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Synthesis, crystal structure, and reactivity of a D-xylose based oxepine

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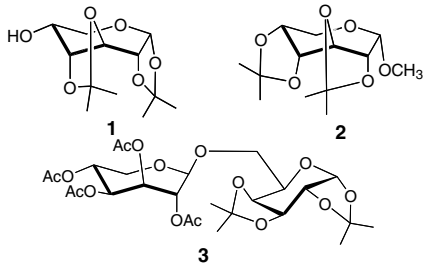
Abstract—The synthesis and X-ray crystal structure of a D-xylose-based oxepine (**9**) are reported. The oxepine was prepared from 2,3,4-tri-*O*-benzyl-D-xylose by the three-step sequence (Wittig olefination, vinyl ether formation, and ring closing metathesis) we recently reported. Epoxidation of this cyclic enol ether (**9**) using dimethyldioxirane (DMDO) gave 1,2-anhydro-β-D-idoseptanose (**10**), which was trapped by a number of nucleophiles to give α-idoseptanosides. The stereochemistry of epoxidation was assigned based on product analysis. Spectroscopic data of methyl 2,3,4,5-tetra-*O*-acetyl-α-D-idoseptanoside, derived from the methanolysis product **11**, was compared to data of its enantiomer, the known methyl 2,3,4,5-tetra-*O*-acetyl-α-L-idoseptanoside.

Keywords: Septanose carbohydrates; Oxepine; D-Idoseptanoside; Glycosylation

1. Introduction

Septanoses, or seven-membered ring sugars are homologs of pyranoses. Their similarity to natural carbohydrates suggests that they should have interesting and potentially useful physical, chemical, and biological properties. There are many examples of hydroxylated oxepines in fused polycyclic marine natural products, but no natural seven-membered ring carbohydrates are known.[1] Septanose carbohydrates are conceptually similar to homologated versions of nucleic acids and protein monomers. Such oligomers of these monomers have provided new unnatural structures and interesting biological activity.[2] The synthesis and conformational analysis of septanose carbohydrates has received only limited attention however. Here we report the synthesis, X-ray crystal structure, and chemical reactivity of an oxepine derived from 2,3,4-tri-*O*-benzyl-D-xylose. Specifically, 1,6-anhydro-3,4,5-tri-*O*-benzyl-2-deoxy-D-xylosept-1-enitol (**9**) was treated with dimethyldioxirane (DMDO) to give 3,4,5-tri-*O*-benzyl-1,2-anhydro-β-D-idoseptanose (**10**) stereoselectively; the anhydroseptanose was then trapped by a number of nucleophiles to give the corresponding septanosides.



1 2 3

An initial challenge to the systematic investigation of septanose structure and function is the identification of general synthetic routes for their preparation. For example, Stevens and co-workers[3–7] have made considerable progress in the preparation of mono-septanosides that correspond to the natural aldohexoses. Treatment of D-glucose with either acidified acetone or acidified acetone–methanol forms 1,2;3,4-di-*O*-isopropylidene-α-D-glucoseptanose (**1**)[3] and methyl 2,3;4,5-di-*O*-isopropylidene-α-D-glucoseptanoside (**2**),[4] respectively.

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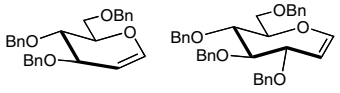
Selective refunctionalization of **1** and **2** have given L-*ido*-,[5] L-*altro*-,[6] D-*gulo*-,[6] and D-*galacto*-[6] derivatives. Preferred conformations of these derivatives have been described in both solution and solid state.[3–7] A general preparation of pyranosyl septanosides has been reported by McAuliffe and Hindsgaul.[8] Acceptors were glycosylated by acyclic chloro-thioethyl acetals to give mixed O,S acetals. The primary alcohol of the acyclic donor was then selectively deprotected and cyclized using a thiophilic promoter to give pyranosyl septanosides such as **3**. Other synthetic strategies for seven-membered ring monosaccharides have also been reviewed.[9]

We endeavored to utilize the known transformations of glycals (**4**)[10] in the preparation of septanose carbohydrates from oxepines (**5**). Toward this end, we have recently reported a concise synthetic preparation of oxepines from protected pyranoses.[11] Here we describe in detail the synthesis of an oxepine using 2,3,4-tri-*O*-benzyl-D-xylose (**6**) as starting material. We report the crystal structure of oxepine **9** and its oxidative coupling with a number of nucleophiles using DMDO as an electrophilic promoter. The results demonstrate the chemical similarity between carbohydrate-based oxepines and glycals and suggest that the synthesis of septanose oligosaccharides should be possible.

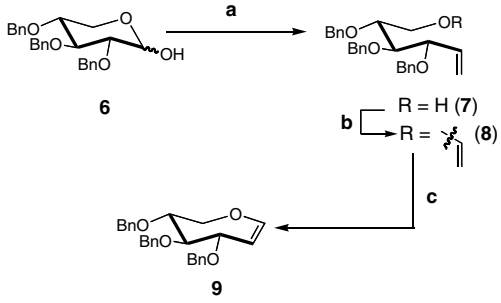


4 **5**

2. Results and discussion

2.1. Synthesis and X-ray crystal structure of oxepine (9)

The preparation of **9** followed a new procedure we recently developed for converting protected pyranoses to the corresponding oxepine using a ring-closing metathesis (RCM) strategy.[11] 2,3,4-Tri-*O*-benzyl-D-xylose (**6**) was treated sequentially with *n*-butyllithium and methylene triphenylphosphane to give heptenitol (**7**) (Scheme 1) in 63% yield.[12] The resulting hydroxyl group was then converted to the vinyl ether **8** using $Pd(OAc)_2$ and 1,10-phenanthroline in the presence of ethyl vinyl ether (90%).[13] The RCM conditions were changed slightly relative to the original report. The initial procedure called for addition of Schrock catalyst[14] to a solution of the diene in toluene followed by heating to 60 °C for 4 h. The new conditions changed only the temperature of the reaction. Schrock catalyst was added to **8** in toluene and stirred at room temperature for 2 h. The revised procedure gave oxepine **9** in 85% yield relative to 82% for the original procedure.[11] The overall yield of **9** over three steps was 48%.



Scheme 1. Reagents and conditions: (a) *n*-BuLi, $CH_2{=}P(Ph)_3$, THF (63%), (b) $Pd(OAc)_2$, 1,10-phenanthroline, $CH_2{=}CHOEt$, CH_2Cl_2 40 °C (90%), (c) 2,6-diisopropylphenylimidoneophylidenemolybdenum(VI) bis(hexafluoro-*t*-butoxide) (Schrock catalyst) 20 mol%, CH_3Ph (85%).

Oxepine **9**, a white solid, was recrystallized from petroleum ether to give crystals suitable for X-ray analysis. The molecular structure of **9** (Fig. 1) showed that it is in a slightly distorted twist chair (TC). It most closely resembled a $^{6,O}TC_{4,5}$ conformation.[15] The deviation from the TC conformation is presumably due to the shortened planar C-1–C-2 (C-6–C-5 in ORTEP numbering) bond. The O–C-6–C-5–C-4 (ORTEP numbering) unit, which includes the enol ether functionality is nearly co-planar, with a dihedral angle about the C-1–C-2 bond of 6.3°. Selected crystal and structural refinement data are given in Table 1.

2.2. Stereoselective oxidation of 9 using dimethyldioxirane (DMDO)

The mild oxidizing agent DMDO has been used extensively to convert glycals into 1,2-anhydro sugars that serve as glycosyl donors when exposed to nucleophiles.[10a] For glycals, epoxide formation *anti* relative to the benzyloxy substituent at C-3 has been most often

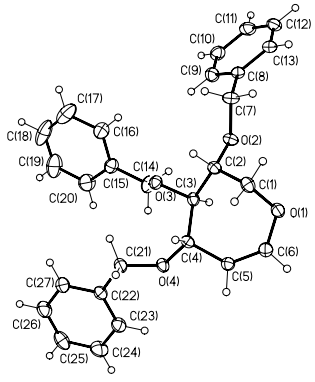
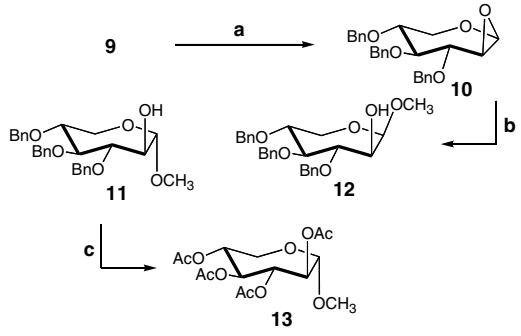


Figure 1. ORTEP diagram of 1,6-anhydro-3,4,5-tri-*O*-benzyl-2-deoxy-D-xylosept-1-enitol (**9**).

Table 1. Crystal data and structure refinement for **9**

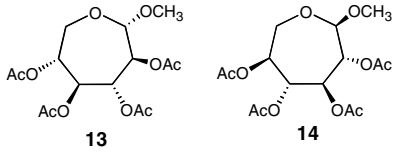
Empirical formula	$C_{27}H_{28}O_4$
Formula weight	416.49
Temperature	183(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_{(1)}$
Unit cell dimensions	$a = 11.512(2)$ Å $\alpha = 90°$ $b = 4.5899(9)$ Å $\beta = 94.97(3)°$ $c = 21.155(4)$ Å $\gamma = 90°$
Volume	1113.6(4) Å^3
Z	2
Density (calculated)	1.242 g/cm^3
Absorption coefficient	0.82 cm^{-1}
$F(000)$	444
Crystal size	$0.35 \times 0.10 \times 0.05$ mm^3
Theta range for data	1.95–28.35°
Index ranges	$-15 <= h <= 15$, $-5 <= k <= 5$, $-28 <= l <= 27$
Reflections collected	4279
Independent reflections	4279 [R(int) = 0.0000]
Completeness to theta = 28.35°	93.8%
Absorption correction	None
Max & min transmiss.	0.9959 and 0.9718
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4279/1/280
Goodness-of-fit on F^2	1.041
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0512$, $wR2 = 0.1159$
R indices (all data)	$R1 = 0.0915$, $wR2 = 0.1336$
Absolute structure parameter	0.3(12)
Largest diff. peak and hole	0.158 and −0.173 eÅ^{-3}



Scheme 2. Reagents and conditions: (a) DMDO, CH_2Cl_2, 0 °C, (b) CH_3OH (60%, two steps) **11**–**12** 4:1, (c) (i) H_2, 10% Pd/CCH_3OH; (ii) Ac_2O, pyridine (80%, two steps).

observed.[16] Epoxidation of **9** was conducted using DMDO in dry dichloromethane (CH_2Cl_2) (Scheme 2) at 0 °C over 0.5 h. Observation of the 1,2-anhydroseptanose species by NMR indicated selective formation (>25:1) of one epoxide. The spectroscopic data were not able to rigorously define the stereochemistry of the epoxide. Rather, spectroscopic data from a methyl septanoside derived from this epoxide was compared to a literature compound.

Specifically, epoxidation of **9** followed by exposure to methanol gave a 60% yield of a mixture of two methyl septanoside isomers **11** and **12** in a 4:1 ratio. The major isomer (**11**) was subjected to hydrogenolysis conditions and subsequently protected as the peracetate to give methyl 2,3,4,5-tetra-*O*-acetyl-α-D-idoseptanoside (**13**) (80% over two steps). Comparison of the $^3J_{H1,H2}$ (6.5 Hz) and $[\alpha]_D$ +79.8 (*c* 1.53) values of **13** with those recently reported for methyl 2,3,4,5-tetra-*O*-acetyl-α-L-idoseptanoside (**14**)[5c] (6.46 Hz, −85.1°, *c* 1.03) indicated that they were enantiomers. A sample of methyl α-L-idoseptanoside supplied by Stevens was acetylated to give **14**. In our hands, **14** gave $^3J_{H1,H2}$ of 6.5 Hz and $[\alpha]_D$ −75.5 (*c* 1.78). These data secured the identity of **10** as 1,2-anhydro-3,4,5-tri-*O*-benzyl-β-D-idoseptanose. The minor product of methanolysis of **10** was assigned as structure **12**, based on spectroscopic data, the high selectivity of epoxidation evidenced by the NMR data for **10**, and the highly selective formation of α-septanosides by other nucleophiles (see later). We propose that **12** arose by formation of an oxonium ion and subsequent β-attack by methanol.



2.3. Addition of nucleophiles to 1,2-anhydro-3,4,5-tri-O-benzyl-β-D-idoseptanose (10)

Table 2 collects the results from the addition of several nucleophiles to 1,2-anhydroseptanose **10**. All reactions that use **10** as a glycosyl donor were conducted as a two-step sequence; **9** was epoxidized to **10** using DMDO, then exposed to the nucleophile under the conditions noted. Similar to the reaction of **10** with methanol, the addition of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose gave two septanosides, **15** and **16** (Fig. 2) in 45% yield with a α/β ratio of 3:2. Addition of 2-propanol or ethanethiol[17] gave exclusively the α-septanosides **17** and **18** in 69% and 32% yields, respectively. All of the above reactions were either under protic or Lewis acidic conditions. We suspected that these reaction conditions may have facilitated oxonium ion formation that resulted in the α/β mixtures in entries 1 and 2. The occurrence of anomeric mixtures in these cases suggested that the thermodynamic stabilities of the α- and β-septanosides may be similar; the specific collection of factors that contribute to their respective energies are expected to be difficult to rationalize. Toward this end, we are currently using a combination of computational and spectroscopic methods to investigate the low energy conformations of septanose carbohydrates.

Table 2. Reactions of various nucleophiles with 1,2-anhydroseptanose **10**

Entry	Nucleophile	Conditions	Product(s)	Yield (%)	α/β
1	CH_3OH	CH_3OH, rt	**11**, **12**	60	4:1
2	1,2;3,4-Di-*O*-isopropylidene-α-D-galactopyranose	$ZnCl_2$, THF, −78 °C to rt	**15**, **16**	45	3:2
3	$(CH_3)_2CHOH$	$(CH_3)_2CHOH$, rt	**17**	69	α
4	CH_3CH_2SH	TFAA, −78 °C	**18**	32	α
5	$NaOCH_3$	CH_3OH, rt	**11**	89	α
6	AllylMgBr	THF, −10 °C	**19**	33	α
7	NaN_3	aq DMF, rt	**20**	69	α
8	LiSPh	THF, 0 °C	**21**	73	α

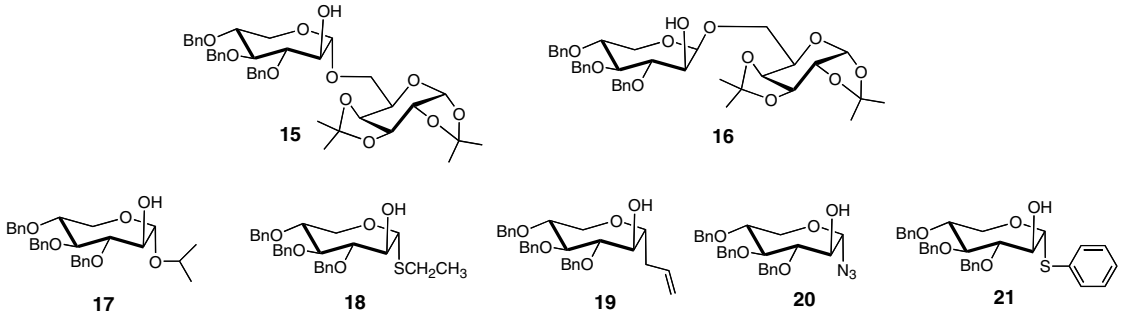


Figure 2. Septanoside products from nucleophilic attack on 1,2-anhydroseptanose **10**.

Anionic additions to 1,2-anhydro sugars have been reported previously.[18] The addition of anionic nucleophiles to **10** gave the α-septanosides **11**, **19**, **20**, and **21** when using oxygen, carbon, nitrogen, and sulfur-based nucleophiles (entries 5–8). The assignment of stereochemistry for septanosides **17**–**21** was done based on the similarity of their NMR spectral data to methyl septanoside **11**. Sodium methoxide addition to **10** cleanly gave **11** in high yield (89%) confirming the selective epoxidation of **9** and demonstrating the enhanced nucleophilicity of anions. The efficiency in forming azido septanoside **20** (69%) and thiophenyl septanoside **21** (73%) are noteworthy. First, azide **20** should be able to be selectively functionalized (via reduction–acylation sequence, for example) to supply new septanoside glycoconjugates. Access to **21** suggests that it too may be used as a glycosyl donor in the preparation of additional septanosides. In all the examples (**11**, **12**, **15**–**21**), the C-2 alcohol can also be selectively functionalized.

In summary, we have demonstrated that 1,2-anhydroseptanoses such as **10**, derived from oxepines can serve as glycosyl donors in the preparation of septanose carbohydrates. The reactivity demonstrated is directly analogous to glycal chemistry. We have also gained access to another class of glycosyl donor such as the thiophenyl septanoside **21** via oxepine **9**. Current efforts are to evaluate the reactivity of oxepines such as **9** under alternative reaction conditions in the synthesis of septanose carbohydrates.[19]

3. Experimental

3.1. General methods

Unless stated otherwise, all reactions were conducted at room temperature (rt) under nitrogen atmosphere. 3,4,5-tri-*O*-benzyl-D-xylose was synthesized by the route of Tsuda et al.[20] Schrock catalyst was purchased from Strem Chemicals (Newburyport, MA). DMDO was generated as described in Ref. 21. Reactions were monitored by TLC (silica gel, 60 Å, F_{254}, 250 μm). Visualization was conducted either under UV light or by charring with 2.5% *p*-anisaldehyde in H_2SO_4, AcOH, and EtOH solution. Preparative chromatography was conducted on silica gel (60 Å, 32–63 μm, Sorbent Technologies, Atlanta, GA). Melting points are uncorrected. Optical rotations were measured at 22 ± 2 °C. ^{1}H NMR spectra were collected at 400 MHz with chemical shifts referenced to $(CH_3)_4Si$ (δ_H 0.00 ppm) or $CHCl_3$ (δ_H 7.27 ppm). ^{13}C NMR were collected at 100 MHz and referenced to $CDCl_3$ (δ_C 77.2 ppm).

3.2. 3,4,5-Tri-*O*-benzyl-1,2-dideoxy-D-xylohept-1-enitol (7)

Into a flame dried round-bottom flask was added methyl triphenylphosphonium bromide (4.46 g, 12.5 mmol) and dry THF (30 mL) to make a white suspension, which was cooled to 0 °C on an ice bath. *n*-Butyllithium

(7.8 mL, 1.6 M) was added dropwise with stirring and gave a clear, dark-orange solution of methylene triphenylphosphane. This solution was stirred at 0 °C for 10 min, then allowed to warm to rt over 30 min. In a separate flask, residual water was removed from 2,3,4-tri-*O*-benzyl-D-xylose (**6**) (1.50 g, 3.57 mmol) via azeotropic distillation from toluene (3 × 15 mL) under reduced pressure. The residue was dissolved in dry THF (5 mL) and cooled to 0°C on an ice bath. *n*-Butyllithium (2.2 mL, 1.6 M) was added dropwise with stirring. This solution was then added to the methylene triphenylphosphane solution via canula and stirred for 24–40 h. The reaction was quenched by addition of aq NH_4Cl and the solvent was removed under reduced pressure. The resulting orange oil was dissolved in CH_2Cl_2 (25 mL) and washed with brine (25 mL) and water (25 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified by column chromatography, using 3:2 hexanes–EtOAc as eluent to give **7** (0.940 g, 63%) as a clear colorless oil. $[\alpha]_D$ +5.6 (*c* 2.43, $CHCl_3$); IR (KBr) cm^{-1} 3447.13, 3063.37, 3029.62, 2870.52, 1496.49, 1454.06, 1209.15, 1064.51, 734.75, 697.14; ^1H NMR ($CDCl_3$) δ 7.38–7.32 (m, 15 H), 5.86 (ddd, 1 H, *J* 17.5, 10.5, 7.5 Hz), 5.30 (d, 1 H, *J* 7.5 Hz), 5.26 (s, 1 H), 4.72 (d, 1 H, *J* 11.7 Hz), 4.69 (d, 1 H, *J* 11.7 Hz), 4.57 (m, 4 H), 4.35 (d, 1 H, *J* 11.7 Hz), 4.18 (dd, 1 H, *J* 7.3, 4.1 Hz, 1) 3.68 (m, 3 H), 3.54 (d, 1 H, *J* 9,2 Hz); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.5, 138.2, 135.3, 128.8, 128.6(3), 128.2, 128.1, 128.0, 127.9, 127.2, 119.1, 81.9, 80.6, 79.8, 75.0, 73.0, 70.9, 61.7; anal. calcd for $C_{27}H_{30}O_4$: C, 77.48; H, 7.22; O, 15.29; found C, 77.14; H, 6.93.

3.3. 3,4,5-Tri-*O*-benzyl-1,2-dideoxy-6-*O*-vinyl-D-xylo-hept-1-ene (8)

Ethylvinyl ether (40 mL) and CH_2Cl_2 (5 mL) were combined in a flame dried round-bottom flask. To this mixture was added 1,10-phenanthroline (0.052 g, 29 mmol) followed by $Pd(OAc)_2$ (0.065 g, 0.29 mmol), which was allowed to stir for 15 min. To this mixture was added **7** (0.81 g, 1.94 mmol) in CH_2Cl_2 (5 mL). The flask was fitted with a condenser and refluxed for 3 days. The solvent was removed under reduced pressure and the dark oily residue was purified by column chromatography using 4:1 hexanes–EtOAc as eluent to give **8** (0.775 g, 90%) as a clear colorless oil. $[\alpha]_D$ +8.4 (*c* 2.65, $CHCl_3$); IR (KBr) cm^{-1} 3063.37, 3029.62, 2871.49, 1616.06, 1496.49, 1454.06, 1321.00, 1200.47, 1087.66, 734.75, 697.14; ^1H NMR ($CDCl_3$) δ 7.41–7.33 (m, 15 H), 6.46 (dd, 1 H, *J* 14.3, 6.8 Hz), 5.90 (ddd, 1 H, *J* 16.9, 10.9, 7.7 Hz), 5.35 (s, 1 H), 5.31 (d, 1 H, *J* 7.4 Hz), 4.84 (dd, 1 H, *J* 11.2, 11.2 Hz), 4.75 (dd, 2 H, *J* 11.5, 3.6 Hz), 4.68 (d, 1 H, *J* 11.7 Hz), 4.61 (d, 1 H, *J* 11.7 Hz), 4.45 (d, 1 H, *J* 11.7 Hz), 4.19 (dd, 1 H, *J* 6.6, 6.6 Hz), 4.12 (dd, 1 H, *J* 14.3, 1.9 Hz), 4.01 (dd, 1 H, *J* 6.7, 1.9 Hz), 3.91 (m, 1 H), 3.85 (dd, 1 H, *J* 10.6, 4.2 Hz), 3.79 (dd, 1 H, *J* 10.5, 5.8 Hz), 3.69 (dd, 1 H, *J* 5.1, 5.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7, 138.7, 138.6, 138.5, 134.6, 128.6, 128.4(2), 128.1, 128.0, 127.7(2), 118.9, 86.9, 81.4, 81.1, 77.8, 75.2, 73.2, 70.8, 68.1; FAB-MS *m*/*z* $[M+H]^+$ calcd 445.2379, found 445.2401.

3.4. 1,6-Anhydro-3,4,5-tri-*O*-benzyl-2-deoxy-D-xylosept-1-enitol (9)

The following reaction was conducted in a glove box. Diene **8** (0.485 g, 1.10 mmol) was dissolved in toluene (195 mL). To this solution was added 2,6-diisopropylphenylimidoneophylidenemolybdenum(VI) bis-(hexafluoro-*t*-butoxide) (Schrock catalyst) (0.168 g, 0.22 mmol) in toluene (5 mL). The mixture was stirred in the glove box for 4 h, then removed from the box and the solvent was removed under reduced pressure to give a brown solid. Purification by column chromatography using 4:1 hexanes–EtOAc gave **9** (0.389 g, 85%) as a white solid. Mp 90–92 °C; $[\alpha]_D$ +2.7 (*c* 0.43, $CHCl_3$); IR (KBr) cm^{-1} 3026.73, 2903.31, 2857.02, 1728.87, 1648.84, 1453.10, 1353.78, 1264.11, 1110.80, 1067.41, 733.78, 691.36; ^1H NMR ($CDCl_3$) δ 7.35–7.26 (m, 15 H), 6.31 (d, 1 H, *J* 7.4 Hz), 4.86 (d, 1 H, *J* 11.2 Hz), 4.74–4.63 (m, 6H), 4.35 (dd, 1 H, *J* 12.9, 4.9 Hz), 4.27 (dd, 1 H, *J* 7.2, 3.4 Hz), 3.98 (d, 1 H, *J* 5.5 Hz) 3.96 (s, 1 H), 3.82 (dd, 1 H, *J* 4.5, 4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 157.5, 138.8, 138.6, 138.3, 128.6(2), 128.5, 128.2, 128.1, 127.9, 127.8, 104.2, 86.6, 82.8, 75.6, 74.6, 72.4, 72.0, 68.8; anal. calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78; O, 15.37; found C, 77.68; H, 6.63; FAB-MS *m*/*z* $[M-H]^+$ calcd 415.1909, found 415.1897.

3.5. 1,2-Anhydro-β-D-idoseptanose (10)

Oxepine **9** (0.015 g, 0.036 mmol) was dried via azeotropic distillation from toluene (3 × 5 mL) under reduced pressure and dissolved in dry CH_2Cl_2 (2 mL). The solution was cooled in an ice bath to 0 °C and a DMDO (0.235 mL, 0.2 M) solution was added dropwise. The mixture was stirred at 0 °C for 30 min and the solvent was removed under reduced pressure. NMR showed quantitative conversion. ^1H NMR ($CDCl_3$) δ 7.44–7.32 (m, 15 H), 4.88 (d, 1 H, *J* 11.2 Hz), 4.85 (d, 1 H, *J* 13.2 Hz), 4.80 (d, 1 H, *J* 2.2 Hz), 4.75 (d, 1 H, *J* 11.5 Hz), 4.69 (d, 1 H, *J* 9.8 Hz), 4.60 (d, 1 H, *J* 11.5 Hz), 3.85 (dd, 1 H, *J* 13.1, 3.5 Hz), 3.77 (m, 2 H), 3.67 (dd, 1 H, *J* 13.1, 6.6 Hz), 3.56 (m, 1 H), 2.99 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.1, 128.7, 128.6, 128.3, 128.1, 127.9 (2), 82.3, 80.6, 79.8, 78.3, 75.4, 73.6, 73.0, 64.1, 58.4.

3.6. Methyl 3,4,5-tri-*O*-benzyl-D-idoseptanoside—[method A]

DMDO epoxidation of **9** (0.046 g, 0.11 mmol) in CH_2Cl_2 (2 mL) at 0 °C over 30 min was followed by solvent removal under reduced pressure. To this residue was added CH_3OH (3 mL) and it was stirred overnight (18 h). The solvent was removed under reduced pressure and the residue was purified by column chromatography, using 4:1 hexanes–EtOAc as eluent to give two products.

3.7. Methyl 3,4,5-tri-*O*-benzyl-α-D-idoseptanoside (11)

The first fraction gave **11** (0.024 g, 48%) as a white solid. R_f 0.33 (4:1 hexanes–EtOAc); Mp 88–90 °C; $[\alpha]_D$ +13.8 (*c* 1.70, $CHCl_3$); IR (KBr) cm^{-1} 3347.82, 3029.62, 2897.52, 1453.10, 1070.30, 750.17, 733.78, 695.21; ^1H NMR ($CDCl_3$) δ 7.34–7.29 (m, 15 H), 5.01 (d, 1 H, *J* 10.8 Hz), 4.92 (d, 1 H, *J* 10.8 Hz), 4.88 (d, 1 H, *J* 10.8 Hz), 4.72 (d, 1 H, *J* 11.3 Hz), 4.65 (d, 1 H, *J* 10.6 Hz), 4.62 (d, 1 H, *J* 10.5 Hz), 4.39 (d, 1 H, *J* 6.2 Hz), 3.69–3.54 (m, 6H), 3.42 (s, 3 H), 3.03 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.3, 137.9, 130.0, 128.9, 128.7, 128.6, 128.3, 128.2, 128.1(2), 128.0, 127.8, 104.4, 87.6, 80.4, 79.6, 76.7, 76.4, 73.9, 72.8, 59.6, 55.5; anal. calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94; O, 20.66; found C, 72.15; H, 6.66; FAB-MS *m/z* $[M-H]^+$ calcd 463.2120, found 463.2113.

3.8. Methyl 3,4,5-tri-*O*-benzyl-β-D-idoseptanoside (12)

The second fraction gave **12** (6 mg, 12%) as a clear colorless oil. R_f 0.21 (4:1 hexanes–EtOAc); $[\alpha]_D$ −49.2 (*c* 0.35, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.35–7.28 (m, 15 H), 5.29 (s, 1 H), 4.85 (d, 1 H, *J* 9.4 Hz), 4.83 (s, 1 H), 4.70 (d, 1 H, *J* 11.9 Hz), 4.59–4.55 (m, 4 H), 4.01 (dd, 1 H, *J* 9.1, 6.2 Hz), 3.97 (d, 1 H, *J* 11.8 Hz), 3.94 (d, 1 H, *J* 12.3 Hz) 3.80 (dd, 1 H, *J* 6.1, 3.7 Hz) 3.76–3.71 (m, 2 H), 3.66 (m, 1 H), 3.46 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.2, 128.7(2), 128.1(2), 128.0, 100.7, 85.2, 80.5, 77.8, 75.0, 73.2, 71.3, 71.2, 58.8, 56.0; FAB-MS *m/z* $[M-H]^+$ calcd 463.2120, found 463.2103.

3.9. Methyl 3,4,5-tri-*O*-benzyl-2-D-idoseptanoside—[method B]

DMDO epoxidation of **9** (0.039 g, 0.09 mmol) in CH_2Cl_2 (2 mL) at 0 °C over 30 min was followed by solvent removal under reduced pressure. To the residue was added $NaOCH_3$ (0.006 g) in CH_3OH (3 mL) and it was stirred overnight (18 h). The reaction was quenched with water (2 mL) and the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (15 mL) and washed with water (2 × 15 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by column chromatography (4:1 hexanes–EtOAc) to give the α anomer (**11**) (0.038 g, 89%).

3.10. Methyl 2,3,4,5-tetra-*O*-acetyl-α-D-idoseptanoside (13)

Methyl septanoside **11** (0.034 g, 0.073 mmol) was dissolved in CH_3OH (15 mL) and 10% Pd/C (10 mg) was added. The solution was stirred under an atmosphere of H_2 for 4 h. The solution was filtered through a short pad of Celite and washed with additional CH_3OH (15 mL). The solvent was removed under reduced pressure and the resulting solid was dissolved in dry pyridine (2 mL) to which Ac_2O (0.5 mL) was added. The mixture was stirred overnight (18 h) and quenched with water. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (2 × 20 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The resulting solid was purified by column chromatography using 2:1 hexanes–EtOAc as eluent to give **13** (0.024 g, 80%, two steps) as a white solid. Mp 126–128 °C; $[\alpha]_D$ +79.8 (*c* 1.53, $CHCl_3$); IR (KBr) cm^{-1} 2924.52, 2852.20, 1752.98, 1378.85, 1222.65, 1125.26, 1071.26, 1049.09; ^1H NMR ($CDCl_3$) δ 5.34–5.20 (m, 3 H), 5.06 (m, 1 H), 4.55 (d, 1 H, *J* 6.5 Hz), 3.83 (dd, 1 H, *J* 12.5, 10.9 Hz), 3.61 (dd, 1 H, *J* 12.8, 4.4 Hz), 3.3 (s, 3 H), 2.05 (s, 3 H), 2.02 (s, 3 H), 2.00 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 169.9, 169.6, 169.4, 169.0, 102.0, 73.9, 71.3, 71.2, 68.1, 59.5, 55.9, 20.9, 20.8, 20.6; anal. calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12; O, 44.16; found C, 49.82; H, 6.47; FAB-MS *m/z* $[M-H]^+$ calcd 415.1909, found 415.1897.

3.11. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(3,4,5-tri-*O*-benzyl-D-idoseptanosyl)-α-D-galactopyranose

Compound **9** (0.053 g, 0.127 mmol) was dried via azeotropic distillation from toluene (3 × 10 mL) under reduced pressure, dissolved in dry CH_2Cl_2 (2 mL), and treated to DMDO (0.444 mL, 0.43 M) at 0 °C for 30 min. The solvent was removed under reduced pressure to afford **10**. It was dissolved in dry THF (0.5 mL) and cooled to −78 °C. To this solution was added 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.050 g, 0.191 mmol) in THF (1 mL), which had previously been azeotroped with toluene (3 × 10 mL). To this mixture was added $ZnCl_2$ (0.191 mL, 1.0 M in Et_2O) and the mixture was allowed to warm to rt overnight. Saturated $NaHCO_3$ (5 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic fractions were dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by column chromatography, using 3:1 hexanes–EtOAc as eluent to give two fractions.

3.12. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(3,4,5-tri-*O*-benzyl-α-D-idoseptanosyl)-α-D-galactopyranose (15)

The first fraction gave **15** (0.027 g, 30%) as a white foam. R_f 0.27 (3:1 hexanes–EtOAc); $[\alpha]_D$ −5.98 (*c* 0.94, $CHCl_3$); IR (KBr) cm^{-1} 3527.17, 2986.23, 2905.24, 1455.03, 1382.71, 1069.33, 735.71, 698.11; ^1H NMR ($CDCl_3$) δ 7.32–7.30 (m, 15 H), 5.53 (d, 1 H, *J* 5.0 Hz), 4.97 (d, 1 H, *J* 10.8 Hz), 4.90 (d, 1 H, *J* 10.8 Hz), 4.85 (d, 1 H, *J* 10.8 Hz), 4.70 (d, 1 H, *J* 11.4 Hz), 4.63 (d, 1 H, *J* 11.5 Hz), 4.60 (dd, 1 H, *J* 8.0, 2.3 Hz), 4.52 (d, 1 H, *J* 6.4 Hz), 4.30 (dd, 1 H, *J* 7.1, 2.3 Hz), 4.28 (m, 1 H), 4.01 (dd, 1 H, *J* 6.3, 6.3 Hz), 3.80–3.76 (m, 2 H), 3.69–3.64 (m, 3 H), 3.57–3.52 (m, 3 H), 1.53 (s, 3 H), 1.44 (s, 3 H), 1.33 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 139.0, 138.4, 138.1, 128.8, 128.7, 128.6, 128.2(2), 128.1, 128.0(2), 127.8, 109.5, 108.9, 103.9, 96.6, 87.4, 80.4, 79.8, 76.6, 76.3, 73.8, 73.0, 71.2, 70.9, 67.2, 66.8, 59.9, 26.3, 26.2, 25.2, 24.7; FAB-MS *m*/*z* $[M-H]^+$ calcd 691.3121, found 691.3118.

3.13. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(3,4,5-tri-*O*-benzyl-β-D-idoseptanosyl)-α-D-galactopyranose (16)

The second fraction gave **16** (0.013 g, 15%), as a white foam. R_f 0.18 (3:1 hexanes–EtOAc); $[\alpha]_D$ −100.54 (*c* 0.68, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.34–7.28 (m, 15 H), 5.53 (d, 1 H, *J* 5.0 Hz), 4.96 (s, 1 H), 4.76 (d, 1 H, *J* 11.2 Hz), 4.68 (d, 1 H, *J* 12.0 Hz), 4.65 (d, 1 H, *J* 12.1 Hz), 4.61–4.55 (m, 4 H), 4.30 (dd, 1 H, *J* 5.0, 2.3 Hz), 4.23 (dd, 1 H, *J* 8.0, 1.7 Hz), 4.05–3.98 (m, 4 H), 3.90 (m, 1 H), 3.78–3.67 (m, 4 H), 1.54 (s, 3 H), 1.43 (s, 3 H), 1.32 (s, 3 H), 1.29 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.5, 138.4(2), 128.8, 128.7, 128.6(2), 128.1, 128.0, 127.9(2), 109.4, 108.8, 100.4, 96.5, 85.0, 80.6, 78.2, 74.6, 73.3, 71.6, 71.4, 71.3, 70.9, 70.8, 67.5, 67.2, 65.6, 59.8, 26.3, 26.2, 25.2, 24.6; FAB-MS *m*/*z* $[M-H]^+$ calcd 691.3121, found 691.3118.

3.14. Isopropyl 3,4,5-tri-*O*-benzyl-α-D-idoseptanoside (17)

DMDO epoxidation of **9** (0.028 g, 0.067 mmol) in CH_2Cl_2 (2 mL) at 0 °C over 30 min was followed by solvent removal. To this residue was added anhydrous 2-propanol (3 mL) and it was stirred overnight (18 h). The solvent was removed under reduced pressure and the residue was purified by column chromatography, using 4:1 hexanes–EtOAc as eluent to give **17** (0.023 g, 69%) as a white solid. Mp 79–81 °C; $[\alpha]_D$ +20.6 (*c* 1.95, $CHCl_3$); IR (KBr) cm^{-1} 3546.45, 3029.62, 2968.87, 2905.24, 1454.06, 1042.34, 735.71, 695.21; ^1H NMR ($CDCl_3$) δ 7.31–7.28 (m, 15 H), 4.99 (d, 1 H, *J* 10.7 Hz), 4.91 (d, 1 H, *J* 10.8 Hz), 4.87 (d, 1 H, *J* 10.8 Hz), 4.72 (d, 1 H, *J* 11.3 Hz), 4.64 (d, 1 H, *J* 11.9 Hz), 4.61 (d, 1 H, *J* 11.2 Hz), 4.57 (d, 1 H, *J* 5.8 Hz), 3.93 (m, 1 H), 3.71–3.49 (m, 6H), 3.00 (s, 1 H), 1.22 (d, 3 H, *J* 6.3 Hz), 1.20 (d, 3 H, *J* 6.1 Hz); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.3, 138.0, 128.9, 128.7, 128.6, 128.3, 128.1, 128.0, 127.9, 127.8, 101.2, 87.6, 80.5, 79.8, 76.7, 76.4, 73.9, 73.1, 69.4, 59.5, 23.6, 21.8; anal. calcd for $C_{30}H_{36}O_6$: C, 73.15; H, 7.37; O, 19.49; found C, 72.76; H, 7.71; FAB-MS *m*/*z* $[M-H]^+$ calcd 491.2434, found 491.2451.

3.15. Ethyl 3,4,5-tri-*O*-benzyl-1-thio-α-D-idoseptanoside (18)

1,2-Anhydroseptanose **10** was prepared from **9** (0.031 g, 0.074 mmol) as described above. Compound **10** was dissolved in dry CH_2Cl_2 (0.8 mL) and ethanethiol (0.2 mL) and cooled to −78 °C. To this solution was added trifluoroacetic anhydride (4 μL) in CH_2Cl_2 (0.196 mL). The mixture was stirred at −78 °C for 1 h, then quenched by with satd $NaHCO_3$ (5 mL). Additional CH_2Cl_2 (10 mL) was added and the organic layer was washed with water (10 mL). The organic layer was dried (Na_2SO_4) and solvent removed under reduced pressure. Purification of the residue by column chromatography using 3:1 hexanes–EtOAc as eluent gave **18** (0.012 g, 32%) as an off-white solid. Mp 64–66 °C; $[\alpha]_D$ +38.8 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3508.85, 3062.41, 3030.59, 2870.52, 1496.49, 1454.06, 1069.33, 735.71, 698.11; ^1H NMR ($CDCl_3$) δ 7.34–7.26 (m, 15 H), 5.00 (d, 1 H, *J* 10.8 Hz), 4.85 (d, 2 H, *J* 10.7 Hz), 4.71 (d, 1 H, *J* 11.4 Hz), 4.64 (d, 1 H, *J* 11.2 Hz), 4.62 (d, 1 H, *J* 10.9 Hz), 3.82 (dd, 1 H, *J* 12.2, 10.6 Hz), 3.76–3.73 (m, 1 H), 3.67 (d, 1 H, *J* 9.0 Hz), 3.59–3.54 (m, 3 H), 3.09 (s, 1 H), 2.75–2.56 (m, 2 H), 1.30 (t, 3 H, *J* 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.3, 137.9, 128.9, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 87.9, 87.1, 81.7, 80.3, 76.7, 76.3, 73.8, 73.4, 61.1, 24.8, 15.3; FAB-MS *m*/*z* $[M+H]^+$ calcd 495.2221, found 495.2205.

3.16. Allyl 3,4,5-tri-*O*-benzyl-α-D-idoseptanoside (19)

DMDO epoxidation of **9** (0.038 g, 0.0091 mmol) in CH_2Cl_2 (2 mL) at 0 °C over 30 min was followed by solvent removal under reduced pressure. The subsequent addition was done in a similar fashion to those described for glucals.[18] **10** was dissolved in dry THF (1 mL) and cooled on an ice bath to −10 °C. Allylmagnesium bromide (0.032 mL, 1.0 M) was added dropwise and the mixture was stirred for 30 min at −10 °C. The reaction was quenched with saturated NH_4Cl (5 mL) solution. EtOAc (10 mL) was added and the reaction placed in a separatory funnel. The EtOAc was separated, and the aqueous layer was extracted with additional EtOAc (10 mL). The combined organic fractions were washed with water (20 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified by column chromatography using 3:1 hexanes–EtOAc as eluent to give **19** (0.015 g, 33%) as a waxy

solid. $[\alpha]_D$ −33.0 (*c* 0.61, $CHCl_3$); IR (KBr) cm^{-1} 3552.24, 3028.66, 2904.27, 1453.10, 1122.37, 1076.08, 740.53, 696.18; ^1H NMR ($CDCl_3$) δ 7.33–7.26 (m, 15 H), 5.90 (m, 1 H), 5.13–5.03 (m, 2 H), 4.89 (d, 1 H, *J* 11.0 Hz), 4.76 (d, 1 H, *J* 10.9 Hz), 4.67 (d, 1 H, *J* 11.6 Hz), 4.63 (d, 1 H, *J* 11.7 Hz), 4.56 (d, 1 H, *J* 11.1 Hz), 4.03 (dd, 1 H, *J* 13.7, 3.9 Hz), 3.79 (dd, 1 H, *J* 8.9, 7.1 Hz), 3.65–3.42 (m, 1 H), 3.56 (d, 1 H, *J* 5.5 Hz), 3.55 (d, 1 H, *J* 3.5 Hz), 3.52 (d, 1 H, *J* 4.0 Hz), 3.46 (dd, 1 H, *J* 9.0, 9.0 Hz), 3.29 (td, 1 H, *J* 8.7, 2.9 Hz), 2.93 (s, 1 H), 2.58–2.54 (m, 1 H), 2.31–2.28 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.4, 138.2, 135.2, 128.9, 128.6(2), 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 117.1, 84.8, 83.5, 82.9, 81.6, 76.3, 75.7, 74.4, 72.5, 68.6, 37.6; FAB-MS *m*/*z* $[M+H]^+$ calcd 475.2485, found 475.2487.

3.17. 3,4,5-Tri-*O*-benzyl-α-D-idoseptanosyl azide (20)

This procedure is based on one described.[18] DMDO epoxidation of **9** (0.032 g, 0.077 mmol) in CH_2Cl_2 (2 mL) at 0 °C over 30 min was followed by solvent removal under reduced pressure. The residue was dissolved in DMF (1 mL) and NaN_3 (0.075 g, 1.54 mmol) in water (0.5 mL) was added. After 4 h, water (5 mL) was added to the solution and it was extracted with EtOAc (2 × 15 mL). The organic layers were dried (Na_2SO_4) and solvent was removed under reduced pressure. The material was purified by column chromatography, using 4:1 hexanes–EtOAc as eluent to give **20** (0.025 g, 69%) as a white waxy solid. Mp 62–64 °C; $[\alpha]_D$ +74.5 (*c* 1.85, $CHCl_3$); IR (KBr) cm^{-1} 3367.10, 3030.59, 2899.45, 2107.81, 1454.06, 1235.18, 1068.37, 749.21, 695.21; ^1H NMR ($CDCl_3$) δ 7.35–7.26 (m, 15 H), 5.01 (d, 1 H, *J* 10.8 Hz), 4.93 (d, 1 H, *J* 6.1 Hz), 4.91 (d, 1 H, *J* 12.5 Hz), 4.87 (d, 1 H, *J* 12.4 Hz), 4.72 (d, 1 H, *J* 11.3 Hz), 4.65 (d, 1 H, *J* 10.7 Hz), 4.62 (d, 1 H, *J* 10.5 Hz), 3.75–3.69 (m, 4 H), 3.59–3.55 (m, 3 H), 3.07 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.0, 137.6, 128.9, 128.7, 128.6, 128.4, 128.2(2), 128.1, 127.9(2), 93.3, 86.9, 80.1, 79.7, 76.7, 76.3, 73.9, 72.5, 62.1; anal. calcd for $C_{27}H_{29}N_3O_5$: C, 68.19; H, 6.15; N, 8.84; O, 16.82; found C, 68.27; H, 5.93; N, 8.80.

3.18. Phenyl 3,4,5-tri-*O*-benzyl-1-thio-α-D-idoseptanoside (21)

DMDO epoxidation of **9** (0.030 g, 0.07 mmol) in CH_2Cl_2 (2 mL) 0 °C over 30 min was followed by solvent removal under reduced pressure. The remainder of this procedure is based on one described.[18] In a separate flame-dried flask, thiophenol (0.073 mL, 0.72 mmol) was dissolved in dry THF (1 mL) and put on a 0 °C ice bath. *n*-Butyllithium (0.446 mL, 1.6 M) was added to this solution dropwise and stirred for 5 min. To this solution was added **10** in dry THF (1 mL). The mixture was stirred at 0 °C for 30 min, and water (10 mL) was added. The reaction mixture was extracted with EtOAc (2 × 10 mL) and dried (Na_2SO_4). The residue was purified by column chromatography, using 4:1 hexanes–EtOAc as eluent to give **21** (0.028 g, 73%) as a clear, slightly yellow syrup. $[\alpha]_D$ +17.8 (*c* 1.15, $CHCl_3$); IR (KBr) cm^{-1} 3450.03, 3029.62, 2889.81, 1454.06, 1071.26, 736.67, 697.14; ^1H NMR ($CDCl_3$) δ 7.52 (d, 2 H, *J* 6.8 Hz), 7.34–7.28 (m, 18H), 5.11 (d, 1 H, *J* 7.8 Hz), 5.00 (d, 1 H, *J* 10.8 Hz), 4.91 (d, 1 H, *J* 10.8 Hz), 4.87 (d, 1 H, *J* 10.8 Hz), 4.71 (d, 1 H, *J* 11.3 Hz), 4.65 (d, 1 H, *J* 9.5 Hz), 4.63 (d, 1 H, *J* 10.7 Hz), 3.91 (dd, 1 H, *J* 12.1, 10.7 Hz), 3.78–3.59 (m, 5 H), 3.17 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.2, 137.8, 134.2, 132.3, 129.3, 129.1, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 91.1, 87.1, 81.4, 80.2, 76.7, 76.3, 73.8, 72.9, 61.2; anal. calcd for $C_{33}H_{34}O_5S$: C, 73.04; H, 6.31; O, 14.74; S, 5.91; found C, 72.74; H, 6.29; S, 5.70.

4. Supplementary Material

Complete crystallographic data for the structural analysis of **9** have been deposited in the Cambridge Crystallographic Data Centre (CCDC), No 223661. Copies of this information may be obtained free of charge from: CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; web: www.ccdc.cam.ac.uk/conts/retrieving.html; email: deposit@ccdc.cam.ac.uk).

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References

1. Yasumoto, T.; Murata, M. *Chem. Rev.* **1993**, *93*, 1897–1909.
2. (a) Eschenmoser, A. *Science* **1999**, *284*, 2118–2124; (b) Gellman, S. H. *Acc. Chem. Res.* **1998**, *31*, 173–180; (c) Porter, E. A.; Wang, X.; Lee, H. S.; Weisblum, B.; Gellman, S. H. *Nature* **2000**, *404*, 585; (d) Porter, E. A.; Weisblum, B.; Gellman, S. H. *J. Am. Chem. Soc.* **2002**, *124*, 7324–7330.
3. Stevens, J. D. *Aust. J. Chem.* **1975**, *28*, 525–557.
4. Ng, C. J.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 241–248.

5. (a) Driver, G. E.; Stevens, J. D. *Aust. J. Chem.* **1990**, *43*, 2063–2081; (b) Ng, C. J.; Craig, D. C.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 249–263; (c) Tran, T. Q.; Stevens, J. D. *Aus. J. Chem.* **2002**, *55*, 171–178.
6. Driver, G. E.; Stevens, J. D. *Carbohydr. Res.* **2001**, *334*, 81–89.
7. (a) Bailey, C. J.; Craig, D. C.; Grainger, C. T.; James, V. J.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 265–270; (b) Craig, D. C.; Stevens, J. D. *Aus. J. Chem.* **1990**, *43*, 2083–2086; (c) Wood, R. A.; James, V. J.; Rae, A. D.; Stevens, J. D.; Moore, F. H. *Aus. J. Chem.* **1983**, *36*, 2269–2277; (d) Choong, W.; McConnell, J. F.; Stephenson, N. C.; Stevens, J. D. *Aus. J. Chem.* **1980**, *33*, 979–985; (e) James, V. J.; Stevens, J. D. *Carbohydr. Res.* **1980**, *82*, 167–174; (f) McConnell, J. F.; Stevens, J. D. *J. Chem. Soc., Perkin Trans. 2* **1974**, 354–358; (g) Stevens, J. D.; Beale, J. P.; Stephenson, N. C. *J. Chem. Soc., Chem. Commun.* **1971**, *10*, 484–486.
8. McAuliffe, J. C.; Hindsgaul, O. *Synlett* **1998**, 307–309.
9. Pakulski, Z. *Pol. J. Chem.* **1996**, *70*, 667–707.
10. (a) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661–6666; (b) Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380–1419.
11. Peczuh, M. W.; Synder, N. L. *Tetrahedron Lett.* **2003**, *44*, 4057–4061.
12. Pougny, J. R.; Nassr, M. A. M.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1981**, 375–376.
13. Handerson, S.; Schlaf, M. *Org. Lett.* **2002**, *4*, 407–409.
14. Schrock, R. R. *Tetrahedron* **1999**, *55*, 8141–8153.
15. (a) Stoddart, J. F. *Stereochemistry of Carbohydrates*; John Wiley and Sons: New York, 1971; (b) Bocain, D. F.; Strauss, H. L. *J. Am. Chem. Soc.* **1977**, *99*, 2876–2882; (c) Bocian, D. F.; Pickett, H. M.; Rounds, T. C.; Strauss, H. L. *J. Am. Chem. Soc.* **1975**, *97*, 687–695; (d) Hendrickson, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 7043–7046; (e) Hendrickson, J. B.. *J. Am. Chem. Soc.* **1967**, *89*, 7047–7061.
16. (a) Gervay, J.; Peterson, J. M.; Oriyama, T.; Danishefsky, S. J. *J. Org. Chem.* **1993**, *58*, 5465–5468, and references therein; (b) Marzabadi, C. H.; Spilling, C. D. *J. Org. Chem.* **1993**, *58*, 3761–3766.
17. Seeberger, P. H.; Eckhardt, M.; Gutteridge, C. E.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 10064–10072.
18. Boulineau, F. P.; Wei, A. *Org. Lett.* **2002**, *4*, 2281–2283.
19. (a) Honda, E.; Gin, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 7343–7352; (b) Kim, J. Y.; Di Bussolo, V.; Gin, D. Y. *Org. Lett.* **2001**, *3*, 303–306; (c) Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656–6660; (d) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 5811–5819; (e) Di Bussolo, V.; Liu, J.; Huffman, L. G., Jr.; Gin, D. Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 204–207; (f) Liu, J.; Gin, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 9789–9797.
20. Tsuda, Y.; Nunozawa, T.; Yoshimoto, K. *Chem. Pharm. Bull.* **1980**, *28*, 3223–3231.
21. (a) Murray, R. W.; Singh, M. *Org. Synth.* **1997**, *74*, 91–100; (b) Gilbert, M.; Ferrer, M.; Sanchez-Baeza, F.; Messeguer, A. *Tetrahedron* **1997**, *53*, 8643–8650.