route outlined in Scheme 1. The formation of an α-deoxyketone from a *cis*-cyclohexanediol derivative **VII** was first required. We reasoned that the treatment of the cyclic sulfate **9** (Scheme 4) with a base should lead to regioselective elimination by abstraction of the proton that is *trans*-diaxially disposed to the sulfate leaving group. Thus, the treatment of **9** with KO*t*Bu led to the formation of a new product with a lower R_f on TLC, presumably the vinyl bisulfate **15**,[15] which, after acidification, afforded the expected ketone **16** in 86% yield. The reaction proceeded cleanly and no other product was detected. Finally, Wittig olefination of **16** with PPh_3MeBr/KHMDS furnished *exo*-methylenecyclohexane **17**.

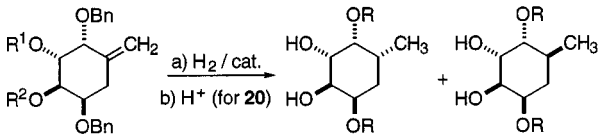


Scheme 4. Reagents and conditions: (a) *t*BuOK, THF; (b) H_2SO_4, H_2O, THF, 86% (2 steps); (c) PPh_3MeBr, $[Me_3Si]_2NK$, THF, 85%; (d) CF_3COOH, MeOH, 98%

Hydrogenation of the double bond was expected to proceed stereoselectively *anti* to the benzyloxy group at the adjacent position, to afford the desired pseudo-L-fucopyranose compound. However, the reaction of the isopropylidene derivative **17** and the diol **18** under different conditions gave mainly the isomeric D-configured pseudosugar. Table 1 summarizes the results of the hydrogenations with Pd, Rh, and Ni catalysts. It is noteworthy that the reaction of **17** with Raney nickel gave the 6-deoxy-5a-carba-D-altropyranose derivative **20** as sole product, isolated in 87% yield. Only with the diol **18** and with the Rh complex as catalyst did the reaction lead to a slight excess of pseudo-L-fuco derivative **19**. Nevertheless, it can be seen that with a given catalyst the relative amount of **19** is always higher in the hydrogenation of **18** than in that of **17**.

We also evaluated the diastereoselectivity of the hydroboration of **17** and **18** (Scheme 5). In this case the fine tuning of the protecting groups resulted in a drastic change in diastereoselectivity: treatment of isopropylidene derivative **17** with BH_3 and subsequent oxidation gave a mixture of

Table 1. Catalytic hydrogenation of **17** and **18**

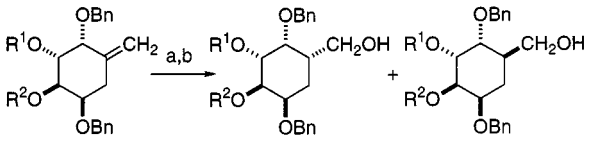


17 $R^1 = R^2 = CMe_2$
18 $R^1 = R^2 = H$
19 R = Bn
1 R = H
20 R = Bn
21 R = H

Compd.	Catalyst	Solvent	**19** : **20**	Yield (%)
17	Pd/ C	EtOAc	0.3 : 1[a]	92
18	Pd/ C	EtOAc	0.6 : 1[a]	90
18	Pd/ C	MeOH/py	0.8 : 1	92
17	$Rh(PPh_3)Cl$	MeOH	0.4 : 1	91
18	$Rh(PPh_3)Cl$	MeOH	1.1 : 1	99
17	Ni-Ra	MeOH	0 : 1	87
18	Ni-Ra	MeOH	0.3 : 1	62

[a] Simultaneous hydrogenolysis of benzyl groups occurred to give **1** and **21**.

the carba-L-galacto- and D-altropyranose derivatives **22** and **23** in the ratio 17:83, from which **23** was isolated in 57% yield. Under similar conditions, diol **18** gave the carba-L-galacto- and D-altropyranose derivatives **24** and **25** in 92:8 ratio, **24** being isolated in 71% yield.

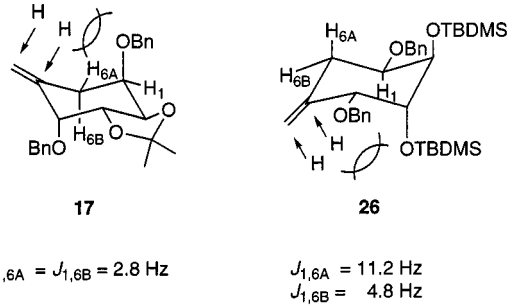


17 $R^1, R^2 = CMe_2$
18 $R^1 = R^2 = H$
22 $R^1, R^2 = CMe_2$ (17 : 83) **23** $R^1, R^2 = CMe_2$
24 $R^1 = R^2 = H$ (92 : 8) **25** $R^1 = R^2 = H$

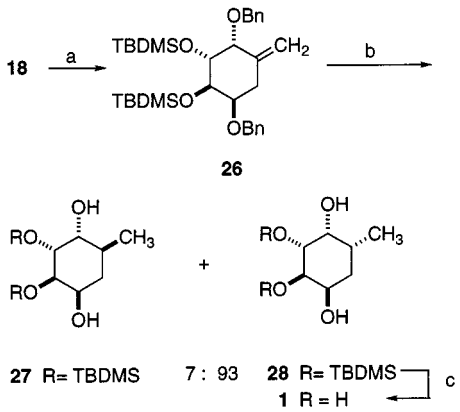
Scheme 5. Reagents and conditions: (a) BH_3·THF, THF; (b) H_2O_2 (30%), NaOH (3 N), 69% (for **17**) and 77% (for **20**)

Although transformation of **24** to the pseudo-L-fucopyranose **1** is feasible, we decided to reexamine the hydrogenation of *exo*-methylenecyclohexanes derived from **18** by changing the substituents at the *C*-2 and *C*-3 positions. We hypothesized that changing the conformation into a form with the substituent at *C*-3 in the axial orientation, the stereochemistry of the process should be the opposite. Thus, we prepared compound **26** in which the presence of two bulky *tert*-butyldimethylsilyl groups at *C*-2 and *C*-3 positions makes the cyclohexane ring adopt the conformation with the two silyl groups *trans*-diaxially disposed (Scheme 6).[16] When **26** was hydrogenated in the presence of Pd–C (Scheme 7), a mixture of pseudo-sugars **27** and **28** (ratio **27**/**28**, 7:93) was obtained. Therefore, hydrogenation on **26** took place selectively on the β-face of the cyclohex-

ane ring. Deprotection of **28** furnished the target carba-5a-α-L-fucopyranose (**1**), whose ^{1}H NMR spectrum was in agreement with the previously reported one.[8e]



Scheme 6. Proposed conformations of **17** and **26**



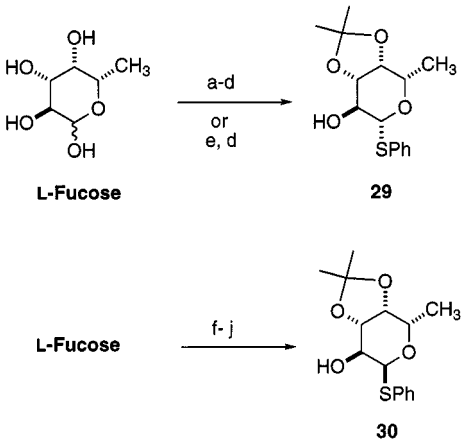
Scheme 7. Reagents and conditions: (a) TBDMSOTf, iPr$_2$EtN, CH_2Cl_2, 89%; (b) H_2, Pd/C (10%), EtOAc, 96%; (c) Bu_4NF, CH_2Cl_2, 51%.

In conclusion, we found a stereoselective route to pseudo-L-fucopyranose **1** from D-mannitol to afford, in addition to the target carbasugar **1**, epimeric pseudosugars. These can be prepared by hydrogenation or hydroboration of a common *exo*-methylenecyclitol, the stereoselectivity of which can be controlled by the substitution on the cyclitol.

Synthesis of 1-*C*-Fucopyranosides

Our approach to the synthesis of these compounds required the preparation of a nucleophilic glycosyl donor. Nonstabilized anomeric carbanions bearing oxygenated substituents at position 2 were previously generated by sequential two-electron transfer with either lithium naphthalenide[17] (from glycosyl chlorides) or samarium diiodide (from glycosyl sulfones,[18] phosphates[19] or chlorides[20]), or by lithium exchange with *n*-butyllithium[21] (from glycosyl stannanes). We investigated new methods to generate anomeric carbanions; these methods are based on the use of glycosyl sulfones and their reductive lithiation, or glycosyl sulfoxides through a sulfinyllithium exchange. Direct *C*-1-lithiation of sugars generally leads to the β-elimination of functional groups in the 2-position; this was prevented by leaving the 2-hydroxyl group unprotected.[17] Therefore, we first prepared the phenyl 1-thio-β- and α-fucopyranosides, with a 2-OH group free, from which the corresponding sulfones and sulfoxides can be obtained.

The synthesis of the β-thioglycoside **29** was carried out by a classical route (Scheme 8) involving thioglycosidation of L-fucose tetraacetate; this was followed by deacetylation and isopropylidenation (four steps, 69% overall yield). Alternatively, a shorter route to **29** was also achieved by direct sulfenylation[22] of L-fucose with $(PhS)_2/Bu_3P$ and subsequent isopropylidenation. Of the solvents tested for the sulfenylation step, acetonitrile gave the best results in terms of yield and stereoselectivity (β:α = 91:9). By the two-step procedure, **29** was obtained in 60% yield.

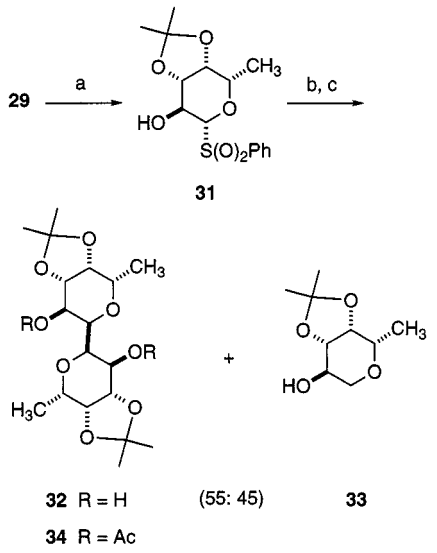


Scheme 8. Reagents and conditions: (a) Ac_2O, Py; (b) PhSH, $SnCl_4$, CH_2Cl_2; (c) NaOMe, MeOH; (d) 2,2-DMP, *p*TsOH, Me_2CO, 69% (4 steps); (e) $(PhS)_2$, Bu_3P, CH_3CN, then step d, 59% (2 steps); (f) TMSCl, Et_3N, DMF; (g) TMSI, CH_2Cl_2; (h) PhSH, DTBMP, CH_2Cl_2, 5 °C; (i) MeOH, room temp.; (j) 2,2-DMP, *p*TsOH, Me_2CO, 77% (5 steps)

The preparation of the α-thioglycoside was tried by a procedure described for the α-thioglucopyranoside,[23] but only a small excess of desired α-thioglycoside was obtained (α:β, 60:40) in low yield (38%). This result confirmed the difficulties often encountered when preparing α-L-thiofucopyranosides.[24] Eventually, the α-thioglycoside **30** could be stereoselectively prepared by an original route (Scheme 8), whose thioglycosylation step was performed by a modified procedure for the synthesis of α-fucopyranosides,[25] in 77% overall yield. Remarkably, all of the five steps are performed in the same flask. Control of the temperature during the thioglycosylation step was crucial for achieving α-stereoselectivity (the ratios α/β were 95:5 and 66:33 at 5 and 20 °C, respectively).

From the 1-thio-β-L-fucopyranoside derivative **29**, the corresponding sulfone **31** was obtained (Scheme 9), and was submitted to reductive lithiation with lithium naphthalenide (LN).[26] The reaction of the oxyanion of **31** with lithium naphthalenide in the presence of isobutyraldehyde as electrophile at –78 °C did not afford the desired *C*-glycoside. Instead, the main products were the dimer **32**[27] and the 1,5-anhydro-L-fucitol **33**, isolated in 36% and 29% yields, respectively. The selective formation of **32** with an α,α-configuration at the anomeric carbons suggests that the α-radical intermediate was generated upon one-electron transfer from lithium naphthalenide to the phenylsulfonyl group

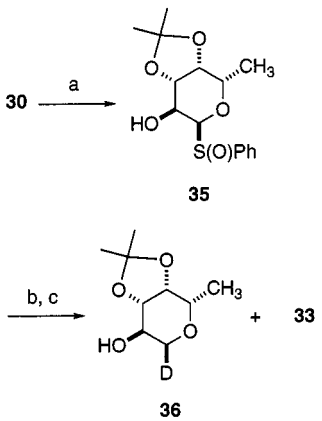
and subsequent C(1)–S fragmentation. The second electron transfer onto the anomeric position, to form a carbanion, seems to be slower than dimerization or proton abstraction, probably due to the presence of the oxyanion at *C*-2.



Scheme 9. Reagents and conditions: (a) *m*CPBA, $NaHCO_3$, CH_2Cl_2, room temp., 90%; (b) BuLi, THF, –78 °C; (c) LN, *i*PrCHO, –78 °C, 65% (2 steps)

All attempts, with different amounts of lithium naphthalenide and with different lengths of time, to get the *C*-fucopyranoside from the reaction of the fucosyl sulfone **31**, for the reductive lithiation, failed. Hence, we focused our attention on the fucosyl sulfoxides and the possibility of performing a phenylsulfinyllithium exchange, which has been used for the generation of oxiranyl carbanions and its further reaction with electrophiles,[28] and for the preparation of glycals.[29]

Since phenylsulfinyllithium exchange would proceed, in principle, with retention of configuration,[28] sulfoxide **35** would be the appropriate anomer for the generation of an α-oriented anomeric carbanion (Scheme 10). Compound **35** was prepared by partial oxidation of **30** at low temperature;



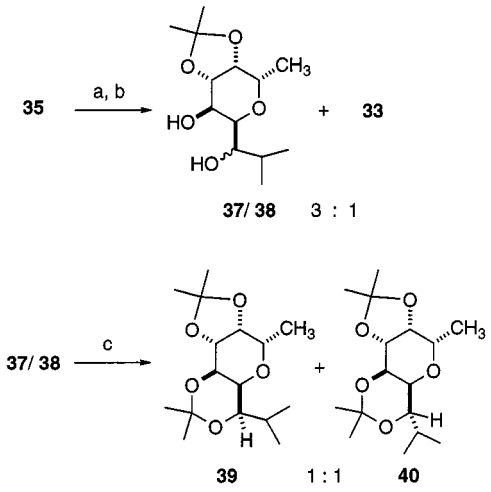
Scheme 10. Reagents and conditions: (a) *m*CPBA, $NaHCO_3$, CH_2Cl_2, –78 °C, 96%; (b) *t*BuLi, THF, –78 °C; (c) CD_3OD (see Table 2)

it was the sole diastereoisomer formed, and its relative configuration was not determined. Deprotonation and phenylsulfinyllithium exchange on **35** was performed by treatment with *t*BuLi. The dianion intermediate was quenched with deuterated methanol, and a mixture of the corresponding α-deuterated and protonated 1,5-anhydrofucitols **36** and **33**, respectively, plus recovered starting material (Scheme 10) formed. The best yields of metallation were obtained in THF and Et_2O, and in the presence of MeLi·LiBr[30] prior to *t*BuLi treatment (Table 2). The ^1H NMR spectra of the crude mixtures showed, in all experiments, that only the above-mentioned products were present. No β-deuterated 1,5-anhydrofucitol could be detected; this indicates that the deuteration is completely stereoselective. Hence, the anomeric carbanion seems to be configurationally stable. This was further supported by the results obtained from the reaction of the fucopyranosyllithium, generated in this way with isobutyraldehyde, which led to a diastereomeric mixture of the α-configured *C*-glycosides **37/38** (Scheme 11). Again, no β-*C*-glycoside could be detected by ^1H NMR. The structures of diastereoisomers **37/38** were confirmed by

Table 2. Phenylsulfinyllithium exchange of **35**

Exp.	Solvent	Equiv./*t* (min)[b]	Equiv./*t* (min)[c]	Yield (%)[a]	**36:33**
1	THF	5/0.5	3/0.5	61	2.3:1
2	THF	5/5	6/5	80	2:1
3	Et_2O	5/5	6/5	63	3.3:1
4[d]	Et_2O	5/5	6/5	54	8.0:1
5[d]	Et_2O	5/20	6/5	77	6.7:1

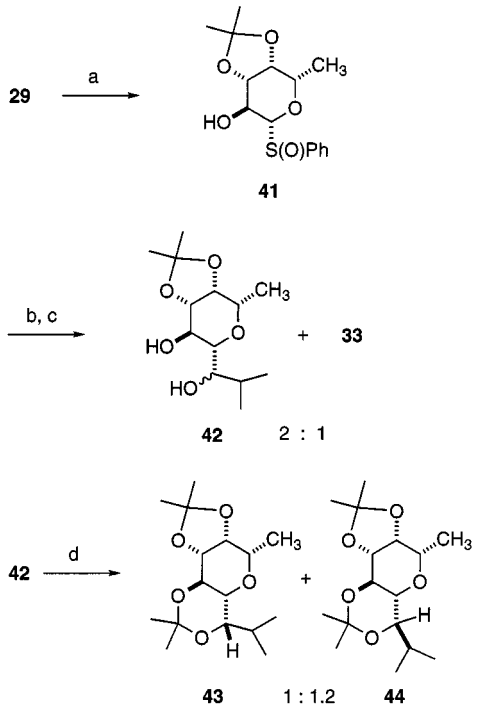
[a] Yields and ratio of **36**: **33** were determined by ^1H NMR spectroscopy. – [b] Equiv. means equivalents of *t*BuLi; *t*: time of metalation step. – [c] Equiv. means equivalents of CD_3OD; *t*: time of deuteration step. – [d] 1 equiv. of MeLi·LiBr was added prior to *t*BuLi treatment (ref.[30])



Scheme 11. Reagents and conditions: (a) MeLi·LiBr, –78 °C, then, *t*BuLi, Et_2O; (b) *i*PrCHO, 81% (2 steps); (c) 2,2-DMP, *p*TsOH, Me_2CO

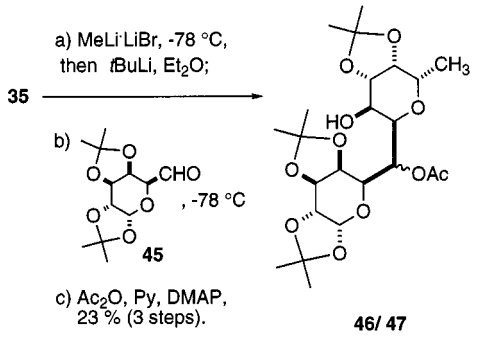
their transformation into the diacetals **39** and **40**, which gave further information[31] about the new chiral center created during the *C*-glycosylation.

Additional evidence for the stereospecificity of the process was obtained from the reaction of fucosyl phenyl sulfoxide **41**, prepared analogously to **35** from phenyl thioglycoside **29** (Scheme 12). In this case, phenylsulfinyllithium exchange was slower, and the corresponding β-configured fucopyranosyllithium species proved to be less efficient in the *C*-glycosylation, although it afforded only the corresponding β-*C*-glycosides **42**, whose structures were again secured after acetylation to **43** and **44** (Scheme 12).



Scheme 12. Reagents and conditions: (a) *m*CPBA, $NaHCO_3$, CH_2Cl_2, –78 °C, 89%; (b) MeLi·LiBr, –78 °C, then, *t*BuLi, Et_2O; (c) *i*PrCHO, 69% (2 steps); (d) 2,2-DMP, *p*-TsOH, Me_2CO

An attempt to widen the scope of the *C*-glycosylation to more complex aldehydes was carried out (Scheme 13) by reaction of the fucopyranosyllithium generated from **35** with the aldehyde **45**[32] derived from D-galactose. In this



Scheme 13. Synthesis of compounds **46/47**

preliminary experiment, only one equiv. of the more valuable aldehyde was used and, after acetylation, a mixture of diastereomeric *C*-disaccharides **46/47** was obtained[33] in 23% (not optimized) combined yield. We are currently investigating the scope and limitation of this new method to generate anomeric carbanions from different sugars and electrophiles.

Conclusion

This paper describes an original route to the preparation of 5a-carba-α-L-fucopyranose (**1**) from D-mannitol, which allows the stereoselective synthesis of other related carbasugars, and a new method for the preparation of *C*-glycosides on the basis of glycosyl sulfoxides. The key steps for the synthesis of **1** were the SmI_2-promoted carbocyclization, the regioselective elimination of a cyclic sulfate, and the stereoselective hydrogenation of a double bond, controlled by substitution on the substrate. The synthesis of 1-*C*-fucopyranosides was carried out stereospecifically by the generation of an anomeric carbanion through phenylsulfinyllithium exchange. The required fucosyl phenyl sulfoxides were efficiently prepared from L-fucose by highly stereoselective thioglycosylation reactions. These fucopyranoside analogs are useful compounds for the synthesis of fucosidase and fucosyltransferase inhibitors and for conformational studies around the anomeric center. Our future studies will focus on these areas.

Experimental Section

General Methods: Separation and purification of all synthesized compounds were carried out by flash chromatography (FC) with silica gel (Merck, 230–400 mesh). The eluent used is indicated, and solvent ratios refer to volume. – TLC was performed with the TLC plates GF_{234} Merck (0.2 mm); detection was done with 5% PMA in EtOH or 5% H_2SO_4 in EtOH. Solvents were dried and distilled as follows: THF, PhMe, and Et_2O (Na/benzophenone), MeCN and CH_2Cl_2 (CaH_2), DMF (3Å molecular sieves), pyridine (NaOH). – Melting points were determined in a Kofler hot-stage apparatus and are not corrected. – ^1H NMR and ^{13}C NMR spectra were measured on a Varian XL-300 (300 MHz and 75 MHz, respectively) spectrometer, or on a Bruker AM-200 (200 MHz and 50 MHz, respectively) spectrometer, in $CDCl_3$ or in the solvent indicated. Chemical shifts (δ) refer to TMS, which was used as an internal reference. – Optical rotations were measured at room temp., in quartz cells (d = 1 dm), in a Perkin–Elmer 241 MC polarimeter, with Na 589 light, at the concentration indicated, in $CHCl_3$ or in the solvent indicated. – Elemental analysis were determined in a Perkin–Elmer 240 analyzer. The preparation of compounds **3–8** is described in ref.[6a]

2,5-Di-*O*-benzyl-1,6-*O*-isopropylidene-D-*allo*-inositol 3,4-Cyclic Sulfate (9): To a solution of Et_3N (140 μL, 1.0 mmol) in CH_2Cl_2 (0.9 mL) was added **8** (R = Bn) (100 mg, 0.25 mmol); the mixture was stirred at 0 °C for 10 min. A solution of thionyl chloride (29 μL, 0.400 mmol, 1.6 equiv.) in dry CH_2Cl_2 (65 μL) was then slowly added (20 min), and the mixture was further stirred for 10 min at 0 °C. The reaction was then diluted with cold Et_2O (1 mL), washed with H_2O (1 mL), dried (Na_2SO_4), and concentrated. The residue

was dissolved in CCl_4 (0.5 mL), CH_3CN (0.5 mL) and H_2O (1.0 mL) and cooled to 0 °C. Ruthenium trichloride (13 mg, 0.05 mmol, 0.2 equiv.) and $NaIO_4$ (107 mg, 0.50 mmol, 2.0 equiv.) were added, while stirring continued vigorously at 0 °C for 1 h. After this time period, the mixture was diluted with Et_2O (5 mL), filtered through a pad of celite, and washed with H_2O (2 mL). The organic layer was dried (Na_2SO_4), concentrated and purified by FC (hexane/EtOAc, 100:1) to give **9** (99 mg, 86%): m.p. 107–109 °C. – $[\alpha]_D$ = –62.0 (*c* = 0.50). – ^{1}H NMR (200 MHz): δ = 7.37–7.18 (m, 10 H), 4.95 (dd, *J* = 1.9 Hz, *J* = 6.7 Hz, 1 H), 4.86 (d, *J* = 4.4 Hz, 1 H), 4.85 (d, *J* = 5.6 Hz, 1 H), 4.81 (d, *J* = 6.1 Hz, 1 H), 4.65 (d, *J* = 12.8 Hz, 1 H), 4.61 (d, *J* = 11.7 Hz, 1 H), 4.43 (dd, *J* = 2.9 Hz, *J* = 6.7 Hz, 1 H), 4.39 (t, *J* = 2.4 Hz, 1 H), 4.28 (dd, *J* = 2.0 Hz, *J* = 4.6 Hz, 1 H), 3.94 (dd, *J* = 2.0 Hz, *J* = 10.0 Hz, 1 H), 1.43 (s, 3 H), 1.42 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 137.42, 136.95, 128.59, 128.29, 127.88, 127.75, 112.06, 81.69, 80.77, 75.18, 74.72, 73.30, 72.61, 72.10, 70.65, 26.87, 26.71.

1,4-Di-*O*-benzyl-2,3-*O*-isopropylidene-L-conduritol E (10): A suspension of tellurium powder (50 mg, 0.39 mmol, 4.0 equiv.) and $NaBH_4$ (18 mg, 0.48 mmol, 5.0 equiv.) in dry DMF (1 mL) containing *t*BuOH (10 μL) was heated at 80 °C under argon without stirring; after 10 min, the solution was stirred at this temperature for another 45 min. The purple solution was cooled at room temperature, a solution of **9** (45 mg, 0.10 mmol, 1 equiv.) in pyridine/DMF/benzene (9 μL/0.4 mL/130 μL) was added, and the mixture was stirred at room temp. for 10 min. Then Et_2O (2 mL) was added, and the mixture was filtered through Celite and washed with EtOAc, CH_2Cl_2 and MeOH. The combined filtrates were washed with NaCl (1 mL), and H_2O (4 × 1 mL), dried (Na_2SO_4) and concentrated. The residue was purified by FC (hexane/EtOAc, 30:1) to give **10** (35 mg, 95%): m.p. 60–62 °C. – $[\alpha]_D$ = +90.0 (*c* = 0.70). – ^{1}H NMR (200 MHz): δ = 7.37–7.30 (m, 10 H), 5.91 (m, 2 H), 4.99 (d, *J* = 11.7 Hz, 2 H), 4.65 (d, *J* = 11.7 Hz, 2 H), 4.35 (m, 2 H), 4.21 (m, 2 H), 1.55 (s, 6 H). – ^{13}C NMR (50 MHz): δ = 139.20, 129.55, 128.44, 127.80, 127.66, 110.90, 75.00, 73.58, 72.13, 27.03. – $C_{23}H_{26}O_4$ (366.46): calcd. C 75.38, H 7.15; found C 75.17, H 7.19.

2,3-*O*-Isopropylidene-L-conduritol E (11): Sodium metal (52 mg, 1.184 mmol, 8 equiv.) was added to a solution of liquid ammonia (3 mL) cooled at –70 °C until a deep color persisted for 30 min. Then, a solution of **10** (100 mg, 0.27 mmol, 1 equiv.) in Et_2O (1 mL) was added and the reaction was stirred for 2 h. Then sat. aq. NH_4Cl (1 mL) was added, and the ammonia was allowed to evaporate at room temp. The residue was purified by FC (hexane/EtOAc, 1:1) to give **11** (28 mg, 56%) and recovered **10** (18 mg, 15%).

11: M.p. 142–144 °C. – $[\alpha]_D$ = –251.8 (*c* = 0.90). – ^{1}H NMR (200 MHz): δ = 6.04 (dd, *J* = 1.4 Hz, *J* = 3.2 Hz, 2 H), 4.55 (s, 2 H), 3.98 (dd, *J* = 1.2 Hz, *J* = 1.8 Hz, 2 H), 2.39 (d, *J* = 2.0 Hz, 2 H), 1.50 (s, 6 H). – ^{13}C NMR (50 MHz): δ = 130.46, 107.52, 73.37, 64.83, 26.89. – $C_9H_{14}O_4$ (186.21): calcd. C 58.04, H 7.58; found C 57.95, H 7.45.

1-*O*-Acetyl-2,3-*O*-isopropylidene-L-conduritol E (12): To a solution of **11** (75 mg, 0.40 mmol) in dry CH_2Cl_2 (15 mL) was added vinyl acetate (171 μL, 2.02 mmol, 5 equiv.), 4 Å molecular sieves (1 g), and lipase PS (0.63 g). The mixture was stirred at 30 °C and at 250 rpm in an orbital shaker for 4 h, and then it was filtered through celite. The filtrate was concentrated, and the residue fractionated by FC (hexane/EtOAc, 8:1→ 2:1→1:1) to give **12** (61 mg, 66%): m.p. 110–114 °C. – $[\alpha]_D$ = –313.4, (*c* = 0.60). – ^{1}H NMR (200 MHz): δ = 6.11 (dd, *J* = 5.0 Hz, *J* = 9.6 Hz, 1 H), 6.00 (dd, *J* = 5.2 Hz, *J* = 9.7 Hz, 1 H), 5.64 (dd, *J* = 3.7 Hz, *J* = 5.0 Hz, 1 H), 4.57 (dd, *J* = 3.8 Hz, *J* = 4.9 Hz, 1 H), 4.08 (dd, *J* = 3.6 Hz, *J* = 10.0 Hz, 1 H), 3.95 (dd, *J* = 3.6 Hz, *J* = 10.0 Hz, 1 H), 2.27 (d, *J* = 2.0 Hz, 1 H), 2.09 (s, 3 H), 1.48 (s, 3 H), 1.45 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 177.06, 132.14, 127.67, 110.67, 73.81, 71.51, 66.07, 64.51, 35.31, 26.74. – $C_{11}H_{16}O_5$ (228.24): calcd. C 57.87, H 7.07; found C 58.14, H 7.42.

(2*R*,3*R*,4*R*,5*R*)-2,5-Di-benzyloxy-3,4-(isopropylidendioxy)cyclohexan-1-one (16): Compound **9** (450 mg, 1 mmol) was dissolved in THF (22 mL) and this solution was treated with *t*BuOK (353 mg, 3.15 mmol, 2.8 equiv.) at room temp. for 90 min. Then the mixture was treated with THF/H_2SO_4/H_2O (300:3:1, 3.5 mL) at room temp. for 30 min. The reaction was diluted with CH_2Cl_2 (30 mL), washed with sat. $NaHCO_3$ solution (20 mL), dried (Na_2SO_4) and concentrated to give a residue which was purified by FC (hexane/EtOAc 20: 1), giving **16** (320 mg, 86%): m.p. 91–94 °C. – $[\alpha]_D$ = –4.0 (*c* = 1.0). – ^{1}H NMR (300 MHz): δ = 7.30–7.17 (m, 10 H), 4.73 (d, *J* = 12.0 Hz, 1 H), 4.63 (d, *J* = 11.7 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 4.51 (d, *J* = 11.7 Hz, 1 H), 4.49 (d, *J* = 2.4 Hz, 1 H), 4.22 (dd, *J* = 2.6 Hz, *J* = 10.0 Hz, 1 H), 4.19 (m, 1 H), 4.15 (dd, *J* = 2.8 Hz, *J* = 10.0 Hz, 1 H), 2.77 (dd, *J* = 3.9 Hz, *J* = 15.2 Hz, 1 H), 2.46 (ddd, *J* = 1.1 Hz, *J* = 2.6 Hz, *J* = 15.2 Hz, 1 H), 1.45 (d, *J* = 11.7 Hz, 6 H). – ^{13}C NMR (50 MHz): δ = 204.61, 138.14, 137.85, 128.39, 128.31, 127.37, 127.61, 127.56, 127.35, 111.78, 82.14, 75.29, 75.06, 72.82, 72.62, 70.75, 41.91, 26.83, 26.76. – $C_{23}H_{26}O_5$ (382.46): calcd. C 72.23, H 6.85; found C 72.89, H 6.81.

(1*R*,2*R*,3*R*,4*R*)-1,4-Di-benzyloxy-2,3-isopropylidenedioxy-5-methylenecyclohexane (17): To a suspension of PPh_3MeBr (1.46 g, 4.1 mmol) in dry THF (5.0 mL) under argon at –78 °C was added KHMDS (0.5 M, 6.8 mL, 3.4 mmol). The temperature was raised to 0 °C and the mixture was stirred for 1 h. Then the reaction was cooled at –40 °C, a solution of **16** (434 mg, 1.14 mmol) in dry THF (5.0 mL) was added dropwise, and stirring was continued for 30 h at 5 °C. The mixture was then quenched with NH_4Cl (10 mL) and was extracted with CH_2Cl_2 (20 mL). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by FC (hexane/EtOAc, 30:1) to give **17** (373 mg, 85%): m.p. 30–31 °C. – $[\alpha]_D$ = +14.1 (*c* = 0.62). – ^{1}H-NMR (300 MHz, [D$_6$]acetone): δ = 7.37–7.24 (m, 10 H), 5.14 (m, 1 H), 5.08 (m, 1 H), 4.61 (d, *J* = 12.1 Hz, 1 H), 4.58 (d, *J* = 12.2 Hz, 1 H), 4.52 (d, *J* = 12.2 Hz, 1 H), 4.38 (d, *J* = 2.7 Hz, 1 H), 4.29 (dd, *J* = 2.4 Hz, *J* = 10.0 Hz, 1 H), 4.15 (q, *J* = 2.8 Hz, 1 H), 4.08 (dd, *J* = 2.7 Hz, *J* = 9.9 Hz, 1 H), 2.47 (m, 2 H), 1.39 (s, 3 H), 1.38 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 141.18, 139.00, 138.65, 128.19, 127.59, 127.21, 127.15, 118.40, 109.83, 79.67, 75.92, 75.72, 72.68, 72.10, 70.31, 34.72 26.85, 26.79. – $C_{24}H_{28}O_4$ (380.48): calcd. C 75.76, H 7.42; found C 74.51, H 7.32.

(1*R*,2*R*,3*R*,4*R*)-1,4-Di-benzyloxy-5-methylenecyclohexane-2,3-diol (18): To a solution of **17** (64 mg, 0.17 mmol) in MeOH (2 mL) was added dropwise CF_3COOH (6.5 μL, 0.85 mmol, 5 equiv.); the mixture was stirred at room temp. for 30 min. The solvents were then removed to give a residue which was purified by FC (hexane/EtOAc 2:1), affording **18** (59 mg, 98%): m.p. 49–50 °C. – $[\alpha]_D$ = –2.6 (*c* = 1.00). – ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 7.40–7.22 (m, 10 H), 5.08 (s, 1 H), 5.02 (s, 1 H), 4.61 (d, *J* = 6.1 Hz, 2 H), 4.57 (d, *J* = 12.1 Hz, 1 H), 4.45 (d, *J* = 12.1 Hz, 1 H), 4.13 (d, *J* = 3.2 Hz, 1 H), 4.01 (ddd, *J* = 2.8 Hz, *J* = 4.7 Hz, *J* = 8.2 Hz, 1 H), 3.92 (td, *J* = 3.2 Hz, *J* = 6.8 Hz, 1 H), 3.82 (q, *J* = 3.2 Hz, 1 H), 3.59 (d, *J* = 5.1 Hz, 1 H), 3.48 (d, *J* = 5.1 Hz, 1 H), 2.50 (dd, *J* = 6.0 Hz, *J* = 13.6 Hz, 1 H), 2.44 (dd, *J* = 3.7 Hz, *J* = 13.6 Hz, 1 H). – ^{13}C NMR (75 MHz): δ = 140.59, 138.19, 138.0, 128.41, 128.39, 127.71, 127.61, 127.61, 116.37, 80.98, 76.52, 72.56, 72.18,

71.09, 70.12, 32.37. – $C_{21}H_{24}O_4$ (340.42): calcd. C 74.09, H 7.11; found C 74.62, H 7.38.

Catalytic Hydrogenation of 17 and 18 with Pd/C. – Method a: A solution of **17** or **18** (0.08 mmol) in EtOAc (1.5 mL), was hydrogenated in the presence of 10% Pd/C (3 mg, 0.002 mmol, 0.05 equiv.) at room temperature for 10 min. The mixture was filtered and concentrated to give a mixture of **1** and **21**, whose ratio (see Table 1) was determined by ^{1}H NMR (200 MHz, D_2O): **1**, see below; **21**,[8a][8e] 3.92–3.88 (m, 3 H), 3.41 (dd, J = 1.5 Hz, J = 10.6 Hz, 1 H), 1.92–1.62 (m, 1 H), 1.52–1.43 (m, 1 H) 1.33 (q, J = 12.4 Hz, 1 H),0.89 (d, J = 6.95 Hz, 3 H). – **Method b:** To a solution of **18** (0.08 mmol) in MeOH (1.0 mL) was added pyridine (3 μL, 0.04 mmol, 0.5 equiv.); this mixture was hydrogenated in the presence of 10% Pd/C (8 mg, 0.008 mmol, 0.1 equiv.) at room temperature for 48 h. The mixture was filtered and concentrated to give a residue which was purified by FC (hexane/EtOAc 7:1) to give **19** (11 mg, 41%) and **20** (14 mg, 51%).

With Rhodium from 17: A solution of **17** (30 mg, 0.08 mmol) in MeOH (1.0 mL) was hydrogenated in the presence of $Rh(PPh_3)Cl$ (10 mg, 0.01 mmol, 0.1 equiv.) at room temperature for 24 h. CF_3COOH (3 μL, 0.03 mmol, 0.5 equiv.) was then added. The mixture was concentrated to give a residue which was purified by FC (hexane/EtOAc, 7:1), to give **19** (7 mg, 25%) and **20** (18 mg, 66%). – **From 18:** A solution of **18** (27 mg, 0.08 mmol) in MeOH (1.0 mL) was hydrogenated in the presence of $Rh(PPh_3)Cl$ (10 mg, 0.01 mmol, 0.1 equiv.) at room temperature for 24 h and then at 60 °C for 8 h. The mixture was concentrated and the residue was purified by FC (hexane/EtOAc, 7:1) to give **19** (14 mg, 51%) and **20** (13 mg, 48%).

With Raney Nickel from 17: A solution of **17** (30 mg, 0.08 mmol) in MeOH (1.0 mL) was hydrogenated in the presence of Raney nickel (100 mg) at room temperature for 30 min. CF_3COOH (3 μL, 0.03 mmol, 0.5 equiv.) was then added, and the solution was separated by decantation and concentrated to give a residue which was purified (see above), to give **20** (24 mg, 87%). – **From 18:** A solution of **18** (27 mg, 0.08 mmol) in MeOH (1 mL) was hydrogenated in the presence of Raney nickel (100 mg) at room temperature for 16 h. The reaction mixture was concentrated and the residue was purified by FC (hexane/EtOAc, 7:1) to give **19** (4 mg, 14%) and **20** (13 mg, 48%).

1,4-Di-*O*-benzyl-5a-carba-α-L-fucopyranose (19): – $[\alpha]_D$ = –4.4 (c = 1.0). – ^{1}H NMR (300 MHz): δ = 7.39–7.30 (m, 10 H), 4.86 (d, J = 11.6 Hz, 1 H), 4.68 (d, J = 5.8 Hz, 1 H), 4.64 (d, J = 5.8 Hz, 1 H), 4.45 (d, J = 11.6 Hz, 1 H), 3.86 (q, J = 2.7 Hz, 1 H), 3.79 (m, 2 H), 3.73 (m, 1 H), 2.32–2.26 (br s, 2 H), 2.09–1.95 (m, 1 H), 1.75 (dtd, J = 0.8 Hz, J = 2.8 Hz, J = 14.4 Hz, 1 H), 1.62 (dt, J = 2.0 Hz, J = 14.4 Hz, 1 H), 1.03 (d, J = 6.8 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 139.21, 138.36, 128.31, 127.90. 127.71, 127.53, 127.50, 81.82, 77.21, 75.34, 74.38, 72.50, 71.25, 30.31, 29.99, 17.67. – $C_{21}H_{26}O_4$ (342.43): calcd. C 73.66, H 7.65; found C 73.17, H 7.91.

1,4-Di-*O*-benzyl-6-deoxy-5a-carba-α-D-altropyranose (20): m.p. 81–83 °C. – $[\alpha]_D$ = +29.5 (c = 0.52). – ^{1}H NMR (300 MHz): δ = 7.39–7.29 (m, 10 H), 4.64 (d, J = 11.2 Hz, 1 H), 4.58 (d, J = 2.3 Hz, 2 H), 4.51 (d, J = 11.2 Hz, 1 H), 4.25 (m, 2 H), 3.83 (ddd, J = 2.4 Hz, J = 4.7 Hz, J = 11.4 Hz, 1 H), 3.39 (dd, J = 2.3 Hz, J = 10.2 Hz, 1 H), 2.34–2.24 (m, 2 H), 1.98–1.84 (m, 1 H), 1.79 (dt, J = 4.1 Hz, J = 12.9 Hz, 1 H), 1.51 (c, J = 12.1 Hz, 1 H), 1.04 (d, J = 6.6 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 138.31, 138.13, 128.48, 127.90, 127.77, 127.60, 81.73, 75.11, 70.09, 68.68, 71.94, 70.77, 31.94, 29.76, 18.44. – $C_{21}H_{26}O_4$ (342.43): calcd. C 73.66, H 7.65; found C 73.51, H 7.59.

1,4-Di-*O*-benzyl-2,3-isopropylidene-5a-carba-β-D-altropyranose (23): To a solution of BH_3·THF (1 M, 287 μL, 0.287 mmol, 3 equiv.) in dry THF (362 μL), cooled at 0 °C, was added, dropwise, a solution of **17** (37 mg, 0.096 mmol) in dry THF (362 μL). The mixture was stirred at room temp. for 2 h and then 3 N NaOH (108 μL, 0.324 mmol, 3.4 equiv.) and 30% H_2O_2 (108 μL, 0.105 mmol, 1.1 equiv.) were added dropwise; stirring was continued for 30 min. The mixture was then diluted with CH_2Cl_2 (1 mL), washed with sat. aq. NaCl (1 mL), dried (Na_2SO_4), and concentrated. FC (hexane / EtOAc, 5:1) gave **23** (21 mg, 57%): m.p. 81–83 °C. – $[\alpha]_D$ = +5.4 (c = 1.3). – ^{1}H NMR (300 MHz, [D$_6$]benzene): δ = 7.38–7.08 (m, 10 H), 4.90 (d, J = 11.9 Hz, 1 H), 4.85 (d, J = 11.9 Hz, 1 H), 4.55 (d, J = 11.9 Hz, 1 H), 4.46 (d, J = 11.9 Hz, 1 H), 4.42 (dd, J = 2.3 Hz, J = 10.3 Hz, 1 H), 4.18 (m, 1 H), 4.14 (dd, J = 2.3 Hz, J = 8.9 Hz, 1 H), 3.88 (q, J = 2.5 Hz, 1 H), 3.52–3.36 (m, 2 H), 2.03 (m, 1 H), 1.73 (dd, J = 4.7 Hz, J = 11.7 Hz, 1 H), 1.66 (ddd, J = 3.2 Hz, J = 6.9 Hz, J = 15.1 Hz, 1 H), 1.47 (s, 3 H), 1.45 (s, 3 H). – ^{1}H NMR (300 MHz): δ = 7.29–7.20 (m, 10 H), 4.89 (d, J = 11.8 Hz, 1 H), 4.83 (d, J = 11.9 Hz, 1 H), 4.55 (d, J = 11.6 Hz, 1 H), 4.46 (d, J = 11.9 Hz, 1 H), 4.24 (dd, J = 2.4 Hz, J = 10.1 Hz, 1 H), 4.14–4.05 (m, 3 H), 3.61–3.52 (m, 2 H), 2.65 (dd, J = 5.0 Hz, J = 7.1 Hz, 1 H), 2.16–2.13 (m, 1 H), 1.94 (ddd, J = 3.0 Hz, J = 7.1 Hz, J = 15.1 Hz, 1 H), 1.71 (d br, J = 13.9 Hz, 1 H), 1.49 (s, 6 H). – ^{13}C NMR (50 MHz): δ = 139.06, 138.27, 129.80, 128.26, 127.62, 127.36, 108.99, 76.57, 76.18, 74.86, 74.12, 73.31, 73.07, 65.79, 42.58, 29.50, 26.86. – $C_{21}H_{26}O_5$ (358.43): calcd. C 70.37, H 7.31; found C 70.17, H 7.02.

1,4-Di-*O*-benzyl-5a-carba-α-L-galactopyranose (24): This compound was prepared from **18** (50 mg, 0.15 mmol) under the same conditions as described for **23**. The residue was purified by FC (hexane/EtOAc, 2:1) to give **24** (37 mg, 71%). – $[\alpha]_D$ = –24.7 (c = 0.60). – ^{1}H NMR (300 MHz): δ = 7.29–7.18 (m, 10 H), 4.88 (d, J = 11.6 Hz, 1 H), 4.62 (d, J = 11.5 Hz, 1 H), 4.57 (d, J = 11.6 Hz, 1 H), 4.38 (d, J = 11.6 Hz, 1 H), 4.00 (m, 1 H), 3.86 (q, J = 2.7 Hz, 1 H), 3.77–3.74 (m, 2 H), 3.51 (d, J = 5.6 Hz, 2 H), 2.40–2.34 (br s, 1 H), 2.30–2.22 (br s, 2 H), 1.98–1.88 (m, 1 H), 1.74 (m, J = 1.0 Hz, J = 3.8 Hz, J = 14.6 Hz, 1 H), 1.57 (dt, J = 2.2 Hz, J = 15.1 Hz, 1 H). – ^{13}C NMR (50 MHz): δ = 138.13, 129.79, 128.48, 127.99, 127.82, 127.78, 127.58, 76.80, 76.36, 74.27, 72.52, 76.80, 71.33, 64.19, 37.14, 25.02. – $C_{21}H_{26}O_5$ (358.43): calcd. C 70.37, H, 7.31; found C 70.61, H, 7.22.

(1*R*,2*R*,3*R*,4*R*)-1,4-Di-benzyloxy-2,3-(*tert*-butyldimethyl)silyloxy-5-methylenecyclohexane (26): To a solution of **18** (150 mg, 0.44 mmol) in CH_2Cl_2 (1.5 mL) and iPr$_2$EtN (226 μL, 0.017 mmol, 0.05 equiv.) was added, dropwise, *tert*-butyldimethylsilyl triflate (258 μL, 1.0 mmol, 2.4 equiv.); the mixture was stirred at room temp. for 5 min. The mixture was then diluted with CH_2Cl_2 (2 mL) and washed with H_2O (3 mL). The organic layer was dried (Na_2SO_4) and concentrated, giving a residue which was purified by FC (hexane/EtOAc 100:1) to give **26** (225 mg, 89%). – $[\alpha]_D$ = –3.8 (c = 0.95). – ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 7.40–7.24 (m, 10 H), 4.92 (m, 1 H), 4.67 (d, J = 12.4 Hz, 1 H), 4.55 (m, 2 H), 4.54 (d, J = 12.7 Hz, 1 H), 4.18 (d, J = 1.8 Hz, 1 H), 4.09–4.00 (m, 2 H), 3.68 (ddd, J = 2.3 Hz, J = 5.0 Hz, J = 6.8 Hz, 1 H), 2.50 (ddd, J = 0.9 Hz, J = 4.5 Hz, J = 12.0 Hz, 1 H), 2.40 (t, J = 12.3 Hz, 1 H) 0.84 (s, 9 H), 0.81 (s, 9 H), 0.07–0.04 (m, 12 H). – ^{13}C NMR (50 MHz): δ = 141.71, 139.00, 138.96, 128.20, 127.49, 127.38, 127.29, 108.05, 77.90, 76.43, 74.05, 72.97, 71.70, 70.70, 34.01, 25.78, 25.76, 18.10, 18.06, –4.40, –4.51, –5.04, –5.12. – $C_{33}H_{52}O_4Si_2$ (568.94): calcd. C 69.67, H 9.22; found C 69.67, H 8.98.

2,3-(*tert*-Butyldimethyl)silyloxy-5a-carba-α-L-fucopyranose (28): A mixture of **26** (200 mg, 0.350 mmol), EtOAc (8 mL), and 10% Pd/C (26 mg, 0.017 mmol, 0.05 equiv.), was hydrogenated at room temp. for 4 h. The reaction mixture was then diluted with EtOAc (20 mL), filtered, and concentrated to give a residue which was purified by FC (hexane/EtOAc, 100:1) to give, first, **27** (8 mg, 7%): – ^{1}H NMR (300 MHz): δ = 3.88–3.83 (m, 3 H), 3.32 (t, *J* = 9.7 Hz, 1 H), 1.69–1.61 (m, 2 H), 1.29–1.24 (m, 1 H), 1.01 (d, *J* = 6.2 Hz, 3 H), 0.92 (s, 9 H), 0.91 (s, 9 H), 0.05 (s, 6 H), 0.04 (s, 6 H). Further elution gave **28** (125 mg, 89%): m.p. 92–95 °C. – $[\alpha]_D$ = –36.72 (*c* = 0.50). – ^{1}H NMR (300 MHz): δ = 3.86–3.85 (m, 1 H), 3.76–3.72 (m, 2 H), 3.69–3.67 (m, 1 H), 2.46 (br s, 1 H), 2.30 (br s, 1 H), 2.04–1.99 (m, 1 H), 1.64–1.63 (m, 1 H), 1.60–1.59 (m, 1 H), 1.03 (d, *J* = 6.9 Hz, 3 H), 0.90 (s, 18 H), 0.09–0.03 (m, 12 H). – ^{13}C NMR (50 MHz): δ = 75.09, 73.98, 73.32, 70.53, 31.50, 28.34, 26.08, 18.00, 18.06, 17.21, –4.59, –4.64. – $C_{19}H_{42}O_4Si_2$ (390.71): calcd. C 58.41, H 10.85; found C 58.23, H 10.31.

5a-Carba-α-L-fucopyranose (1): To a solution of **28** (85 mg, 0.22 mmol) in THF (7 mL) was added Bu_4NF (224 mg, 0.87 mol, 4 equiv.); the reaction mixture was stirred at room temp. for 2 h. The solvent was then evaporated and the residue was purified by FC (CH_2Cl_2/MeOH 10:1) to give a mixture which was purified by filtration through florisil and eluted with CH_2Cl_2/MeOH (5:1) to give **1** (19 mg, 51%): m.p. 112–115 °C (ref.[8a,8e] 115 °C). – $[\alpha]_D$ = –49.9 (*c* = 0.40, EtOH) (ref.[8a,8e] $[\alpha]_D$ = –58). – ^{1}H NMR (300 MHz, D_2O): 4.07 (q, *J* = 3.0 Hz, 1 H), 3.88 (t, *J* = 2.6 Hz, 1 H), 3.76 (dd, *J* = 3.0 Hz, *J* = 10.3 Hz, 1 H), 3.69 (dd, *J* = 3.0 Hz, *J* = 10.3 Hz, 1 H, H-3), 2.03–1.94 (m, 1 H), 1.61 (m, 2 H), 0.99 (d, *J* = 6.95 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 75.47, 72.65, 72.11, 70.81, 33.67, 29.83, 17.75.

Phenyl 3,4-*O*-Isopropylidene-1-thio-β-L-fucopyranoside (29). – Method a: A suspension of L-fucose (5.00 g, 30.5 mmol) in pyridine (15 mL) was treated with Ac_2O (60 mL, 64.9 g, 636 mmol, 21 equiv.) and was heated to 100 °C for 1 h. The mixture was cooled to room temp. and was concentrated (coevaporating with PhMe, 2 × 50 mL) to give a residue which was dissolved in CH_2Cl_2 (100 mL) and cooled to –20 °C. PhSH (3.68 mL, 3.97 g, 36.0 mmol, 1.2 equiv.) and $SnCl_4$ (3.65 mL, 8.12 g, 31.2 mmol, 1.0 equiv.) were added dropwise, and the temperature was raised to 0 °C within 1 h. After 2 h, the temperature was raised to room temp., and the mixture was diluted with CH_2Cl_2 (100 mL) and washed with 1 N H_2SO_4 (75 mL), sat. $NaHCO_3$ (75 mL), and H_2O (75 mL). Evaporation of the solvent gave a residue which was dissolved in MeOH (100 mL) and treated with NaOMe (0.7 M in MeOH, 10 mL) at room temp. for 20 h. The reaction was then neutralized with Amberlyst IR-120 (H^+), filtered and concentrated to give crude phenyl 1-thio-α- and -β-L-fucopyranoside. This mixture was dissolved in Me_2CO (100 mL) and treated with 2,2-dimethoxypropane (15.0 mL, 12.7 g, 122 mmol, 4.0 equiv.) and *p*TsOH·H_2O (580 mg, 3.05 mmol, 0.10 equiv.). After 12 h, the reaction was neutralized with Et_3N (1.00 mL) and concentrated to give a residue which was purified by FC (hexane/EtOAc, 5:1 → 3:1), giving **29** (6.30 g, 69%) and **30** (331 mg, 4%). – **29:** M.p. 82–83 °C. – $[\alpha]_D$ = +35.1 (*c* = 1.0, MeOH). – ^{1}H NMR (200 MHz): δ = 7.55–7.51 (m, 2 H), 7.30–7.26 (m, 3 H), 4.40 (d, *J* = 10.3 Hz, 1 H), 4.07–3.99 (m, 2 H), 3.85 (dt, *J* < 1 Hz, *J* = 6.4 Hz, 1 H), 3.52 (ddd, *J* = 2.3 Hz, *J* = 6.5 Hz, *J* = 10.3 Hz, 1 H), 2.58 (d, *J* = 2.3 Hz, 1 H), 1.41 (d, *J* = 6.4 Hz, 3 H), 1.40 (s, 3 H), 1.32 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 132.58, 132.12, 128.90, 127.94, 109.81, 87.76, 79.04, 76.25, 72.71, 71.22, 28.08, 26.30, 16.90. – $C_{15}H_{20}O_4S$ (396.38): calcd. C 60.79, H 6.80, S 10.82; found C 60.59, H 6.97, S 10.73. – **Method b:** To a suspension of L-fucose (1.00 g, 6.09 mmol) in MeCN (15 mL) was added diphenyldisulfide (1.73 g, 7.92 mmol, 1.3 equiv.) and Bu_3P (3.00 mL, 2.44 g, 12.0 mmol, 2.0 equiv.) at 0 °C. The temperature was raised to room temp., and the reaction was allowed to proceed for 24 h. Then the solvent was evaporated to give a residue which was cromatographed (hexane/EtOAc, 2:1 → 1:1 → EtOAc), giving crude phenyl 1-thio-α- and -β-L-fucopyranoside, which were dissolved in Me_2CO (30 mL) and treated with 2,2-dimethoxypropane (2.90 mL, 2.46 g, 23.6 mmol, 3.9 equiv.) and *p*TsOH·H_2O (250 mg, 1.31 mmol, 0.22 equiv.). After 24 h, the reaction was neutralized with Et_3N (1.0 mL) and was concentrated to give a residue which was purified by FC (hexane/EtOAc, 5:1 → 3:1), giving **29** (1.06 g, 59%) (whose physical properties were identical to the material described above) and **30** (105 mg, 6%).

Phenyl 3,4-*O*-Isopropylidene-1-thio-α-L-fucopyranoside (30): To a solution of L-fucose (4.00 g, 24.4 mmol) in DMF (12.0 mL) containing Et_3N (20 mL, 14.5 g, 14 mmol, 5.9 equiv.), cooled to 0 °C, was added, dropwise, TMSCl (18.0 mL, 15.4 g, 142 mmol, 5.8 equiv.). The mixture was warmed to room temp. and stirred for 2 h. Then the reaction was quenched with H_2O/ice (160 mL) and extracted with pentane (400 mL). The organic phase was washed with H_2O/ice (3 × 120 mL), dried (Na_2SO_4), and concentrated to give a residue which was dissolved in CH_2Cl_2 (60 mL) and treated with TMSI (3.52 mL, 5.17 g, 25.9 mmol, 1.1 equiv.) at room temp. for 1 h. The reaction was then cooled to 5 °C, and a solution of PhSH (2.64 mL, 2.85 g, 25.8 mmol, 1.1 equiv.) and 2,6-di-*tert*-butyl-4-methylpyridine (5.00 g, 24.3 mmol, 1.0 equiv.) in CH_2Cl_2 (60 mL) was added. After 21 h, MeOH (120 mL) was added, and stirring was continued for 30 min. Evaporation of the solvent gave crude phenyl 1-thio-α- and -β-L-fucopyranoside, which was dissolved in Me_2CO (120 mL) and treated with 2,2-dimethoxypropane (6.00 mL, 5.08 g, 48.8 mmol, 2.0 equiv.) and *p*TsOH·H_2O (240 mg, 1.26 mmol, 0.052 equiv.). After 90 min, the reaction was neutralized with Et_3N (4.00 mL) and concentrated to give a residue which was purified by FC (hexane/EtOAc, 6:1 → 3:1 → 1:1), giving **29** (340 mg, 4%) (see above physical and spectroscopic data) and **30** (5.55 g, 77%): m.p. 72–74 °C. – $[\alpha]_D$ = –278.0 (*c* = 1.1, MeOH). – ^{1}H NMR (200 MHz): δ = 7.52–7.47 (m, 2 H), 7.30–7.27 (m, 3 H), 5.55 (d, *J* = 4.7 Hz, 1 H), 4.57 (dt, *J* = 2.0 Hz, *J* = 6.7 Hz, 1 H), 4.20–4.04 (m, 3 H), 2.65 (d, *J* = 5.8 Hz, 1 H), 1.53 (s, 3 H), 1.37 (s, 3 H), 1.35 (d, *J* = 6.7 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 134.16, 131.31, 129.02, 127.26, 109.42, 88.24, 76.27, 75.73, 69.98, 65.35, 27.90, 25.92, 16.22. – $C_{15}H_{20}O_4S$ (296.38): calcd. C 60.79, H 6.80, S 10.82; found C 60.59, H 7.01, S 10.87.

Phenyl 1,1-Dioxo-3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside (31): To a solution of **29** (805 mg, 2.72 mmol) in CH_2Cl_2 (25 mL) was added $NaHCO_3$ (550 mg, 6.55 mmol, 2.4 equiv.) and 86% *m*CPBA (1.30 g, 6.46 mmol, 2.4 equiv.) at room temp. After 2 h, CH_2Cl_2 (25 mL) was added and the solution was washed with sat. $NaHCO_3$ (3 × 25 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a residue which was purified by FC (hexane/EtOAc, 4:1 → 3:1 → 1:1), affording **31** (800 mg, 90%): m.p. 141–143 °C. – $[\alpha]_D$ = –33.0 (*c* = 1.1). – ^{1}H NMR (200 MHz): δ = 7.97–7.93 (m, 2 H), 7.72–7.55 (m, 3 H), 4.16 (d, *J* = 9.9 Hz, 1 H), 4.11 (dd, *J* = 5.5 Hz, *J* = 6.3 Hz, 1 H), 3.99 (dd, *J* = 5.5 Hz, *J* = 2.0 Hz, 1 H), 3.87 (ddd, *J* = 1.7 Hz, *J* = 6.3 Hz, *J* = 9.9 Hz, 1 H), 3.84 (dt, *J* = 2.0 Hz, *J* = 6.4 Hz, 1 H), 2.58 (d, *J* = 1.7 Hz, 1 H), 1.33 (s, 3 H), 1.32 (d, *J* = 6.4 Hz, 3 H), 1.31 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 135.30, 134.25, 129.76, 128.86, 110.06, 91.20, 78.79, 75.41, 73.24, 68.64, 27.77, 26.23, and 16.46. – $C_{15}H_{20}O_6S$ (328.38): calcd. C 54.86, H 6.14; found C 54.84, H 5.98.

Reaction of 31 with Lithium Naphthalenide: To a solution of **31** (50 mg, 0.15 mmol) in THF (1 mL), cooled to –78 °C, was added

BuLi (1.38 M in THF, 0.11 mL, 0.152 mmol, 1.0 equiv.). After 30 min, isobutyraldehyde (43 μL, 34.0 mg, 0.47 mmol, 3.1 equiv.) and lithium naphthalenide (1 M in THF, 0.80 mL, 0.8 mmol, 5.3 equiv.) were added, and stirring was continued for an additional 30 min. Then the reaction was quenched with 20% AcOH in THF (1.00 mL), warmed to room temp., diluted with CH_2Cl_2 (20 mL), and washed with H_2O (10 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a residue which was purified by FC. Elution with hexane/EtOAc (8:1) afforded **32** (10.2 mg, 36%), which was characterized as its diacetate **34**: m.p. 131–134 °C. – $[\alpha]_D$ = –111.1, (*c* = 1.0). – ^{1}H NMR (400 MHz, [D$_6$]benzene): δ = 5.37 (dd, *J* = 3.0 Hz, *J* = 3.2 Hz, 1 H), 4.32 (d, *J* = 2.4 Hz, 1 H), 4.18 (dd, *J* = 3.9 Hz, *J* = 7.2 Hz, 1 H), 4.09 (dt, *J* = 1.8 Hz, *J* = 6.6 Hz, 1 H), 3.74 (dd, *J* = 1.8 Hz, *J* = 7.2 Hz, 1 H), 1.76 (s, 3 H), 1.49 (s, 3 H), 1.28 (d, *J* = 6.5 Hz, 3 H), 1.17 (s, 3 H). – ^{13}C NMR (50 MHz): δ = 169.85, 109.52, 75.86, 73.35, 70.69, 70.33, 66.94, 27.05, 24.91, 18.06. – MS (FAB, *m*-NBA); *m*/*z*: 459.3 [M + 1]$^+$. – $C_{22}H_{34}O_{10}$ (458.50): calcd. C 57.63, H 7.47; found C 57.21, H 7.48. Further elution with hexane/EtOAc (2:1) gave **33** (8.3 mg, 29%): m.p. 82–86 °C. – $[\alpha]_D$ = –68.8 (*c* = 1.0). – ^{1}H NMR (200 MHz): δ = 4.05 (dd, *J* = 5.4 Hz, *J* = 2.2 Hz, 1 H), 3.96 (dd, *J* = 5.4 Hz, *J* = 6.3 Hz, 1 H), 3.94 (dd, *J* = 5.3 Hz, *J* = 11.0 Hz, 1 H), 3.84 (dddd, *J* = 3.6 Hz, *J* = 5.3 Hz, *J* = 6.3 Hz, *J* = 9.9 Hz, 1 H), 3.78 (dt, *J* = 2.2 Hz, *J* = 6.5 Hz, 1 H), 3.12 (dd, *J* = 9.9 Hz, *J* = 11.0 Hz, 1 H), 2.14 (d, *J* = 3.6 Hz, 1 H), 1.54 (s, 3 H), 1.38 (s, 3 H), 1.37 (d, *J* = 6.5 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 119.46, 79.64, 76.24, 72.35, 69.36, 68.15, 28.20, 26.24, 16.84. – $C_9H_{16}O_4$ (188.22): calcd. C 57.43, H 8.57; found C 57.14, H 8.41.

Phenyl 1-Oxo-3,4-*O*-isopropylidene-1-thio-α-L-fucopyranoside (35): A solution of **30** (1.55 g, 3.88 mmol) in CH_2Cl_2 (70 mL) containing $NaHCO_3$ (390 mg, 4.64 mmol, 1.2 equiv.) was cooled to –78 °C and treated with a solution of 85% *m*CPBA (780 mg, 3.84 mmol, 0.99 equiv.) in CH_2Cl_2 (20 mL). After 60 min, the reaction was warmed to room temp., diluted with CH_2Cl_2 (75 mL), and washed with $Na_2S_3O_3$ (50 mL) and $NaHCO_3$ (50 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a residue which was purified by FC (hexane/EtOAc, 3:1→2:1→1:2), affording **35** (1.16 g, 96%): m.p. 122–125 °C. – $[\alpha]_D$ = –86.3 (*c* = 1.0). – ^{1}H NMR (200 MHz): δ = 7.73–7.69 (m, 2 H), 7.59–7.54 (m, 3 H), 5.75 (br. s, 1 H), 4.64 (dt, *J* = 1.4 Hz, *J* = 6.5 Hz, 1 H), 4.55 (d, *J* = 3.0 Hz, 1 H), 4.49 (t, *J* = 3.0 Hz, 1 H), 4.45 (dd, *J* = 3.0 Hz, *J* = 7.5 Hz, 1 H), 4.21 (dd, *J* = 1.4 Hz, *J* = 7.5 Hz, 1 H), 1.36 (s, 3 H), 1.31 (s, 3 H), 1.30 (d, *J* = 6.5 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 140.11, 131.36, 129.05, 125.29, 109.61, 93.15, 74.54, 73.87, 68.87, 64.27, 26.15, 24.22, 16.49. – $C_{15}H_{20}O_5S$ (312.38): calcd. C 57.67, H 6.45; found C 57.37, H 6.39.

Deuteration Experiments (Table 2): Under argon, a solution of **35** (0.033 M) in dry solvent at –78 °C was treated with MeLi·LiBr (1.5 M in Et_2O, 1.1 equiv.), followed by slow addition of *t*BuLi (1.64 M in hexanes, 5 equiv.). After 20 min, CD_3OD (5 equiv.) was added, the mixture was stirred for 5 min at –78 °C, and it was then quenched with saturated aqueous solution of NH_4Cl. After separating the water and CH_2Cl_2 layers, the organic layer was dried (Na_2SO_4) and concentrated. The crude mixture was analyzed by ^{1}H NMR (200 MHz). – ^{1}H NMR (200 MHz, selected data): δ = 4.20 (dd, $J_{4,5}$ = 1.5 Hz, $J_{3,4}$ = 7.5 Hz, H-4 of **36**), 4.05 (dd, $J_{4,5}$ = 2.2 Hz, $J_{3,4}$ = 7.5 Hz, H-4 **36** and **33**), 3.12 (dd, $J_{1ax,2}$ = 9.9 Hz, $J_{1ax,1eq}$ = 11.0 Hz, H-1ax of **33**).

4,8-Anhydro-3,5:6,7-di-*O*-isopropylidene-2-*C*-methyl-1,2,9-trideoxy-L-*threo*-D-*ido* and L-*threo*-D-*gulo*-nonitol (39 and 40): To a suspension of **35** (47 mg, 0.15 mmol) in Et_2O (4.5 mL), cooled to –78 °C, was added, dropwise, MeLi·LiBr (1.5 M in Et_2O, 105 μL, 0.16 mmol, 1.1 equiv.). After 5 min, *t*BuLi (1.64 M in pentane, 740 μL, 1.21 mmol, 8.1 equiv.) was added dropwise, and after another 20 min, isobutyraldehyde (70 μL, 55.3 mg, 0.767 mmol, 5.1 equiv.) was added. After 100 additional min, the reaction was quenched at –78 °C with sat NH_4Cl (0.50 mL), was warmed to room temp., diluted with H_2O (5 mL), and washed with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give a residue which was purified by FC. Elution with hexane/EtOAc 10:1 gave first **37** (12.2 mg, 31%), then **38** (11.1 mg, 28%) and **33** (4 mg, 22%). To a solution of **37** (12 mg) in acetone (1.2 mL) was added dimethoxypropane (30 μL) and *p*TsOH·H_2O (1 mg). After 24 h, the reaction mixture was neutralized with Et_3N and concentrated. The residue was purified by FC (hexane/EtOAc, 20:1) to give **39** as an oil. – $[\alpha]_D$ = –19.7 (*c* = 1.1). – ^{1}H NMR (200 MHz): δ = 4.30 (dt, *J* = 1.4 Hz, *J* = 6.7 Hz, 1 H), 4.27 (dd, *J* = 2.7 Hz, *J* = 7.9 Hz, 1 H), 4.11 (ddd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1 H), 3.98 (t, *J* = 2.7 Hz, 1 H), 3.73 (dd, *J* = 1.4 Hz, *J* = 2.5 Hz, 1 H), 3.16 (dd, *J* = 1.4 Hz, *J* = 9.4 Hz, 1 H), 2.09 (dtt, *J* = 6.7 Hz, *J* = 6.7 Hz, *J* = 9.4 Hz, 1 H), 1.49 (s, 3 H), 1.41 (s, 6 H), 1.36 (s, 3 H), 1.23 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 108.27, 98.03, 75.73, 74.54, 72.23, 76.84, 75.93, 61.49, 29.09, 27.15, 23.72, 23.60, 18.57, 18.35, 17.55, 16.86. – $C_{16}H_{28}O_5$ (280.32): calcd. C 63.97, H 9.40; found C 63.56, H 9.66. – A solution of **38** was treated according to the method described for **39** and the residue was purified by FC (hexane/EtOAc, 20:1) to give **40**: m.p. 40–42 °C. – $[\alpha]_D$ = +27.3 (*c* = 1.1). – ^{1}H NMR (200 MHz): δ = 4.86 (dd, *J* = 2.7 Hz, *J* = 7.5 Hz, 1 H), 4.13 (dd, *J* = 5.3 Hz, *J* = 2.7 Hz, 1 H), 4.11–4.00 (m, 2 H), 4.08 (dd, *J* = 5.3 Hz, *J* = 8.4 Hz, 1 H), 3.34 (dd, *J* = 8.4 Hz, *J* = 5.4 Hz 1 H), 1.82 (dtt, *J* = 5.4 Hz, *J* = 6.5 Hz, 1 H), 1.51 (s, 3 H), 1.37 (s, 3 H), 1.36 (s, 3 H), 1.31 (s, 3 H), 1.18 (d, *J* = 6.4 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 109.16, 100.86, 74.01, 73.43, 72.93, 72.74, 65.26, 63.99, 30.48, 26.21, 24.77, 24.21, 23.66, 18.93, 17.47, 16.37. – $C_{16}H_{28}O_5$ (280.32): calcd. C 63.97, H 9.40; found C 64.22, H 9.68.

Phenyl 1-Oxo-3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside (41): A solution of **29** (3.75 g, 12.7 mmol) in CH_2Cl_2 (150 mL) containing $NaHCO_3$ (1.20 g, 14.3 mmol, 1.1 equiv.) was cooled to –78 °C and treated with a solution of 85% *m*CPBA (2.39 g, 11.8 mmol, 0.93 equiv.) in CH_2Cl_2 (50 mL). After 30 min, the reaction was warmed to room temp. and was washed with $Na_2S_3O_3$ (100 mL) and $NaHCO_3$ (100 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a residue which was purified by FC (hexane/EtOAc, 1:1 → EtOAc), affording **41** (3.54 g, 89%): m.p. 97–101 °C. – $[\alpha]_D$ = –80.4 (*c* = 1.0, $CHCl_3$). – ^{1}H NMR (200 MHz): δ = 7.75–7.67 (m, 2 H), 7.56–7.52 (m, 3 H), 4.37 (ddd, *J* = 1.7 Hz, *J* = 5.9 Hz, *J* = 8.2 Hz, 1 H), 4.29 (d, *J* = 1.7 Hz, 1 H), 4.14 (t, *J* = 5.9 Hz, 1 H), 4.05 (dd, *J* = 2.2 Hz, *J* = 5.9 Hz, 1 H), 3.99 (d, *J* = 8.2 Hz, 1 H), 3.79 (dt, *J* = 2.2 Hz, *J* = 6.5 Hz, 1 H), 1.60 (s, 3 H), 1.38 (s, 3 H), 1.34 (d, *J* = 6.5 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 141.95, 131.46, 128.95, 124.72, 119.95, 94.11, 77.00, 74.95, 71.52, 68.58, 27.14, 25.50, 16.37. – $C_{15}H_{20}O_5S$ (312.38): calcd. C 57.67, H 6.45; found C 57.36, H 6.50.

4,8-Anhydro-3,5:6,7-di-*O*-isopropylidene-2-*C*-methyl-1,2,9-trideoxy-L-*threo*-D-*galacto*- and -L-*threo*-D-*talo*-nonitol (43 and 44): To a suspension of **41** (47 mg, 0.15 mmol) in Et_2O (4.5 mL), cooled to –78 °C, was added, dropwise, MeLi·LiBr (1.5 M in Et_2O, 105 μL, 0.158 mmol, 1.1 equiv.). After 5 min, *t*BuLi (1.64 M in pentane, 740 μL, 1.21 mmol, 8.1 equiv.) was added dropwise, and after another 20 min, isobutyraldehyde (70 μL, 55.3 mg, 0.78 mmol, 5.1 equiv.) was added. After an additional 100 min, the reaction was quenched at –78 °C with sat. NH_4Cl (0.50 mL); it was warmed to room temp.,

diluted with H_2O (5 mL), and washed with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give a residue which was chromatographed (hexane/EtOAc, 5:1 → 2:1) to remove remaining **41**. The diastereomeric mixture of *C*-glycosides, which contained **33**, were treated with isopropylidene according to the method described for **39** afforded **43** and **44**, which were separated by FC. Elution with hexane/EtOAc (50:1) gave **43** (8.6 mg, 19%): m.p. 145–147 °C. – $[\alpha]_D$ = –43.3 (*c* = 1.1). – ^{1}H NMR (200 MHz): δ = 4.11–3.99 (m, 2 H), 3.84 (dt, *J* = 1.9 Hz, *J* = 6.6 Hz, 1 H), 3.71 (dd, *J* = 7.0 Hz, *J* = 9.7 Hz, 1 H), 3.60 (dd, *J* = 3.4 Hz, *J* = 9.4 Hz, 1 H), 2.89 (t, *J* = 9.6 Hz, 1 H), 1.96 (dtt, *J* = 3.4 Hz, *J* = 6.8 Hz, *J* = 7.0 Hz, 1 H), 1.56 (s, 3 H), 1.49 (s, 3 H), 1.41 (s, 3 H), 1.37 (d, *J* = 6.6 Hz, 3 H), 1.36 (s, 3 H), 0.96 (d, *J* = 7.0 Hz, 3 H), 0.90 (d, *J* = 6.8 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 109.306, 101.81, 76.57, 76.37, 74.80, 72.70, 72.09, 29.27, 28.65, 28.45, 26.28, 19.31, 18.86, 16.83, 16.10. – $C_{16}H_{28}O_5$ (300.39): calcd. C 63.97, H 9.40; found C 64.02, H 9.41. – Further elution with hexane/EtOAc 20:1 gave **44** (10.7 mg, 24%): m.p. 75–76 °C. – $[\alpha]_D$ = –30 (*c* = 1.2). – ^{1}H NMR (200 MHz): 4.14–4.01 (m, 2 H), 3.78 (dt, *J* = 2.3 Hz, *J* = 6.7 Hz, 1 H), 3.66 (dd, *J* = 8.6 Hz, *J* = 9.6 Hz, 1 H), 3.42 (dd, *J* = 6.3 Hz, *J* = 9.5 Hz, 1 H), 3.19 (dd, *J* = 6.3 Hz, *J* = 9.6 Hz, 1 H), 2.04 (dtt, *J* = 6.5 Hz, *J* = 6.7 Hz, *J* = 9.5 Hz, 1 H), 1.56 (s, 3 H), 1.41 (s, 3 H), 1.37 (d, *J* = 6.6 Hz, 3 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.5 Hz, 3 H). – ^{13}C NMR (50 MHz): δ = 109.32, 99.31, 77.00, 76.62, 76.31, 74.99, 74.42, 70.87, 28.52, 27.08, 26.31, 25.17, 22.94, 19.30, 16.75. – $C_{16}H_{28}O_5$ (300.39): calcd. C 63.97, H 9.40; found C 64.66, H 9.59. – Further elution with hexane/EtOAc (2:1) gave **33** (7.4 mg, 26%), whose physical properties were identical to the material described above.

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[1] [1a] J. H. Musser, *Ann. Rep. Med. Chem*. **1992**, *27*, 301–310. – [1b] Z. J. Witczak in *Carbohydrates in Drug Design* (Eds.: Z. J. Witczak, K. A. Nieforth), Marcel Dekker Inc., New York, **1997**; pp 1–37.

[2] [2a] A. Varki, *Glycobiology* **1993**, *3*, 97–130. – [2b] R. A. Dwek, *Chem. Rev.* **1996**, *96*, 683–720.

[3] *Carbohydrate Mimics. Concepts and Methods* (Ed.: Y. Chapleur), Wiley-VCH, Weinheim, **1998**.

[4] P. Sears, C.-H. Wong, *Chem. Commun*. **1998**, 1161–1170.

[5] [5a] B. Aguilera, A. Fernández-Mayoralas, *Chem. Commun.* **1996**, 127–128. – [5b] B. Aguilera, A. Fernández-Mayoralas, *J. Org. Chem*. **1998**, *63*, 2719–2723.

[6] [6a] For a preliminary account of this work, see: M. Carpintero, A. Fernández-Mayoralas, C. Jaramillo, *J. Org. Chem*. **1997**, *62*, 1916–1917. – [6b] C. Jaramillo, G. Corrales, A. Fernández-Mayoralas, *Tetrahedron Lett*. **1998**, *39*, 7783–7786.

[7] For a review of silyl Lewis^X mimics, see: E. E. Simanek, G. J. McGarvey, J. A. Jablonowski, C.-H. Wong, *Chem. Rev.* **1998**, *98*, 833–862.

[8] [8a] H. Redlich, W. Sudau, A. K. Szardenings, R. Vollerthun, *Carbohydr. Res.* **1992**, *226*, 57–78. – [8b] S. Cai, M. R. Stroud, S. Hakomori, T. Toyokuni, *J. Org. Chem*. **1992**, *57*, 6693–6696. – [8c] R. Verduyn, S. H. van Leeuwen, G. A. van der Marel, J. H. van Boom, *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 67–71. – [8d] H. A. J. Carless, S. S. Malik, *J. Chem. Soc., Chem. Commun*. **1995**, 2447–2448. – [8e] C. H. Tran, D. H. G. Crout, *Tetrahedron: Asymmetry* **1996**, *7*, 2403–2406. – [8f] R. Angelaud, Y. Landais, *Tetrahedron Lett*. **1997**, *38*, 8841–8844.

[9] D. E. Levy, C. Tang, *The Chemistry of C-Glycosides*, Pergamon, Exeter, **1995**.

[10] For samarium diiodide promoted pinacol coupling of related carbohydrate derivatives, see: [10a] J. L. Chiara, W. Cabri, S. Hanessian, *Tetrahedron Lett.* **1991**, *32*, 1125–1128. – [10b] J. Uenishi, S. Masuda, S. Wakabayashi, *Tetrahedron Lett.* **1991**, *32*, 5097–5100. – [10c] J. L. Chiara, M. Martín-Lomas, *Tetrahedron Lett.* **1994**, *35*, 2969–2972. – [10d] J. P. Guidot, T. Le Gall, C. Mioskowski, *Tetrahedron Lett.* **1994**, *35*, 6671–6672. – [10e] J. L. Chiara, N. Valle, *Tetrahedron: Asymmetry* **1995**, *6*, 1895–1898. – [10f] T. Sawada, R. Shirai, S. Iwasaki, *Tetrahedron Lett.* **1996**, *37*, 885–886.

[11] E. J. Corey, R. A. E. Winter, *J. Am. Chem. Soc.* **1963**, *85*, 2677–2678.

[12] For selective lipase-catalyzed acylations controlled by solvent, see: [12a] R. López, E. Montero, F. Sánchez, J. Cañada, A. Fernández Mayoralas, *J.Org. Chem*. **1994**, *59*, 7027–7032. – [12b] D. A. MacManus, E. N. Vulfson, *Enzyme Microb. Technol.* **1997**, *20*, 225–228.

[13] [13a] G. Stork, T. Y. Chan, G. A. Breault, *J. Am. Chem. Soc.* **1992**, *114*, 7578–7579. – [13b] L. Pingli, M. Vandewalle, *Tetrahedron* **1994**, *50*, 7061–7074. – [13c] L. Fensterbank, A-L. Dhimane, S. Wu, E. Lâcote, S. Bogen, M. Malacria, *Tetrahedron* **1996**, *52*, 11405–11420.

[14] The formation of **13** was evidenced by the presence of a singlet at δ = 4.04, assigned to the methylene of the bromomethylsilyl group, in its ^{1}H NMR ($CDCl_3$) spectrum.

[15] Elimination of a cyclic sulfate derived from dimethyl L-tartrate to give a vinyl sulfate salt was reported previously: K. S. Kim, G. W. Lee, I. H. Cho, Y. H. Joo, *Bull. Korean Chem. Soc*. **1993**, *14*, 660–661.

[16] This was evidenced by comparison of the coupling constants $J_{1,6A}$ and $J_{1,6B}$ in the ^{1}H NMR spectra of **17** and **26** (see Scheme 6).

[17] V. Wittman, H. Kessler, *Angew. Chem.* **1993**, *105*, 1138–1140; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1091–1093.

[18] [18a] T. Skrydstrup, O. Jarreton, D. Mazéas, D. Urban, J.-M. Beau, *Chem. Eur. J.* **1998**, *4*, 655–671. – [18b] D. Mazéas, T. Skrydstrup, J.-M. Beau, *Angew. Chem.* **1995**, *107*, 990–993; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 909–912. – [18c] P. de Pouilly, A. Chénedé, J.-M. Mallet, P. Sinaÿ, *Bull. Soc. Chim. Fr.* **1993**, *130*, 256–265.

[19] S.-C. Hung, C.-H. Wong, *Angew. Chem.* **1996**, *108*, 2829–2832; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2671–2674.

[20] S.-C. Hung, C.-H. Wong, *Tetrahedron Lett.* **1996**, *37*, 4903–4906.

[21] [21a] O. Frey, M. Hoffmann, V. Wittman, H. Kessler, P. Uhlmann, A. Vasella, *Helv. Chim. Acta* **1994**, *77*, 2060–2069. – [21b] P. Lesimple, J.-M. Beau, *Bioorg. Med. Chem.* **1994**, *2*, 1319–1330.

[22] A. Furstner, *Liebigs Ann. Chem*. **1993**, 1211–1217.

[23] K. C. Nicolaou, R. E. Dolle, D. P. Papahatjis, J. L. Randall, *J. Am. Chem. Soc.* **1984**, *106*, 4189–4192.

[24] P. Smid, G. A. van der Marel, F. M. Rombouts, J. H. van Boom, *J. Carbohydr. Chem.* **1991**, *10*, 833–849.

[25] T. Uchiyama, O. Hindsgaul, *Synlett* **1996**, 499–501.

[26] J.-M. Beau, P. Sinaÿ, *Tetrahedron Lett.* **1985**, *26*, 6185–6188; 6189–6192.

[27] Dimer **32** was characterized as its diacetate **34**, the ^{1}H NMR of which showed signals for an α-configured fucopyranosyl unit ($J_{1,2}$ = 3.0 Hz), but no signals were observed for an aglycon moiety. The mass spectral data agreed with a structure whose mass was composed of two fucopyranosyl units.

[28] T. Satoh, K. Horiguchi, *Tetrahedron Lett*. **1995**, *36*, 8235–8238.

[29] M. Casillas, A. M. Gómez, J. C. López, S. Valverde, *Synlett* **1996**, 628–630.

[30] M. Hoffmann, H. Kessler, *Tetrahedron Lett.* **1997**, *38*, 1903–1906.

[31] Large values for $J_{3,4}$ and small values for $J_{1,2}$ indicated that the fucopyranosyl ring of **39** and **40** has a skew conformation. The small $J_{1,7}$ for **39** (1.4 Hz) was indicative of the *R* configuration at *C*-7 with a boat conformation of the dioxane ring. On the other hand, the large $J_{1,7}$ (8.4 Hz) for **40** agreed with the *S* configuration at *C*-7 with a chair conformation of the dioxane ring.

[32] G. B. Howart, D.G. Lance, W. A. Szarek, J. K. N. Jones, *Can. J. Chem*. **1969**, *47*, 75.

[33] Selected ^{1}H NMR (200 MHz) data for **46:** δ = 5.50 (d, *J* = 5.1 Hz, 1 H), 5.32 (dd, *J* = 8.0, 4.0 Hz, 1 H), 5.11 (dd, *J* = 3.9, 4.3 Hz, 1 H), 4.60 (dd, *J* = 3.0, 7.5 Hz 1 H), 4.53 (dd, *J* = 4.7, 3.9 Hz, 1 H), 4.34 (dd, *J* = 7.7, 1.7 Hz, 1 H), 3.96 (dd, *J* = < 1.0, 7.9 Hz, 1 H), 2.09 (s, 3 H), 2.05 (s, 3 H). For **47:** δ = 5.53 (d, *J* = 5.0 Hz, 1 H), 5.42 (dd, *J* = 5.0, 8.5 Hz, 1 H), 5.21 (t, *J* = 2.6 Hz, 1 H), 4.60 (dd, *J* = 2.2, 7.9 Hz, 1 H), 4.40 (dd, *J* = 1.9, 7.9 Hz, 1 H), 4.38 (dd, *J* = 2.7, 8.6 Hz, 1 H), 4.29 (dd, *J* = 2.3, 5.0 Hz, 1 H), 4.26 (dd, *J* = 2.7, 7.6 Hz, 1 H), 4.16 (dd, *J* = 1.7, 5.0 Hz, 1 H), 2.08 (s, 3 H), 2.00 (s, 3 H).

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