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A de novo approach to C-branched inositols: synthesis of a *myo*-inositol precursor for C-linked glycosyl phosphatidylinositols

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Abstract—C-Linked glycosyl inositols are valuable structure-activity probes because of their greater hydrolytic stability and different conformational behavior compared with their parent O-glycosides. Simple C-branched inositols are synthetic precursors to these and other groups of inositol mimetics. Herein is described a de novo synthesis of C-branched inositols that contain a versatile ethenyl side chain for elaboration into more complex appendages. The approach centers on a stereoselective oxocarbenium ion–allylsilane cyclization and provides C-branched inositols with different stereochemical motifs. The synthesis of C-ethenyl-di-*O*-isopropylidene-*myo*-, *neo*-, *epi*-, and *allo*-inositols is discussed.

Keywords: C-Branched inositol; Oxocarbenium ion; Allysilane

1. Introduction

Glycosylinositols are subunits of the glycosyl phosphatidylinositols (GPI)[1] anchors that covalently link certain proteins to the outer leaflet of eukaryotic cell membranes, and related phosphatidyl inositol mannosides (PIM)[2] structures in the cell wall of mycobacteria. Both GPI and PIM contain a *myo*-inositol residue that is connected at O6 via an α-glycoside linkage to mannose (in PIM, cf **1**) or glucosamine (in GPI, cf **2**), which is attached at the reducing end of a trimannan chain (Fig. 1). The *myo*-inositol segment is also connected at O1 to a phosphatidyldiacylglycerol residue. In GPIs, the O2 position bears a fatty acid ester, whereas PIMs are linked to a mannose or oligomannan at this position. Both GPIs and PIMs may contain an additional fatty acid ester at O4.

The hydrophobic nature of the *myo*-inositol residue is believed to facilitate lipid clustering and translocation in the bilayer surface, and the specificity of aggregation is likely controlled by lipid substitution and the conformation of this subunit.[3] The formation of such lipid microdomains has been associated with signaling mechanisms.[4] Components of GPIs have also been suggested as second messengers of insulin action.[5] In parasites such as *Trypanosoma brucei*, the GPI anchoring system provides a protective protein coating, which undergoes antigenic variation and constitutes a defense mechanism against the host immune response.[1,6] The

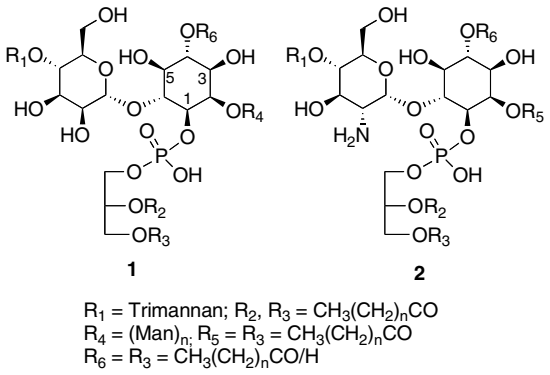

Figure 1. Generalized GPIs and PIMs.

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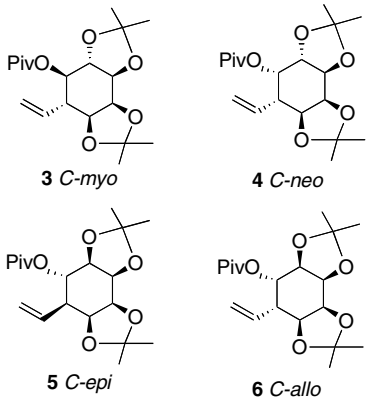
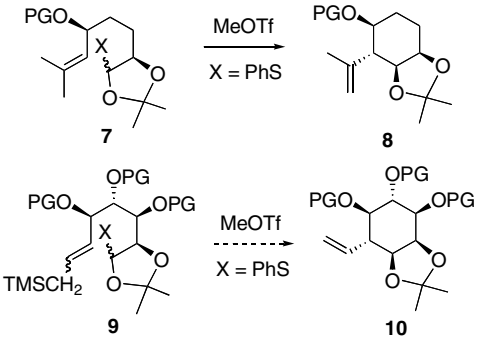


Figure 2. C-Branched inositols.



Scheme 1. Oxocarbenium ion cyclizations for C-branched inositols.

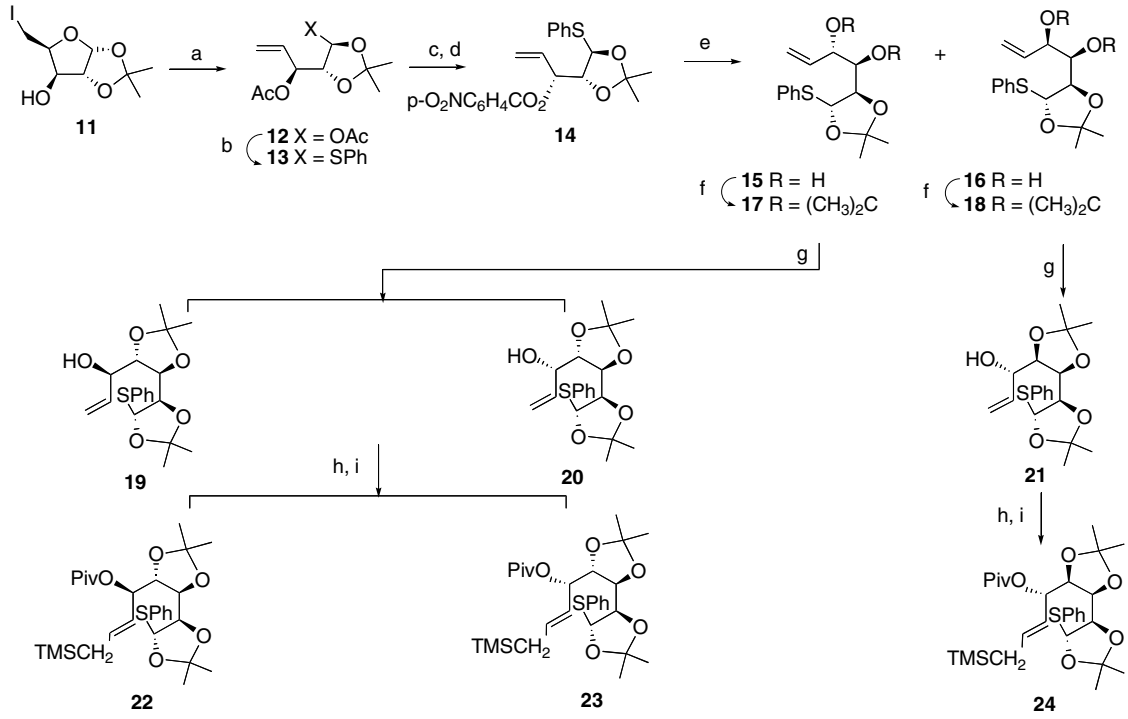
implication of GPIs and PIMs in a variety of disease mechanisms has led to interest in several areas of GPI biochemistry,[1,2] including the design of inhibitors of GPI biosynthesis,[7,8] immunological studies on the specificity of GPI-membrane integration,[9] and investigation of glycosyl inositol analogues of putative insulin mimics.[10] C-Linked glycosyl inositols are potentially valuable mechanistic probes, because of their greater hydrolytic stability and different conformational behavior compared with their parent O-glycosides.[11] In this vein, we were interested in the 6-*C*-ethenyl-*myo*-inositol analogue **3**, a synthetic precursor to more complex C-branched *myo*-inositols (Fig. 2). Herein, we describe the synthesis of **3** and the diastereomeric analogues **4**, **5**, and **6**.

Previous syntheses of C-branched cyclitols include the modification of naturally occurring cyclitols,[12] the de novo formation of the cyclitol framework through cyclization of acyclic precursors,[13] or cycloaddition[14] strategies. A 6-C-branched *myo*-inositol related to **3**, involving an intramolecular silyl nitronate cycloaddition, has been reported.[13e] We were interested in a de novo synthesis because of the versatility of such an approach for providing different substitution patterns. In this context, we have been developing an oxocarbenium ion–alkene cyclization strategy for C-branched, oxygenated cyclohexanes, and the synthesis of **3** provided an opportunity to evaluate the scope of this methodology.[15]

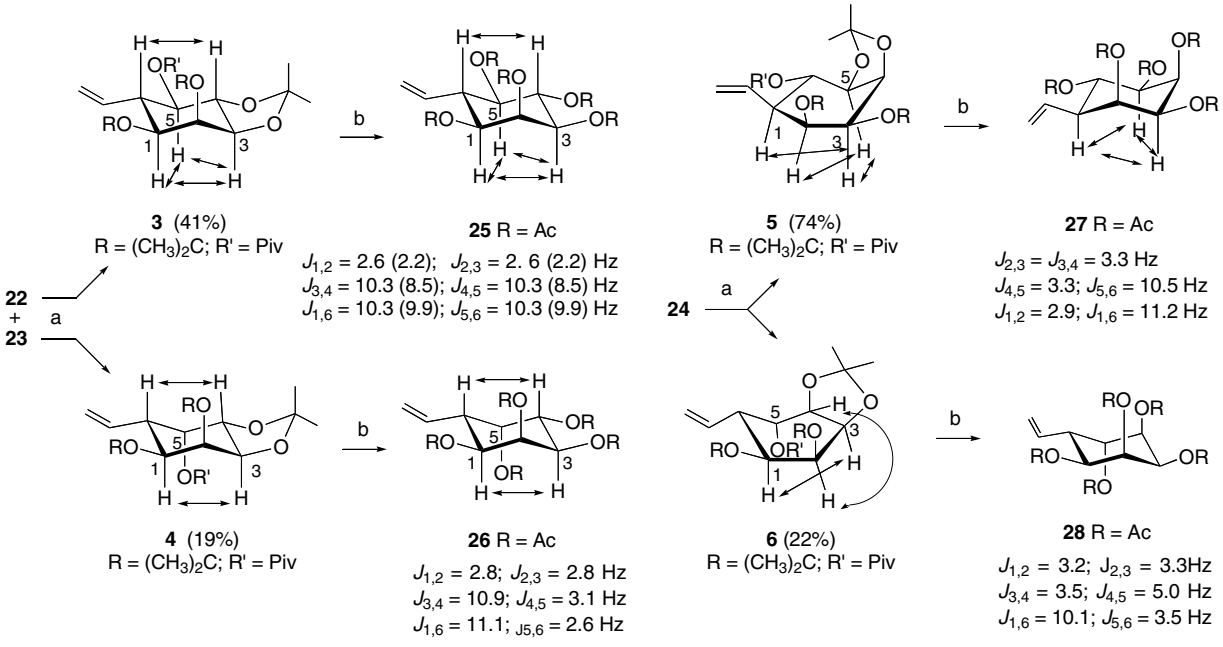
2. Results and discussion

In the aforementioned study, it was observed that treatment of thioacetal–alkene **7** with methyl triflate led to one of the four possible diastereomeric cyclization products (Scheme 1). The favored isomer contained a cis-fused *O*-isopropylidene and a vicinal isopropenyl substituent that was trans to the isopropylidene residue. The stereoselectivity of this transformation was rationalized in terms of the cyclic nature of the oxocarbenium ion intermediate and conformational factors in the transition state leading to **8**. By analogy, we envisaged that cyclization of a precursor such as **9** should lead to the C-branched *myo*-inositol **10** with high stereoselectivity. While the use of an allylsilane (in place of the isobutenyl residue in **7**), was expected to facilitate the trapping of the oxocarbenium ion, the more complex substitution in **9** compared with **7** led to concerns about both competing side reactions and stereoselectivity. Indeed, preliminary investigations on the derivatives of **9** with benzyl ether or ester protecting groups suggested that products arising from attack on the intermediate oxocarbenium ion by neighboring oxygen substituents were predominant. We argued that strategic positioning of cyclic and ester protecting groups would limit these processes because of unfavorable ring strain and electronic effects in the cyclization reaction. Accordingly, substrate **22** was proposed as a suitable precursor to **3** (Schemes 2 and 3).

To evaluate the generality of the cyclization methodology, a divergent synthesis that led to **22** as well as diastereomeric cyclization precursors was developed. The synthesis started with commercially available 1,2-*O*-isopropylidene-α-D-xylofuranose, which was converted to the known 5-iodo derivative **11**.[16] Treatment of **11** with 2 equiv of *n*-butyl lithium at low temperature followed by quenching of the reaction with acetic anhydride provided diacetate **12** as a mixture of acetal isomers. Exposure of this mixture to boron trifluoride etherate and thiophenol at low temperature led to 1-thio-1,2-*O*-isopropylidene acetal **13** as a single isomer, which was presumed to have the trans stereochemistry by analogy with the earlier investigation.[15] Ester hydrolysis on **13** and treatment of the resulting alcohol under Mitsunobu conditions provided nitrobenzoate **14**. Hydrolysis of **14** provided an allylic alcohol that was diastereomeric to the substrate for the Mitsunobu reaction, confirming that the reaction proceeded with inversion of configuration. Ozonolysis of **14** provided the aldehyde derivative, which was treated without purification with an excess of vinylmagnesium bromide. This two-step sequence provided a mixture of diastereomeric diols **15** and **16** in a 3:1 ratio. The configuration at the



Scheme 2. Synthesis of cyclization precursors. Reagents and conditions: (a) *n*-BuLi, THF, −78 °C, then Ac_2O, pyridine, DMAP, 86%; (b) PhSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78→−40 °C, 88%; (c) $NaOCH_3$, CH_3OH, 99%; (d) *p*-O_2N–C_6H_4COOH, DIAD, THF, 98%; (e) (i) O_3, CH_3OH/CH_2Cl_2, −78 °C then Ph_3P; (ii) $CH_2{=}CHMgBr$, THF, 0 °C, **15/16** (3:1), 60%; (f) DMP, CH_2Cl_2, CSA, **17** (87%), **18** (82%); (g) see (e), **19/20** (2:1), 66%; **21**, 63% (h) $TMSCH_2CH{=}CH_2$, CH_2Cl_2, Grubbs II catalyst; (i) PivCl, CH_2Cl_2, pyridine, DMAP, **22/23** (68%), **24** (59%) two steps.



Scheme 3. Cyclization reactions and stereochemical assignment of products. Average of mutual *J* values indicated. Calculated *J* values for idealized chair are shown in parentheses. Double headed arrows indicate unambiguous NOE's. Reagents and conditions: (a) CH_3OTf, CH_2Cl_2, DTBMP; (b) (i) DIBALH, THF, −78 °C; (ii) CH_3OH, HCl; (iii) Ac_2O, pyridine, EtOAc.

newly formed carbinol center in **15** and **16** was assigned by correlation with the subsequent cyclization products, the structures of which were analyzed through ^1H NMR analysis (vide infra). The major isomer **15** corresponds to the stereochemistry required for the *myo*-inositol target **3**. Diols **15** and **16** were converted to their respective

di-*O*-isopropylidene derivatives **17** and **18**, which were individually processed using an ozonolysis/Grignard addition protocol that was similar to that used on alkene **14**. This reaction sequence gave an approximately 2:1 mixture of allylic alcohols **19/20** from **17**, and a single product **21** from **18**. Once again, the configuration at the newly introduced stereogenic center in **19**–**21** relied on the assignment of stereochemistry in the later cyclization products. Unseparated mixture **19/20** and **21** were then individually subjected to olefin cross-metathesis with allyltrimethylsilane.[17] Treatment of the metathesis product arising from **19/20** with pivaloyl chloride provided an inseparable 2:1 mixture of isomers **22/23** in overall yield of 68% from **19/20**. ^{1}H NMR analysis of this mixture suggested that the stereoselectivity of the cross-metathesis was greater than 90% in favor of the *E*-alkene. Similarly, the cross-metathesis-pivaloylation sequence on **21** led to **24** in 59% yield.

The cyclization reactions on unseparated mixture of **22/23** and **24** were promoted with methyl triflate in the presence of 2,6-di-*t*-butyl-4-methylpyridine (DTBMP) and freshly activated 4 Å molecular sieves in anhydrous dichloromethane (Scheme 3). Under these conditions, an approximately 2:1 mixture of **22/23** afforded **3** (41%) and **4** (19%). Stereochemical analysis of the products (vide infra) indicated that **3** was produced from **22**, and **4** from **23**. In comparison, the reaction of **24** produced a mixture of **5** (74%) and **6** (22%). Thus, the reactions of **22** and **23** were both highly stereoselective, giving in each case a single diastereomer in which the newly formed *O*-isopropylidene was cis-fused to the cyclitol ring, and the adjacent isopropenyl substituent was trans to the isopropylidene ring. The cyclization of **24** was less selective giving a mixture of products which also contained a cis-fused *O*-isopropylidene, but differed with respect to the configuration at the ethenylated carbon.

The stereochemistry of **3**–**6** was assigned by considering the synthetic sequence leading to the cyclization precursors in connection with ^{1}H NMR analysis of the cyclization products **3**–**6** and their pentaacetate derivatives **25**–**28** (Scheme 3). Due to the uncertainty in predicting well-defined conformations for the di-*O*-isopropylidene derivatives, structural assignments were based on vicinal $J_{H,H}$ values and NOE's in **25**–**28**, and corroborated with NOE's for **3**–**6**. Thus, the stereochemistry at C2 and C3 in **3**, **4**, and **6** (cf. C3 and C4 in **5** due to different numbering) is set in the common precursor **14**. Di-*O*-isopropylidene **3**, the major product from the cyclization of a mixture of **22/23**, was determined to have the *myo* configuration by comparison of the experimental coupling constants for the derived pentaacetate **25**, with those expected by application of the Haasnoot–Altona equation[18,19] to an idealized chair conformation (Scheme 3). This assignment was confirmed by NOE's between H4 and H6, and mutual NOE's between H1, H3, and H5. Similar NOE's were observed for the di-*O*-isopropylidene precursor **3**. In addition to setting the configurations at the two stereogenic centers that were generated in the cyclization reaction (C1 and C6), the structure for **3** (and **25**) established the configurations at C4 and C5 in the corresponding cyclization precursor **22**, that is, the new stereogenic centers that were formed in the two Grignard reactions leading to **22**. Based on the synthetic grounds, **22** and **23** differ only with respect to the configuration at C5, and therefore the assignment of structure **22** established the structure of **23**. The epimeric relationship between **22** and **23** was independently confirmed by $J_{H,H}$ analysis on **26**, the pentacetate derivative of the other cyclization product (i.e., **4**), from the mixture **22/23**. Thus, for **26**, $J_{4,5} = 3.1$ and $J_{5,6} = 2.6$ Hz, which was in line with an equatorial–axial relationship between H5, and both H4 and H6. Unambiguous NOE's between H1 and H3, and H4 and H6 in both **4** and **26** confirmed the *neo* configuration. Using similar arguments, the cyclization products **5** and **6** and their respective pentaacetates **27** and **28** were assigned as *epi* and *allo*, and the structure of the corresponding precursor deduced as **24**. Of note is the observation that the coupling constant data for **25** and **26** were consistent with a predominant conformation with a chair-like geometry, even though the presence of the 1,3-diaxial oxygen substituents might have been expected to lead to significant distortion.

The stereochemistry of the cyclization reaction appears to be controlled by conformational factors. Thus, the high stereoselectivity observed for the reactions of **22** and **23** is consistent with a clear preference for chair-like transition states **29A** and **30A**, respectively, over the other diastereomeric possibilities (Fig. 3). The particular flip chair conformation in these structures is determined by the 3,4-*O*-isopropylidene residue (in which the oxygens of the cyclic acetal are in a trans diequatorial relationship in the forming six-membered ring). The configuration at C1 is controlled by the preference for a 1,2-*O*-isopropylidene that is cis-fused (vs trans-fused) in the resulting tricyclic framework. The constraints imposed by the two cyclic acetal residues are met in a pair of low energy transition states, **29A**/**29A′** and **30A/30A′**, corresponding to precursors **22** and **23**, respectively. Of these **29A** and **30A**, in which the C6 substituent adopts the pseudo-equatorial (vs the pseudo-axial orientation in **29A′** and **30A′**), in the forming six-membered ring, are expected to be highly favored, thereby leading to single cyclization products from **22** and **23**, respectively. Analysis of transition states for the cyclization of **24** is complicated by the fact that both *O*-isopropylidene rings in the diastereomeric products **5** and **6** are cis-fused, and therefore a wider range of low energy transition state conformations are possible, compared to the cyclizations leading to **3** and **4**. In addition, chair-like geometries would probably

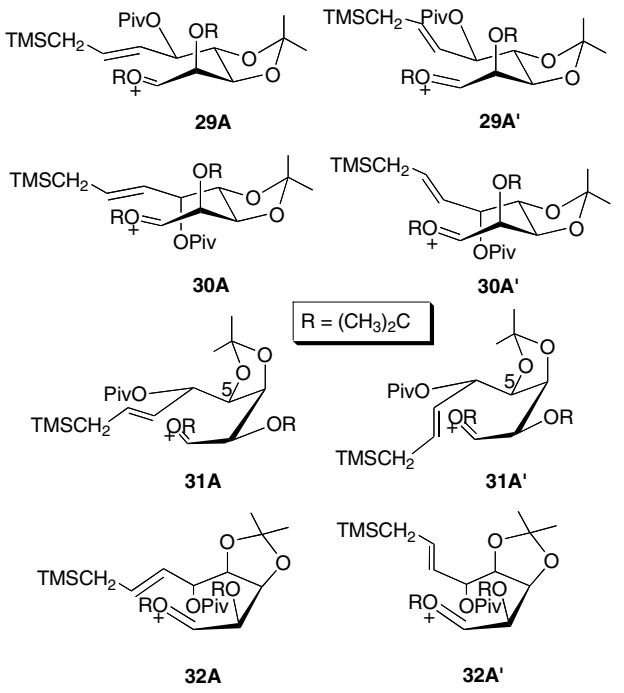


Figure 3. Transition state models for oxocarbenium ion cyclization.

be disfavored because of severe 1,3-diaxial interactions between oxygen substituents of the two isopropylidene rings. Assuming a half-chair like geometry, four low energy pathways **31A/31A′** and **32A/32A′** corresponding to pairs of 'flip' conformations may be considered for **5** and **6**, respectively. Of these **31A** and **32A**, in which the alkene substituent adopts a pseudo-equatorial position, are expected to be favored (over **31A′** and **32A′**). While **31A** should be preferred over **32A**, and as a result **5** should predominate over **6**, the high degree of steric congestion in both structures would be expected to have a leveling effect on their relative energies, thereby leading to low product selectivity. The observed ratio of **5/6** (3:1) appears to be consistent with this argument.

3. Conclusion

A novel oxocarbenium ion–allylsilane synthetic strategy for the *C*-ethenyl inositols has been described. Noteworthy aspects of this methodology are the easy accessibility of the 1-thio-1,2-*O*-isopropylidene-alkene precursor from 1,2-*O*-isopropylidene-α-D-xylofuranose and the stereoselectivity of the key oxocarbenium ion cyclizations. The potential for obtaining diastereomeric precursors from other common 1,2-*O*-isopropylidene sugars, and the synthetic versatility of the 1-thio-1,2-*O*-isopropylidene–alkene building blocks suggest that C-branched inositols with a variety of substitution patterns, and other groups of highly oxygenated cyclohexanes may be possible through this approach.

4. Experimental

4.1. General methods

Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere in oven-dried glassware using standard syringe and septa technique. Optical rotations were recorded at room temperature using a Rudolph Autopol III polarimeter. ^{1}H and ^{13}C NMR spectra were obtained on a Varian Unity Plus 500 (500 MHz) spectrometer. Chemical shifts are relative to the deuterated solvent peak or the tetramethylsilane (TMS) peak at (δ 0.00) and are in parts per million (ppm). Assignments for selected nuclei were determined from ^{1}H COSY experiments. High resolution mass spectrometry (HRMS) was performed on an Ultima Micromass Q-Tof instrument at the Mass Spectrometry Laboratory of the University of Illinois, Urbana-Champaign. Thin layer chromatography (TLC) was done on 0.25 mm thick precoated silica gel HF_{254} aluminum sheets. Chromatograms were observed under UV (short and long wavelength) light, and/or were visualized by heating plates that were dipped in a solution of ammonium(VI) molybdate tetrahydrate (12.5 g) and cerium (IV) sulfate tetrahydrate (5.0 g) in 10% aq sulfuric acid (500 mL). Flash column chromatography (FCC) was performed using Silica Gel 60 (230–400 mesh) and employed a stepwise solvent polarity gradient, correlated with TLC mobility.

4.2. 1,3-Di-*O*-acetyl-4,5-dideoxy-1,2-*O*-isopropylidene-4-eno-L-*threo*-pentose (12)

To a solution of **11** (6.24 g, 20.8 mmol) in THF (100 mL) was added *n*-BuLi (33 mL of a 2.5 M solution in THF, 83.2 mmol) dropwise at −78 °C, under an atmosphere of argon. The reaction was stirred at this temperature for 1 h, then pyridine (6.73 mL, 83.2 mmol), acetic anhydride (15.7 mL, 83.2 mmol) and DMAP (2.50 g, 20 mmol) were added. The mixture was warmed to −40 °C, stirred for an additional 1 h at this temperature, then poured into ice-cold satd aq $NaHCO_3$, and extracted with Et_2O. The combined organic phase was dried (Na_2SO_4), filtered, and evaporated in vacuo. FCC of the residue afforded **12** as an approximately 1:1 mixture of diastereomers (4.60 g, 86%). A portion of this mixture was subjected to further FCC for characterization purposes. For the less polar component: $R_f = 0.80$ (20%, EtOAc/petroleum ether); $[\alpha]_D$ −20.6 (*c* 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.41, 1.51 (each 3H, both s, $(CH_3)_2C$), 2.09, 2.13 (each 3H, both s, $CH_3CO \times 2$), 4.23 (1H, dd, $J = 3.4$, 3.5 Hz, H-2), 5.31 (1H, d, $J = 10.6$ Hz, H-5), 5.39 (1H, d, $J = 17.2$ Hz, H-5′), 5.53 (1H, t, $J = 7.6$ Hz, H-3), 5.73 (1H, m, H-4), 6.20 (1H, d, $J = 3.4$ Hz, H-1); ^{13}C NMR ($CDCl_3$): δ 21.0, 21.1, 27.1, 30.5, 73.1, 82.8, 96.3, 113.7, 120.1, 131.9, 170.2,

170.2; ESIMS m/z 281.1 $[M+Na]^+$. For the more polar component: $R_f = 0.70$ (20%, EtOAc/petroleum ether); $[\alpha]_D$ −80.3 (c 4.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.40, 1.51 (each 3H, both s, $(CH_3)_2C$), 2.80, 211 (each 3H, both s, $CH_3CO \times 2$), 4.23 (1H, dd, $J = 3.5$ Hz, 10.6 Hz, H-2), 5.29 (1H, d, $J = 10.6$ Hz, H-5), 5.37 (1H, d, $J = 17.3$ Hz, H-5′), 5.54 (1H, t, $J = 7.7$ Hz, H-3), 5.70 (1H, m, H-4), 5.20 (1H, d, $J = 3.5$ Hz, H-1); ^{13}C NMR ($CDCl_3$): δ 21.3, 21.4, 26.2, 28.3, 72.9, 80.1, 93.4, 113.0, 120.3, 131.9, 169.9, 170.0; ESIMS m/z 281.1 $[M+Na]^+$.

4.3. 3-*O*-Acetyl-4,5-dideoxy-1,2-*O*-isopropylidene-4-eno-L-*threo*-pentose-*S*-phenyl-monothiohemiacetal (13)

$BF_3{\cdot}OEt_2$ (3.05 mL, 24.2 mmol) was slowly added at −78 °C, under argon, to a solution of **12** (4.17 g, 16.2 mmol) and thiophenol (4.15 mL, 40.4 mmol), in anhydrous CH_2Cl_2 (70 mL). The mixture was warmed to −40 °C, and stirring was continued at this temperature for 1 h (or until the TLC indicated complete disappearance of the starting material). The reaction mixture was quenched by the addition of Et_3N (3 mL), then poured into 1 N aq NaOH and extracted with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. FCC of the residue gave **13** (4.40 g, 88%): $R_f = 0.7$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ +118.7 (c 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.50, 1.57 (each 3H, both s, $(CH_3)_2C$), 2.12 (3H, s, CH_3CO), 4.25 (1H, t, $J = 5.6$ Hz, H-2), 5.34 (1H, d, $J = 6.5$ Hz, H-1), 5.35 (1H, d, $J = 10.8$ Hz, H-5), 5.42 (1H, d, $J = 17.6$ Hz, H-5′), 5.49 (1H, t, $J = 5.9$ Hz, H-3), 5.79 (1H, m, H-4), 7.34 (3H, m, Ar–H), 7.54 (2H, d, $J = 7.1$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 21.6, 26.8, 27.8, 74.1, 82.2, 86.2, 112.9, 120.9, 128.2, 129.6, 132.5, 132.5, 134.6, 170.4; ESIMS m/z 331.1 $[M+Na]^+$.

4.4. 4,5-Dideoxy-1,2-*O*-isopropylidene-3-*O*-*p*-nitrobenzoyl-4-eno-D-*erythro*-pentose-*S*-phenyl-monothiohemiacetal (14)

$NaOCH_3$ (100 mg, 1.85 mmol) was added to a solution of **13** (2.23 g, 7.24 mmol) in anhydrous CH_3OH (20 mL). The reaction was stirred at rt for 2 h and the pH was then adjusted to 7 by addition of a solution of HCl in CH_3OH. The mixture was concentrated under reduced pressure and the residue purified by FCC to give the derived alcohol (1.93 g, 99%): $R_f = 0.50$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ +158 (c 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.40, 1.43 (each 3H, both s, $(CH_3)_2C$), 2.19 (1H, br s, OH), 3.96 (1H, dd, $J = 4.0$ Hz, H-2), 4.13 (1H, m, H-3), 5.18 (1H, dt, $J = 1.2$, 10.5 Hz, H-5), 5.31 (1H, dt, $J = 1.4$, 17.2 Hz, H-5′), 5.33 (1H, d, $J = 6.6$ Hz, H-1), 5.84 (1H, m, H-4), 7.20 (3H, m, Ar–H), 7.43 (2H, d, $J = 7.1$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.2, 27.5, 71.9, 83.4, 85.8, 112.1, 117.4, 127.7, 128.5, 129.2, 131.8, 134.2, 136.8; ESIMS m/z calcd for $C_{14}H_{18}O_3NaS$ $[M+Na]^+$: 289.0874. Found: 289.0887. Diisopropylazodicarboxylate (2.05 mL, 10.6 mmol) was added dropwise at 0 °C to a mixture of the product from the previous step (1.88 g, 7.05 mmol), Ph_3P (2.2 g, 8.46 mmol), and p-nitrobenzoic acid (1.77 g, 10.6 mmol) in anhydrous toluene (30 mL). The reaction was maintained at this temperature for 2 h, then quenched by the addition of satd aq $NaHCO_3$. The mixture was then extracted with Et_2O and the organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. FCC of the residue gave **14** (2.81 g, 98%): $R_f = 0.85$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ +142 (c 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.34, 1.47 (each 3H, both s, $(CH_3)_2C$), 4.26 (1H, q, $J = 4.3$ Hz, H-2), 5.35 (1H, d, $J = 10.6$ Hz, H-5), 5.38 (1H, d, $J = 6.3$ Hz, H-1), 5.37–5.42 (1H, d, $J = 17.2$ Hz, H-5′), 5.70 (1H, t, $J = 5.4$ Hz, H-3), 5.95 (1H, m, H-4), 7.24 (3H, m, Ar–H), 7.41 (2H, dd, $J = 1.1$, 1.5 Hz, Ar–H), 8.20 (2H, d, $J = 8.7$ Hz, Ar–H), 8.24 (2H, d, $J = 8.7$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.3, 27.5, 75.4, 82.2, 85.9, 112.6, 120.6, 123.8, 128.0, 129.3, 131.1, 131.4, 132.3, 135.5, 152.1, 164.1; ESIMS m/z calcd for $C_{21}H_{21}NO_6NaS$ $[M+Na]^+$: 438.0987. Found: 438.0996.

4.5. 5,6-Dideoxy-1,2-*O*-isopropylidene-5-eno-L-*lyxo*-hexose-*S*-phenyl-monothiohemi-acetal (15) and 5,6-dideoxy-1,2-*O*-isopropylidene-5-eno-D-*ribo*-hexose-*S*-phenyl-monothiohemiacetal (16)

Alkene **14** (2.71 g, 6.28 mmol) was dissolved in a 5/1 mixture of CH_2Cl_2/CH_3OH (35 mL). The solution was cooled to −78 °C and treated with a stream of O_3 in O_2 until TLC indicated the complete disappearance of the starting material. The reaction was then purged with nitrogen, and Ph_3P (3.29 g, 12.5 mmol) was added. The mixture was warmed to rt, stirred for 1 h at this temperature, and concentrated under reduced pressure. The crude material was dried under high vacuum and dissolved in anhydrous THF (30 mL). The resulting solution was added dropwise at 0 °C to a mixture of vinylmagnesium bromide (50 mL of a 1 M solution in THF, 50.0 mmol) in THF (60 mL). The reaction was stirred for 1 h at this temperature, then poured into satd aq NH_4Cl and extracted with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. FCC of the residue afforded **15/16** as a 3:1 mixture (0.90 g, 60%). Further FCC of the mixture provided separate samples of **15** and **16**. For **15**: $R_f = 0.53$ (40%, EtOAc/petroleum ether); $[\alpha]_D$ +127.4 (c 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.40, 1.47 (each 3H, both s, $(CH_3)_2C$), 2.40 (2H, br d, $J = 7.7$ Hz, OH), 3.62 (1H, br d, $J = 4.4$, 8.8 Hz, H-3), 4.14 (1H, t, $J = 5.3$ Hz, H-2), 4.25 (1H, br s, H-4), 5.24 (1H, dt, $J = 1.3$, 10.6 Hz, H-6), 5.4 (1H, dt, $J = 1.4$, 17.3 Hz, H-6′), 5.51 (1H, d, $J = 6.0$ Hz, H-1), 5.90 (1H, m,

H-5), 7.22 (3H, m, Ar–H), 7.45 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.1, 27.7, 71.8, 74.1, 81.6, 86.0, 111.9, 118.0, 127.6, 129.2, 131.7, 134.7, 136.8; ESIMS *m/z* calcd for $C_{15}H_{20}O_4NaS$ $[M+Na]^+$: 319.0980. Found: 319.1031. For **16**: $R_f = 0.30$ (40%, EtOAc/petroleum ether); $[\alpha]_D$ +392.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.49, 1.55 (each 3H, both s, $(CH_3)_2C$), 2.29 (1H, d, $J = 3.6$ Hz, OH), 2.38 (1H, d, $J = 4.4$ Hz, OH), 3.81 (1H, m, H-3), 4.23 (1H, t, $J = 5.7$ Hz, H-2), 4.30 (1H, m, H-4), 5.30 (1H, dt, $J = 1.2$, 10.5 Hz, H-6), 5.40 (1H, dt, $J = 1.3$, 17.3 Hz, H-6′), 5.65 (1H, d, $J = 5.9$ Hz, H-1), 6.01 (1H, m, H-5), 7.30 (3H, m, Ar–H), 7.51 (2H, d, $J = 7.1$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.1, 27.7, 73.8, 74.0, 81.6, 85.8, 111.9, 118.3, 127.7, 129.2, 131.7, 134.3, 136.5; ESIMS *m/z* calcd for $C_{15}H_{20}O_4NaS$ $[M+Na]^+$: 319.0980. Found: 319.0982.

4.6. 5,6-Dideoxy-1,2,3,4-di-*O*-isopropylidene-5-eno-L-*lyxo*-hexose-*S*-phenyl-monothiohemiacetal (17)

A solution of diol **15** (0.599 g, 2.16 mmol), dimethoxypropane (5.30 mL, 43.2 mmol) and camphorsulfonic acid (0.05 g, 0.22 mmol) in anhydrous CH_2Cl_2 (20 mL) was stirred at 0 °C for 1 h. The reaction was then quenched by the addition of satd aq $NaHCO_3$ and extracted with Et_2O. The organic extract was dried (Na_2SO_4) and concentrated under reduced pressure. FCC of the residue provided **17** (0.592 g, 87%): $R_f = 0.70$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ −11.3 (*c* 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.34, 1.36, 1.39, 1.47 (each 3H, all s, $(CH_3)_2C \times 2$), 3.85 (1H, dd, $J = 4.7$, 8.1 Hz, H-3), 4.14 (1H, dd, $J = 4.8$, 5.6 Hz, H-2), 4.42 (1H, dd, $J = 7.0$, 7.9 Hz, H-4), 5.19 (1H, dt, $J = 1.0$, 10.4 Hz, H-6), 5.38 (1H, dt, $J = 1.1$, 17.2 Hz, H-6′), 5.48 (1H, d, $J = 5.7$ Hz, H-1), 5.81 (1H, m, H-5), 7.22 (5H, m, Ar–H), 7.45 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.5, 27.1, 27.3, 27.8, 79.5, 80.4, 81.3, 85.5, 110.1, 112.2, 119.0, 127.6, 129.2, 131.8, 134.5, 135.7; ESIMS *m/z* 359.1 $[M+Na]^+$.

4.7. 5,6-Dideoxy-1,2,3,4-di-*O*-isopropylidene-5-eno-D-*ribo*-hexose-*S*-phenyl-monothiohemiacetal (18)

Treatment of diol **16** (0.232 g, 0.84 mmol) following the procedure that was described for **17** provided **18** (0.23 g, 82%): $R_f = 0.60$ (15%, EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$): δ 1.37, 1.45, 1.52, 1.58 (each 3H, all s, $(CH_3)_2C \times 2$), 4.09 (1H, dd, $J = 6.0$, 8.6 Hz, H-3), 4.17 (1H, dd, $J = 4.2$, 9.6 Hz, H-2), 4.72 (1H, t, $J = 6.2$ Hz, H-4), 5.32 (1H, dt, $J = 1.4$, 10.5 Hz, H-6), 5.45 (1H, dt, $J = 1.5$, 17.2 Hz, H-6′), 5.66 (1H, d, $J = 4.2$ Hz, H-1), 6.01 (1H, m, H-5), 7.30 (3H, m, Ar–H), 7.51 (2H, d, $J = 7.1$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 25.7, 26.9, 28.0, 28.3, 78.7, 79.0, 80.1, 87.7, 109.4, 112.6, 118.4, 127.3, 129.1, 129.2, 131.5, 133.0, 135.3; ESIMS *m/z* calcd for $C_{18}H_{24}O_4NaSSi$ $[M+Na]^+$: 359.1293. Found: 359.1297.

4.8. 6,7-Dideoxy-1,2,3,4-di-*O*-isopropylidene-6-eno-D-*gulo*-heptose-*S*-phenyl-monothiohemiacetal (19) and 6,7-dideoxy-1,2,3,4-di-*O*-isopropylidene-6-eno-L-*manno*-heptose-*S*-phenyl-monothiohemiacetal (20)

Treatment of alkene **17** (0.592 g, 1.9 mmol) following the ozonolysis-Grignard reaction sequence that was described for the preparation of **15/16** provided **19/20** as an approximately 2/1 inseparable mixture of alcohols (0.42 g, 66%): $R_f = 0.55$ (25%, EtOAc/petroleum ether): ^{1}H NMR ($CDCl_3$): δ 1.40, 1.41, 1.43, 1.44, 1.47, 1.49, 1.57, 1.58, 1.60 (12H, all s, $(CH_3)_2C \times 2$), 2.40 (0.5H, br d, $J = 8.3$ Hz, OH), 2.59 (0.5H, br s, $J = 3.6$ Hz, OH), 4.04 (1H, dd, $J = 6.4$, 11.5 Hz, H-3), 4.09 (1H, dd, $J = 6.8$, 10.4 Hz, H-4), 4.16 (0.5H, t, $J = 5.7$ Hz, H-2), 4.20 (0.5H, t, $J = 5.6$ Hz, H-2), 4.25 (1H, m, H-5), 5.26 (0.5H, dt, $J = 1.4$, 10.6 Hz, H-7), 5.27 (0.5H, dt, $J = 1.4$, 10.5 Hz, H-7), 5.40 (1H, dt, $J = 1.5$, 17.3 Hz, H-7′), 5.61 (1H, dd, $J = 3.7$, 5.1 Hz, H-1), 5.97 (1H, m, H-6), 7.31 (3H, m, Ar–H), 7.65 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ 26.4, 26.7, 27.2, 27.3, 27.4, 27.4, 27.7, 27.9, 29.8, 71.8, 73.2, 78.9, 81.7, 81.8, 82.1, 82.5, 86.4, 86.8, 110.4, 110.5, 112.4, 112.6, 116.9, 117.4, 127.6, 129.2, 131.7, 134.5, 136.4, 137.3; ESIMS *m/z* calcd for $C_{19}H_{26}O_5NaS$ $[M+Na]^+$: 389.1399. Found: 389.1396.

4.9. 6,7-Dideoxy-1,2,3,4-di-*O*-isopropylidene-6-eno-L-*talo*-heptose-*S*-phenyl-monothiohemiacetal (21)

Treatment of alkene **18** (0.208 g, 0.66 mmol) following the ozonolysis-Grignard reaction sequence that was described for the preparation of **15/16** provided alcohol **21** (0.15 g, 63%): $R_f = 0.76$ (20%, EtOAc/petroleum ether); $[\alpha]_D$ +89 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.26,1.37, 1.45, 1.51 (each 3H, all s, $(CH_3)_2C \times 2$), 2.47 (1H, d, $J = 6.9$ Hz, OH), 4.02 (1H, dd, $J = 6.1$, 9.1 Hz, H-3), 4.10 (1H, dd, $J = 4.0$, 6.0 Hz, H-4), 4.48–4.50 (2H, m, H-2, H-5), 5.15 (1H, dt, $J = 1.6$, 10.6 Hz, H-6), 5.36 (1H, dt, $J = 1.6$, 17.3 Hz, H-6′), 5.53 (1H, d, $J = 4.5$ Hz, H-1), 5.96 (1H, m, H-6), 7.23 (3H, m, Ar–H), 7.46 (2H, d, $J = 7.1$ Hz, Ar–H); ^{13}C NMR ($CDCl_3$): δ 25.2, 26.8, 27.6, 28.3, 69.6, 78.4, 79.6, 80.1, 88.3, 109.3, 112.8, 116.0, 127.4, 129.1, 131.6, 135.2, 137.9; ESIMS *m/z* calcd for $C_{19}H_{26}O_5NaS$ $[M+Na]^+$: 389.1399. Found: 389.1385.

4.10. 6,7,8-Trideoxy-1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-8-trimethylsilyl-6(*E*)-eno-D-*gulo*-octose-*S*-phenyl-monothiohemiacetal (22) and 1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-6,7,8-trideoxy-8-trimethylsilyl-6(*E*)-eno-L-*manno*-octose-*S*-phenyl-monothiohemiacetal (23)

Grubbs' catalyst second generation (39 mg, 0.05 mmol) in CH_2Cl_2 (3 mL) was injected at rt into a degassed solution of a mixture of **19/20** (320 mg, 0.93 mmol) and

allyltrimethylsilane (0.89 mL, 10.8 mmol) in CH_2Cl_2 (10 mL). After 2 h at this temperature, the reaction was quenched by the addition of DMSO (1 mL), stirred for an additional 5 h and concentrated in vacuo. The residue was purified by FCC to afford an approximately 2:1 mixture of products (0.369 g, 95%): $R_f = 0.82$ (15%, EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$): δ 0.0 (9H, s, TMS), 1.37, 1.38, 1.39, 1.48, 1.53 (12H, all s, $(CH_3)_2C \times 2$), 1.39–1.50 (2H, m buried under singlets, CH_2-8), 2.25 (1H, br m, OH's), 3.90–4.22 (4H, m, H-2,3,4,5), 5.35 (1H, m, H-6), 5.55 (0.4H, d, $J = 5.3$ Hz, H-1), 5.56 (0.6H, d, $J = 5.5$ Hz, H-1), 5.75 (1H, m, H-7), 7.22–7.30 (3H, m, Ar–H), 7.50 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ 1.68, 1.71, 23.2, 23.3, 26.5, 26.6, 27.2, 27.5, 27.8, 73.0, 73.8, 82.1, 82.3, 86.4, 110.2, 110.4, 112.3, 126.5, 127.1, 127.5, 127.6, 129.2, 131.5, 131.8, 132.0, 134.7; ESIMS m/z calcd for $C_{23}H_{36}O_5NaSSi$ $[M+Na]^+$: 475.1950. Found: 475.1938. DMAP (15 mg, 0.12 mmol), pyridine (0.34 mL, 4.2 mmol) and pivaloyl chloride (0.44 mL, 3.6 mmol) were added to a solution of the product from the previous step (269 mg, 0.59 mmol), in dry CH_2Cl_2 (10 mL). The mixture was stirred at rt for 12 h and then poured into H_2O and extracted with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. FCC of the residue gave an approximately 2:1 inseparable mixture of **22/23** (220 mg, 72%): $R_f = 0.85$ (15%, EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$): δ 0.0 (9H, s, TMS), 1.21 (9H, s, $(CH_3)_3CCO$), 1.39, 1.41, 1.43, 1.44, 1.48, 1.54, 1.56 (12H, all s, $(CH_3)_2C \times 2$), 1.45–1.52 (2H, m buried under singlets, CH_2-8), 4.00 (0.65H, t, H-2), 4.04 (0.35H, dd, $J = 5.5$, 6.8 Hz, H-2), 4.19 (2H, m, H-3,4), 5.28–5.39 (2H, m, H-5,6), 5.57 (1H, d, $J = 5.2$ Hz, H-1), 5.85 (1H, m, H-7), 7.29 (3H, m, Ar–H), 7.54 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ −1.78, 23.4, 23.5, 26.3, 26.6, 27.4, 27.5, 27.6, 27.7, 27.9, 74.0, 74.9, 80.2, 80.8, 82.1, 82.3, 85.9, 86.2, 110.5, 110.6, 112.3, 112.4, 122.4, 123.0, 127.5, 127.6, 129.1, 131.7, 131.8, 134.4, 134.5, 135.1; ESIMS m/z calcd for $C_{28}H_{44}O_6NaSSi$ $[M+H]^+$: 559.2526. Found: 559.2528.

4.11. 6,7,8-Trideoxy-1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-8-trimethylsilyl-6(*E*)-eno-L-*talo*-octose-*S*-phenylmonothiohemiacetal (24)

Allylic alcohol **21** (63 mg, 0.18 mmol) was subjected to the metathesis procedure that was used in the preparation of **22/23**. FCC of the crude product afforded the cross-metathesis product (0.074 g, 90%): $R_f = 0.67$ (10%, EtOAc/petroleum ether); $[\alpha]_D$ +51.2 (c 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.0 (9H, s, TMS), 1.32, 1.44, 1.55, 1.57 (each 3H, all s, $(CH_3)_2C \times 2$), 1.45–1.50 (2H, m buried under singlets, CH_2-8), 2.40 (1H, br d, $J = 5.7$, OH), 4.03 (1H, dd, $J = 6.1$, 8.6 Hz, H-3), 4.09 (1H, dd, $J = 4.6$, 5.9 Hz, H-4), 4.42–4.47 (1H, m, H-5), 4.50 (1H, dd, $J = 4.3$, 8.6 Hz, H-2), 5.45 (1H, dd, $J = 6.3$, 15.4 Hz, H-6), 5.62 (1H, d, $J = 4.3$, H-1), 5.79 (1H, m, H-7), 7.22–7.30 (3H, m, Ar–H), 7.51 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ −1.62, 23.3, 25.4, 27.0, 27.7, 28.3, 69.9, 78.4, 79.9, 80.8, 88.3, 109.1, 112.8, 127.4, 128.0, 129.2, 129.9, 131.6, 135.4; ESIMS m/z calcd for $C_{23}H_{36}O_5NaSSi$ $[M+Na]^+$: 451.1974. Found: 451.1955. Treatment of a sample of the material from the previous step (152 mg, 0.34 mmol) following the pivaloylation procedure that was used for **22/23** provided **24** (141 mg, 65%); $R_f = 0.84$ (15%, EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$): δ 0.0 (9H, s, TMS), 1.24 (9H, s, $(CH_3)_3CCO$), 1.34, 1.44, 1.53, 1.57 (each 3H, all s, $(CH_3)_2C \times 2$), 1.47–1.53 (2H, m, buried under singlets, CH_2-8), 4.03 (1H, dd, $J = 6.0$, 9.3 Hz, H-3), 4.21 (1H, dd, $J = 3.1$, 6.0 Hz, H-4), 4.26 (1H, dd, $J = 4.2$, 9.3 Hz, H-2), 5.42 (1H, m, H-6), 5.55 (1H, dd, $J = 4.0$, 7.5 Hz, H-5), 5.62 (1H, d, $J = 4.2$ Hz, H-1), 5.85 (1H, m, H-7), 7.27 (3H, m, Ar–H), 7.53 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$): δ 1.77, 23.3, 25.6, 26.9, 27.2, 27.4, 28.4, 39.1, 72.0, 78.2, 79.7, 79.8, 88.4, 109.4, 112.8, 124.1, 127.2, 129.1, 131.5, 132.9, 178.2; ESIMS m/z 554.2 ($M+NH_4$).

4.12. 6-Deoxy-6-*C*-ethenyl-1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*myo*-inositol (3) and 6-deoxy-6-*C*-ethenyl-1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*neo*-inositol (4)

A mixture of **22/23** (316 mg, 0.61 mmol), 2,6-di-*t*-butyl-4-methylpyridine (1.38 g, 6.70 mmol), and freshly activated, powdered 4 Å molecular sieves (700 mg) in anhydrous CH_2Cl_2 (4 mL), was stirred under an argon atmosphere for 15 min at rt, then cooled to 0 °C. Methyl triflate (0.62 mL, 5.5 mmol) was introduced, and the reaction warmed to rt and stirred for an additional 18 h, at which time Et_3N (1 mL) was added. The mixture was diluted with Et_2O, washed with satd aq $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and evaporated zunder reduced pressure. FCC of the residue afforded **3** (79 mg, 41%) and **4** (37 mg, 19%). For **3**: $R_f = 0.22$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ −27.5 (c 1.0, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.18 (3H, s, $(CH_3)_2C$), 1.2 (9H, s, $(CH_3)_3CCO$), 1.38, 1.41, 1.45 (each 3H, all s, $(CH_3)_2C$), 2.61 (1H, dt, $J = 7.3$, 6.3 Hz, H-6), 3.37 (1H, dd, $J = 3.1$, 10.0 Hz, H-3), 3.80 (1H, dd, $J = 5.4$, 6.5 Hz, H-1), 4.27 (1H, dd, $J = 3.1$, 5.2 Hz, H-2), 4.48 (1H, t, $J = 9.7$ Hz, H-4), 5.50 (1H, br d, $J = 10.6$ Hz, H-8), 5.12 (1H, br d, $J = 17.1$ Hz, H-8′), 5.21 (1H, t, $J = 8.9$ Hz, H-5), 5.70 (1H, ddd, $J = 17.3$, 10.3, 7.9 Hz, H-7); ^{13}C NMR ($CDCl_3$): δ 25.4, 26.9, 27.2, 27.3, 27.6, 38.9, 51.2, 72.4, 73.0, 74.6, 75.3, 78.8, 111.4, 111.6, 118.6, 135.9, 177.9; ESIMS m/z calcd for $C_{19}H_{31}O_6$ $[M+H]^+$: 355.21. Found 355.21. For **4**: $R_f = 0.39$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ −6.7 (c 0.2, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.15 (9H, s, $(CH_3)_3CCO$),

1.23, 1.33, 1.36, 1.45 (each 3H, all s, $(CH_3)_2C \times 2$), 2.27 (1H, m, H-6), 3.92 (1H, dd, $J = 4.6$, 8.4 Hz, H-1), 4.01 (1H, dd, $J = 1.9$, 10.1 Hz, H-4), 4.05 (1H, dd, $J = 2.7$, 10.1 Hz, H-3), 4.42 (1H, dd, $J = 2.7$, 4.5 Hz, H-2), 5.09 (1H, dt, $J = 1.3$, 10.6 Hz, H-8), 5.19 (1H, dt, $J = 1.4$, 17.4 Hz, H-8′), 5.63 (1H, t, $J = 2.5$ Hz, H-5), 5.71 (1H, ddd, $J = 17.2$, 10.6, 6.3 Hz, H-7); ^{13}C NMR (C_6D_6): δ 27.0, 27.5, 27.6, 28.0, 29.1, 39.6, 48.4, 69.4, 73.7, 74.3, 74.4, 79.0, 111.2, 111.9, 117.9, 136.0, 176.8; ESIMS m/z calcd for $C_{19}H_{31}O_6$ $[M+H]^+$: 355.2121. Found: 355.2119.

4.13. 1-Deoxy-1-*C*-ethenyl-2,3,4,6-di-*O*-isopropylidene-6-*O*-pivaloyl-D-*epi*-inositol (5) and 6-deoxy-6-*C*-ethenyl-1,2,3,4-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*allo*-inositol (6)

Allylsilane **24** (88 mg, 0.17 mmol) was subjected to the procedure that was used for the preparation of **3** and **4**. FCC of the crude product afforded recovered **24** (10 mg), **5** (40 mg, 74% based on recovered **24**) and **6** (12 mg, 22% based on recovered **24**). For **5**: $R_f = 0.59$ (15%, EtOAc/petroleum ether); $[\alpha]_D$ −94.0 (*c* 2.2, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.11 (3H, s, $(CH_3)_2C$), 1.18 (9H, s, $(CH_3)_3CCO$), 1.30 (3H, s, $(CH_3)_2C$), 1.63 (6H, s, $(CH_3)_2C$), 1.77 (1H, ddd, $J = 3.8$, 9.4, 12.7 Hz, H-1), 3.81–3.86 (2H, m, H-2, H-4), 4.16 (1H, dd, $J = 3.6$, 6.8 Hz, H-3), 4.24 (1H, t, $J = 7.4$ Hz, H-5), 4.98 (1H, dd, $J = 2.1$, 17.2 Hz, H-8), 5.02 (1H, dd, $J = 2.1$, 10.2 Hz, H-8′), 5.88 (1H, dd, $J = 7.1$, 12.4 Hz, H-6), 6.08 (1H, ddd, $J = 2,4$, 9.9, 17.2 Hz, H-7); ^{13}C NMR (C_6D_6): δ 24.7, 26.3, 26.8, 27.1, 27.8, 39.0, 48.4, 71.1, 74.5, 74.5, 76.8, 78.9, 109.7, 111.1, 118.4, 136.1, 177.2; ESIMS m/z calcd for $C_{19}H_{31}O_6$ $[M+H]^+$: 355.2121. Found: 355.2129. For **6**: $R_f = 0.63$ (15%, EtOAc/petroleum ether) $[\alpha]_D$ +32.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.18 (9H, s, $(CH_3)_3CCO$), 1.34, 1.41, 1.52, 1.57 (each 3H, s, $(CH_3)_2C \times 2$), 2.95 (1H, ddd, $J = 1.5$, 6.3, 7.7 Hz, H-6), 4.13 (1H, dd, $J = 2.1$, 6.9 Hz, H-4), 4.33 (1H, t, $J = 7.4$ Hz, H-1), 4.38 (1H, dd, $J = 3.9$, 7.2 Hz, H-2), 4.55 (1H, dd, $J = 3.9$, 6.9 Hz, H-3), 4.99 (1H, br s, H-5), 5.20 (1H, d, $J = 10.5$ Hz, H-8), 5.25 (1H, d, $J = 16.3$ Hz, H-8′), 5.83 (1H, ddd, $J = 6.4$, 10.5, 17.1 Hz, H-7); ^{13}C NMR ($CDCl_3$): δ 24.3, 25.5, 26.6, 26.8, 27.3, 39.1, 41.2, 73.3 (2C), 73.4, 74.8, 75.2, 109.8, 110.1, 117.3, 136.8, 177.1; ESIMS m/z calcd for $C_{19}H_{31}O_6$ $[M+H]^+$: 355.2121. Found: 355.2117.

4.14. 1,2,3,4,5-Penta-*O*-acetyl-6-deoxy-6-*C*-ethenyl-D-*myo*-inositol (25)

Compound **3** (37 mg, 0.1 mmol) was dissolved in CH_2Cl_2 (2 mL), and DIBALH (0.16 mL, 0.14 mmol) was added at −78 °C. The reaction was warmed to rt, stirred for an additional 3 h at this temperature, then quenched by the addition of satd aq potassium sodium tartrate tetrahydrate. The mixture was stirred until the appearance of two layers, then extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude material was filtered through a plug of silica gel, and the filtrate evaporated to dryness. The residue was dissolved in CH_3OH (2 mL) and concentrated HCl (0.05 mL) added to the solution. The mixture was stirred for 6 h, then adjusted to pH 7 by addition of a solution of $NaOCH_3$ in CH_3OH. The solvent was removed in vacuo and pyridine (0.2 mL), EtOAc (2 mL), Ac_2O (0.28 mL, 3 mmol) and DMAP (6 mg, 0.05 mmol) were added to the residue. The reaction mixture was stirred at rt for 12 h, then quenched with CH_3OH (0.2 mL) and concentrated under reduced pressure. The residue was purified by FCC to afford **25** (40 mg, 86%): $R_f = 0.42$ (30%, EtOAc/petroleum ether); $[\alpha]_D$ +5.5 (*c* 3.0, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.61, 1.65, 1.68, 1.72, 1.78 (each 3H, s, CH_3CO), 2.93 (1H, dt, $J = 11.2$, 9.4 Hz, H-6), 4.94 (1H, dd, $J = 2.6$, 11.5 Hz, H-1), 4.99 (1H, dd, $J = 1.5$, 10.0 Hz, H-8), 5.06 (1H, dd, $J = 1.0$, 16.7 Hz, H-8′), 5.12 (1H, t, $J = 10.3$ Hz, H-5), 5.19 (1H, dd, $J = 2.8$, 10.5 Hz, H-3), 5.52 (1H, ddd, $J = 2.3$, 9.7, 17.1 Hz, H-7), 5.80 (1H, t, $J = 10.1$ Hz, H-4), 5.87 (1H, t, $J = 2.6$ Hz, H-2); ^{13}C NMR (C_6D_6): δ 20.5 (3C), 20.6, 20.7, 47.6, 69.0, 69.9, 70.0, 71.2, 71.4, 120.4, 135.1, 169.2, 169.5, 169.5, 170.0, 170.0; ESIMS m/z calcd for $C_{18}H_{25}O_{10}$ $[M+H]^+$: 401.1448. Found: 401.1443.

4.15. 1,2,3,4,5-Penta-*O*-acetyl-6-deoxy-6-*C*-ethenyl-D-*neo*-inositol (26)

Treatment of **4** (37 mg, 0.10 mmol) following the identical three-step procedure that was used for **25** provided **26** (38 mg, 90%): $R_f = 0.45$ (30%, EtOAc/petroleum ether); $[\alpha]_D$ −6.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.54, 1.60, 1.63, 1.72, 1.74 (each 3H, all s, CH_3CO), 3.13 (1H, ddd, $J = 2.6$, 8.0, 11.1 Hz, H-6), 4.89 (1H, d, $J = 17.3$ Hz, H-8), 4.9 (1H, d, $J = 10.1$ Hz, H-8′), 5.62 (1H, ddd, $J = 7.9$, 10.6, 17.2 Hz, H-7), 5.6 (1H, dd, $J = 2.8$, 11.7 Hz, H-1), 5.62 (1H, dd, $J = 2.9$, 10.9 Hz, H-4), 5.72 (1H, dd, $J = 2.9$, 10.9 Hz, H-3), 5.79 (1H, t, $J = 2.8$ Hz, H-5), 6.12 (1H, t, $J = 2.8$ Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 20.8, 20.9 (3C), 21.0, 43.0, 67.9, 68.0, 69.6, 69.7, 70.3, 120.1, 132.7, 169.9, 170.0, 170.2 (2C), 170.5; ESIMS m/z calcd for $C_{18}H_{25}O_{10}$ $[M+H]^+$: 401.1448. Found: 401.1439.

4.16. 2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-*C*-ethenyl-D-*epi*-inositol (27)

Treatment of **5** (74 mg, 0.20 mmol) following the identical three-step procedure that was used for **25** provided **27** (66 mg, 80%): $R_f = 0.34$ (30%, EtOAc/petroleum ether); $[\alpha]_D$ −8.84 (*c* 1.9, $CHCl_3$); ^{1}H NMR (C_6D_6): δ 1.66, 1.68, 1.69 (each 3H, all s, CH_3CO), 1.73 (6H, s,

CH_3CO), 1.93 (1H, ddd, $J = 2.9$, 8.5, 11.2 Hz, H-1), 4.84 (1H, t, $J = 3.34$ Hz, H-5), 4.92 (1H, d, $J = 17.2$ Hz, H-8), 4.97 (1H, d, $J = 10.3$ Hz, H-8′), 5.06 (1H, dd, $J = 3.3$, 10.3 Hz, H-3), 5.48 (1H, br t, $J = 3.3$ Hz, H-6), 5.68 (1H, ddd, $J = 8.4$, 10.3, 17.3 Hz, H-7), 5.8 (1H, t, $J = 10.7$ Hz, H-2), 5.84 (1H, br t, $J = 3.3$ Hz, H-4); ^{13}C NMR (C_6D_6): δ 20.5, 20.6, 20.7, 20.8, 46.6, 68.2, 68.9, 70.1, 71.2, 71.8, 119.9, 133.6, 169.3, 169.7, 169.8, 169.9, 170.1; ESI HRMS calcd for $C_{18}H_{25}O_{10}$ $[M+H]^+$: 401.1448. Found: 401.1439.

4.17. 1,2,3,4,5-Penta-*O*-acetyl-6-deoxy-6-*C*-ethenyl-D-*allo*-inositol (28)

Treatment of **6** (19 mg, 0.05 mmol) following the identical three-step procedure that was used for **25** provided **28** (18 mg, 86%): $R_f = 0.32$ (30%, EtOAc/petroleum ether); $[\alpha]_D$ +1.9 (*c* 1.2, $CHCl_3$); ^1H NMR (3% v/v $CDCl_3/C_6D_6$): δ 1.58, 1.73, 1.74, 1.74, 1.79 (each 3H, all s, CH_3CO), 3.16 (1H, m, H-6), 5.03 (1H, dt, $J = 1.1$, 10.5 Hz, H-8), 5.11 (1H, dt, $J = 1.2$, 17.3 Hz, H-8′), 5.38 (1H, t, $J = 3.4$ Hz, H-3), 5.41 (1H, dd, $J = 3.6$, 5.0 Hz, H-5), 5.46–5.51 (2H, m, H-1, H-4), 5.60 (1H, ddd, $J = 7.9$, 10.5, 17.3 Hz, H-7), 5.69 (1H, br t, $J = 3.4$ Hz, H-2); ^{13}C NMR (3% v/v $CDCl_3/C_6D_6$): δ 20.3, 20.6, 20.7 (2C), 20.8, 41.5, 67.9, 68.1 (2C), 69.2, 71.3, 120.0, 133.6, 169.2, 169.4, 169.6, 169.8, 170.0; ESIMS *m/z* calcd for $C_{18}H_{25}O_{10}$ $[M+H]^+$: 401.1448. Found: 401.1435.

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Supplementary data

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