

ADDITIONAL REACTIONS OF LEVOGLUCOSENONE

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ABSTRACT

Several new, $[4 + 2]$ cycloaddition products of levoglucosenone have been synthesized, and the oxidation of products of this type has been accomplished by several methods, including epoxidation and osmium tetroxide oxidation, producing interesting polycyclic molecules. Additions of long-chain hydrocarbons to levoglucosenone have also been investigated *via* Grignard reactions.

INTRODUCTION

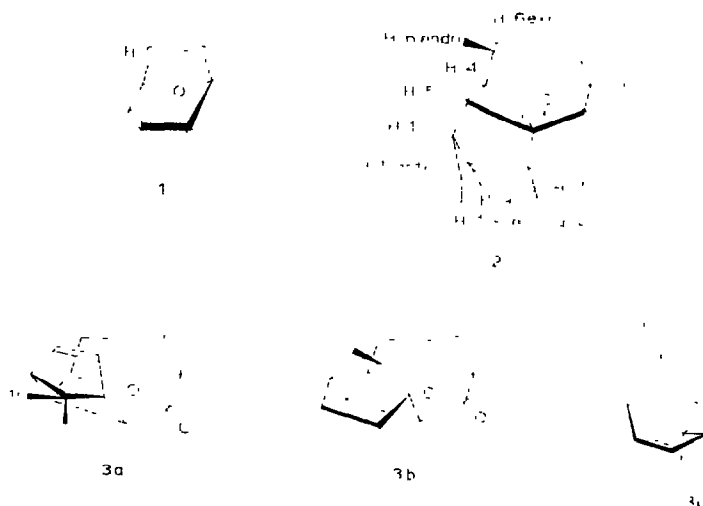
The addition and substitution reactions of the enone function in 1,6-anhydro-3,4-dideoxy- β -D-glycero-hex-3-enopyranos-2-ulose (**1**, levoglucosenone) provide the opportunity for extension of the carbon chain in carbohydrates, and for the synthesis of a variety of branched-chain and polycyclic sugar derivatives. Some compounds of this type, obtained by the Grignard reaction¹, the Diels-Alder² (*i.e.*, $[4 + 2]$ cycloadditions) and Michael additions³, and base-catalyzed oligomerization⁴ of levoglucosenone, have already been described.

We now describe further derivatives of the Diels-Alder addition-products, and investigation of longer chain, alkyl derivatives. Some of these compounds and reactions could be of interest for the synthesis of non-ionic surfactants and of novel, branched-chain sugar derivatives, particularly those involving fused rings.

RESULTS AND DISCUSSION

$[4 + 2]$ Cycloaddition reactions. — The chemistry and stereochemistry of some $[4 + 2]$ cycloaddition products of levoglucosenone have been the subjects of a previous publication². The reaction of **1** with 1,3-cyclopentadiene to produce the cyclic derivative **2** (in 48% yield) was discussed, and the stereochemistry of **2** was deduced on the basis of ¹H-n.m.r.-spectral evidence. The synthesis of **2** was accompanied by the formation of an isomer, **3**, in 3% yield*, and its structure is investigated here.

*Compound **3** has since been reported by Bhaté and Horton⁵.



There are four possible, $[4 + 2]$ cycloaddition products resulting from the reaction between levoglucosenone and cyclopentadiene. The structure of the major product, **2**, has been confirmed by a single-crystal, X-ray diffraction study⁶ of the epoxide **5**, which was synthesized from **2**. Of the three remaining possibilities (*i.e.*, **3a**, **3b**, and **3c**), the magnetic dissimilarity in the ^1H -n.m.r. spectrum of H-11*anti* and H-11*syn* (0.46 p.p.m. apart) seen for **3**, as opposed to the smaller, 0.17 p.p.m. difference in the position of the signals of these protons of **2**, indicates that the pyranose

TABLE I

 ^1H -N.M.R. ASSIGNMENTS FOR COMPOUNDS 2-8^a

Proton	2	3	4	5	6 ^b	7 ^b	8
H-1	4.77(s)	5.05(s)	5.01(s)	5.04(s)	4.93(s)	4.92(s)	5.05(s)
H-3	2.99(m)	2.26(d)	3.42(d)	2.84(dd)	2.91(dd)	2.73(dd)	2.75(dd)
H-4	2.39(dd)	1.67(d)	2.83(d)	2.31(dd)	2.25(dd)	2.29(dd)	2.21(dd)
H-5	4.62(d)	4.82(d)	4.86(dd)	4.82(d)	4.62(d)	4.89(d)	4.80(m)
H-6 <i>exo</i>	3.77(dd)	3.87(dd)	3.87(m)	3.86(m)	3.71(dd)	3.76(dd)	3.87(m)
H-6 <i>endo</i>	3.84(d)	3.81(dd)	3.87(m)	3.86(m)	3.76(d)	3.89(d)	3.87(m)
H-7	3.34(m)	3.29(s)		3.05(d)	2.19(s)	2.51(dd)	2.84(d)
H-8	5.98(dd)	6.31(dd)		3.08(d)	4.06(d)	4.39(dd)	4.75(d)
H-9	6.24(dd)	6.20(dd)		3.50(d)	4.35(s)	3.54(dd)	3.97(dd)
H-10	2.99(m)	2.90(s)		2.78(m)	1.99(m)	2.37(d)	2.55(dm)
H-11 <i>syn</i>	1.41(m)	1.26(m)		1.51(dm)	1.86(dm)	1.90(dm)	1.89(dm)
H-11 <i>anti</i>	1.24(m)	1.72(d)		0.75(d)	1.29(d)	1.19(dm)	1.13(dm)
-CH ₃			3.62(s) 3.57(s)				1.44(s) 1.28(s)

^aAssignments given in δ values relative to Me₄Si; solvent, CDCl₃, **2** at 90 MHz, all others at 360 MHz.^bSolvent was acetone-*d*₆. ^cSignal partially obscured by acetone signal

TABLE II

SELECTED COUPLING-CONSTANTS (Hz) FOR COMPOUNDS 2-8

Coupling constant	2	3	4	5	6	7	8
$J_{3,4}$	8.5	9.0	9.2	10.1	5.4	11.1	10.8
$J_{3,7}$	3.0	~0	—	4.5	~0	5.3	4.3
$J_{4,10}$	3.2	~0	—	3.7	10.4	4.6	4.0
$J_{5,6exo}$	4.0	4.8	2.7	3.9	5.0	5.0	4.5
$J_{7,8}$	3.0	3.1	—	~0	~0	9	~0
$J_{7,11syn}$	2.0	1.7	—	2	~0	~0	~0
$J_{8,9}$	6	5.6	—	3.6	—	5.9	5.3
$J_{9,10}$	~0	3.0	—	~0	~0	~0	~0
$J_{10,11anti}$	1.5	1.7	—	~0	—	~0	1.4
$J_{6exo,6endo}$	7.0	7.0	—	—	6.4	7.4	—
$J_{11syn,11anti}$	8.5	8.0	—	10.1	10.2	10.2	10.4

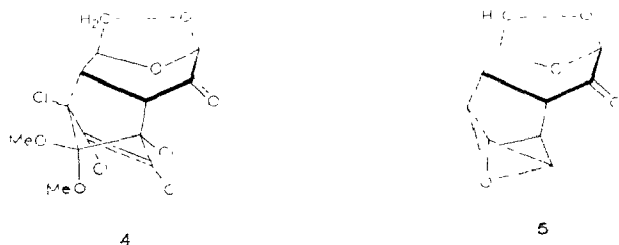
ring is attached to the norbornyl portion of the molecule in the *exo* position (see Table I). The two structures, **3b** and **3c**, containing this orientation would be expected to have similar ^1H -n.m.r. spectra, and thus it would be difficult to distinguish between them. Inspection of molecular models indicated that the dihedral angle between H-3 and H-4 is similar, and small, in both **3b** and **3c**, despite the orientation of the norbornyl ring "above" the parent ring-system in **3b**, and "below" in **3c**. Thus, the $J_{3,4}$ value of 9.0 Hz (see Table II) does not indicate which of the two structures, **3b** or **3c**, is correct. The H-3 and H-4 resonances of **3** are both farther upfield than those in **2**, consistent with anisotropic effects of the $\text{C}=\text{C}$ bond, which, according to the model of ApSimon *et al.*⁷, would have a shielding effect on both H-3 and H-4 of either **3b** or **3c**. In unsubstituted norbornene, this effect is evident in the position of the *endo* protons, whose resonances occur at⁸ 0.94 p.p.m. (δ), 0.63 p.p.m. farther upfield than those of the *exo* protons, which occur at 1.57 p.p.m.

Inspection of a molecular model of **3b** indicated that the steric interaction between H-6*endo* and H-11*anti* would produce considerable strain. Also, addition reactions of levoglucosenone previously reported gave products arising from attack from "below" the 1,6-anhydro bridge^{2,3,9}. Therefore, despite the similarities expected in the n.m.r. spectra of **3b** and **3c**, the latter structure, in which the norbornyl ring is oriented "below" the parent ring-system, is most probably the structure of **3**.

The facile, $[4 + 2]$ cycloaddition reaction between levoglucosenone and cyclopentadiene offers the possibility of introducing a variety of new functionalities onto the levoglucosenone skeleton. This was demonstrated by the cycloaddition reaction between **1** and a cyclopentadiene derivative, 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene.

The reaction proceeded readily on heating, and crystalline **4** was isolated in 68% yield. As this reaction is analogous to that producing **2**, and similar $[4 + 2]$

cycloaddition products have been deduced to have added from "below" the levoglucosenone ring-system², we concluded that the substituted cyclopentadiene is also oriented from "below". The magnetic similarity of the two methoxyl substituents (0.05 p.p.m. apart in the ¹H-n.m.r. spectrum) indicates that the levoglucosenone molecule is attached *endo* to the norbornyl ring, with the methoxyl groups in similar environments. In addition, molecular models show that considerable steric hindrance results when the levoglucosenone molecule is attached in the *exo* position. Therefore, it is reasonable to assume that the levoglucosenone is attached to the substituted norbornyl ring in the *endo* position.

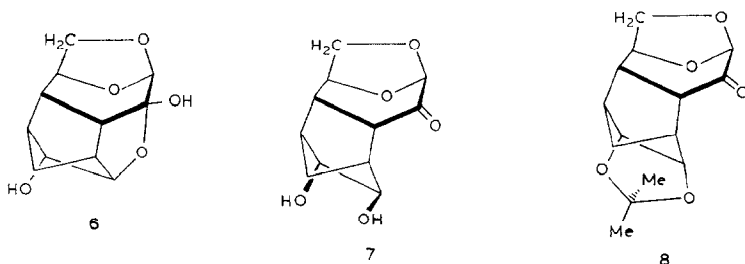


The oxidation of 2. -- On treatment of **2** with *m*-chloroperoxybenzoic acid, the 8,9-epoxide **5** was produced in 86% yield. An X-ray crystallographic study confirmed its structure, as well as that⁶ of **2**. The ¹H-n.m.r. assignments, and selected coupling-constants, of this compound are given in Tables I and II.

Hydrolysis of norbornyl epoxides with acid had led to rearrangement *via* nonclassical-ion formation^{10,11}. To determine whether this rearrangement occurs with the substituted norbornyl epoxide **5**, it was hydrolyzed with acid. Following hydrolysis, t.l.c. indicated only one product, namely, **6**, which was isolated in 49% yield. Its i.r. spectrum contained bands at 3387 and 3327 cm⁻¹, showing the presence of hydroxyl functionality, however the expected band due to carbonyl stretch was absent. Dreiding models showed the possibility of hemiacetal formation between C-2 and an *endo* hydroxyl group on C-9. The coupling constants of *trans* protons in norbornyl systems is on the order of 2-5 Hz, whereas that for *cis* protons is^{12,13} in the range of 6-10 Hz. No observable coupling between H-8 and H-9 was detected in the ¹H-n.m.r. spectrum of **6**, indicating that the protons are in the *trans* orientation, with the strain of the added ring changing the conformation of the norbornyl unit enough to eliminate even small coupling between H-8 and H-9. The geminally coupled protons, H-11_{syn} and H-11_{anti}, were readily assigned, eliminating the possibility of a rearrangement's having occurred. There is a considerable difference in the ¹H-n.m.r. shifts of H-11_{anti} and H-11_{syn} (0.57 p.p.m.), indicating a deshielding effect of the *exo* 9-hydroxyl group on H-11_{syn}. This is an interesting molecule, containing five fused rings, and functionality through which it may be further modified.

The 8,9-*cis,exo*-diol was also synthesized from the alkene **2** using osmium tetroxide as the oxidizing agent in 1:1 molar ratio. After addition of the osmium

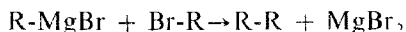
tetraoxide to **2**, the black solution resulting was stirred for 2 h at room temperature. Cleavage of the osmic ester was accomplished with hydrogen sulfide at room temperature, and the *cis,exo*-diol **7** was isolated in a yield of 74%. The formation of *cis-exo*-diols from the osmium tetraoxide or permanganate oxidation of norbornene^{10,14,15} is well established, and the value of $J_{8,9}$ for **7** (5.9 Hz) is on the order of that measured for *cis* protons in a norbornyl system^{12,13}, as mentioned earlier.



The oxidation of the double bond of **2** was attempted in another experiment by using the method of Akashi *et al.*¹⁶ where osmium tetraoxide was utilized in a catalytic amount, with *tert*-butyl hydroperoxide as the oxidizing agent, and acetone as the solvent. After ether extraction of the reaction solution, t.l.c. showed the presence of a major product (R_F 0.14). The ether extract was dried (anhydrous sodium sulfate) for 72 h, and t.l.c. then showed the disappearance of this product, and the appearance of a new one (R_F 0.59). The major product, **8**, isolated in 19% yield, crystallized. The i.r. spectrum of **8** contained no O–H stretch, and high-resolution mass spectrometry indicated a mass higher than that of the expected *cis* diols. After examining the chemical-ionization, and high-resolution, mass spectra, and the ^1H - and ^{13}C -n.m.r. spectra, it was determined that the isopropylidene derivative of the *exo, cis*-diol **7** had been fortuitously formed. Although the expected diol must have been an intermediate, the solvent acetone, which was extracted in the diethyl ether, reacted with the diol under the dehydrating conditions.

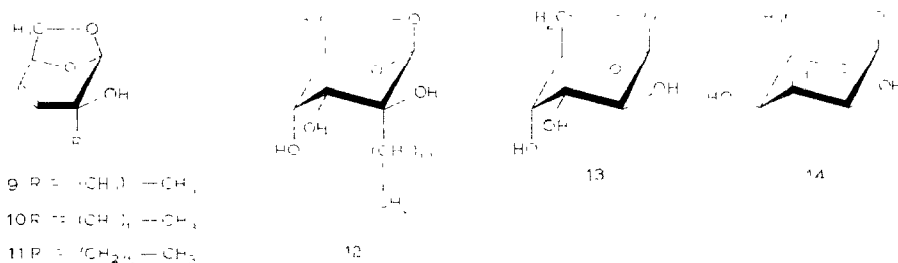
Grignard additions to levoglucosenone. — Nucleophilic addition to α,β -unsaturated carbonyl compounds generally occurs at the β position, and this holds true for the α,β -unsaturated system of levoglucosenone^{3,4,9}. However, nucleophilic attack on the carbonyl group, as well as on the $\text{C}=\text{C}$ bond, can be accomplished by Grignard reagents, and the 1,2 and 1,4 methylGrignard additions to levoglucosenone have been reported¹. The addition of long hydrocarbon chains to levoglucosenone by this technique may be used to produce compounds that have potential as non-ionic surfactants. To this end, 1-bromotetradecane (C_{14}) and 1-bromooctadecane (C_{18}) were used for preparing the corresponding Grignard reagents, which were allowed to react with levoglucosenone. The expected product, **9**, from 1,2 addition of the former, was obtained in 20% yield. Its i.r. spectrum contained the band of an O–H stretch, at 3421 cm^{-1} , and lacked that for $\text{C}=\text{O}$ stretch. The ^1H -n.m.r. spectrum of **9** showed a broad, 26-proton signal from 1.20 to 1.56 p.p.m., a singlet at 2.46 p.p.m. which

was exchangeable with deuterium, and two vinylic protons. A major by-product was octacosane, formed by Wurtz coupling of the Grignard reagent with the bromo compound¹⁷.



Product **10**, obtained by reaction of levoglucosenone with the Grignard reagent from 1-bromooctadecane, was isolated in 11% yield.

In an attempt to lessen Wurtz coupling, a one-step method utilizing alkyl-lithium reagents¹⁸ instead of Grignard reagents was investigated. When 1-bromotetradecane was used, the reaction could not be initiated, even by vigorous refluxing and addition of a drop of methyl iodide as an initiator. Using 1-bromodecane by this method produced the desired product, **11**, but the yield was only 10%, and the Wurtz-coupled by-product, eicosane, was produced.



As already reported¹, the reaction of a methyl Grignard reagent with levoglucosenone gave a major, branched-chain product which was assigned the *D-erythro* configuration. However, in the hydride reduction of levoglucosenone, attack of the reducing agent occurred mainly at the carbonyl group, to give the allylic alcohol having⁹ the *D-threo* configuration. The quaternary center at C-2 in the branched-chain products precluded the use of coupling constants to determine the configuration of products **9** through **12**. However, we tentatively assign the *D-threo* configuration to the products **9** through **12** by analogy with the hydride-reduction products. This is consistent with attack of the Grignard reagent (or alkyl lithium reagent) from the less-hindered side of the carbonyl group of levoglucosenone, and if this is so, the Grignard addition products previously reported should also have the *D-threo* configuration.

The oxidation of 9. - To increase the hydrophilic nature of the Grignard addition-product **9**, a 3,4-*cis*-diol grouping was introduced by using osmium tetroxide in the molar ratio of 1:1. The expected product, **12** obtained in 27% yield, was a white, waxy solid. The *altro* configuration was assigned to **12**, based on a comparison of the ¹H-n.m.r. spectrum of **12** to those of 1,6-anhydro-β-D-altropyranose (**13**) and 1,6-anhydro-β-D-talopyranose¹⁹ (**14**) (see Table III). The difference in the chemical shifts of H-6*endo* and H-6*exo* are small for both **12** and **13**, and, for **14**, the axial hydroxyl group deshields H-6*endo*, resulting in a 0.70 p.p.m. difference between the

TABLE III

SELECTED, ^1H -N.M.R. SHIFTS (δ) AND COUPLING CONSTANTS (Hz) FOR COMPOUNDS **12**–**14**

	12	13 ¹⁹	14 ¹⁹
H-1	5.12	5.30	5.24
H-3	3.58	3.58	4.09
H-4	3.74	3.88	3.87
H-5	4.46	4.59	4.36
H-6 _{exo}	3.68	3.74	3.58
H-6 _{endo}	3.61	3.74	4.28
$J_{3,4}$	5	3.8	4.5
$J_{4,5}$	2	2.5	4.0
$J_{5,6\text{exo}}$	5	4.5	5.0
$J_{5,6\text{endo}}$	0.9	0.8	0.8
$J_{6\text{exo},6\text{endo}}$	7.7	—	7.5

protons on C-6. In addition, the coupling between H-4 and H-5 of **12** ($J_{4,5}$ 2 Hz) is consistent with the axial–equatorial coupling found for the *altro* configuration. This, again, is consistent with the trend of stereospecificity induced by the 1,6-anhydro ring, which directs attack on the levoglucosenone molecule to occur from “below” the plane of the pyranose ring.

EXPERIMENTAL

General. — All t.l.c. assays were conducted on Baker-flex silica gel IB2-F (J. T. Baker Chemical Co.), and detection was achieved by u.v. absorbance, or by spraying with 1 : 2 : 37 anisaldehyde–sulfuric acid–ethanol and heating. Silica gel used for column separations was supplied by E. Merck (silica gel 60; 70–230 mesh, ASTM). ^1H -N.m.r. (90 MHz) and ^{13}C -n.m.r. (22.5 MHz) spectra were recorded with a Jeol FX-90Q instrument; 360 MHz, ^1H -n.m.r. and 90.6 MHz, ^{13}C -n.m.r. spectra were recorded at Colorado State University. Infrared spectra were recorded with a Nicolet MX-1 instrument, and mass spectra with a Varian M.A.T. III spectrometer, except for high-resolution and chemical-ionization mass spectra, which were recorded at the University of Nebraska, Lincoln.

Reaction of levoglucosenone with cyclopentadiene to give compounds 2 and 3. — The [4 + 2] cycloaddition reaction of **1** with cyclopentadiene was performed as reported previously¹. Levoglucosenone (2.0 g) was heated under reflux with dicyclopentadiene (15 mL) for 1.25 h, and column-chromatographic separation of the products yielded **2** (0.63 g, 21 %) and **3** (0.11 g, 3 %), *i.e.*, in the ratio of 7 : 1. I.r. data for **3**: $\nu_{\text{max}}^{\text{NaCl}}$ 3020, 2812, 2720 (C–H stretch), 1721 (C=O), and 1119 cm^{-1} (C–O–C).

Anal. Calc. for $\text{C}_{11}\text{H}_{12}\text{O}_2$: C, 68.74; H, 6.29. Found: C, 68.85; H, 6.56.

Reaction of levoglucosenone with 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene to give 4. — Levoglucosenone (0.35 g, 2.8 mmol) was heated under reflux with

1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene (0.73 g, 2.8 mmol). After several minutes, the solution was black, and heating was discontinued. T.l.c. showed the absence of starting material. The black material was passed through two columns (52 × 110 mm) of silica gel, the first eluted with 5:4 acetone-ethyl acetate, and the second with 1:1 hexane-ethyl acetate, to remove the dark-colored impurities. All of the fractions from the second column were combined. The product could not be detected by t.l.c., on spraying with either sulfuric acid, or the sulfuric acid-anisaldehyde-ethanol solution. The solvent was removed by rotary evaporation, and the orange oil remaining crystallized immediately; yield of crude product, 0.74 g (68%). Recrystallization from hexane-ethyl acetate afforded colorless needles having m.p. 124–125°; $\nu_{\text{max}}^{\text{KBr}}$ 2951 (C–H stretch), 1732 (C=O), 1611 (C=C), and 1200 cm^{-1} (C–O–C); $^1\text{H-n.m.r.}$ (360 MHz, $\text{CDCl}_3\text{--Me}_4\text{Si}$): see Tables I and II.

Anal. Calc. for $\text{C}_{13}\text{H}_{12}\text{Cl}_4\text{O}_5$: C, 40.03; H, 3.10; Cl, 36.36. Found: C, 40.08; H, 3.21; Cl, 36.18.

Oxidation of 2 with m-chloroperoxybenzoic acid to give 5. The reaction of **2** with *m*-chloroperoxybenzoic acid yielded **5** in 86% yield.

Acid hydrolysis of epoxide 5 to give 6. — To a solution of epoxide **5** (0.12 g, 0.57 mmol) in oxolane (THF; 5 mL) was added 25M H_2SO_4 (12 mL). The solution was kept for 72 h at room temperature, BaCO_3 was added to neutralize the acid, the solid was filtered off, and the filtrate concentrated by rotary evaporation. Colorless crystals of **6** (0.64 g, 49%) were precipitated; m.p. 223–225°; $\nu_{\text{max}}^{\text{KBr}}$ 3381, 3325 (O–H stretch), 2937, 2933 (C–H), and 1098, 1012 cm^{-1} (C–O). $^1\text{H-n.m.r.}$ (360 MHz acetone- $d_6\text{--Me}_4\text{Si}$): see Tables I and II; also δ 2.84 (m, OH, w :2.2 Hz), $J_{3,8}$ 4.9 Hz.

Anal. Calc. for $\text{C}_{11}\text{H}_{14}\text{O}_5$: C, 58.40; H, 6.24. Found: C, 58.49; H, 6.31.

Oxidation of 2 with osmium tetroxide to give 7. To a solution of compound **2** (0.83 g, 3.8 mmol) in 1,4-dioxane (10 mL) was added a solution of osmium tetroxide (0.94 g, 3.7 mmol) in 1,4-dioxane (25 mL). The solution immediately turned black; it was stirred for 2 h at room temperature, and then H_2S was bubbled through the solution for 0.5 h, and the heavy, black precipitate was removed by filtration. T.l.c. of the filtrate with 5:4:1 acetone-ethyl acetate- H_2O showed one product (R_f 0.79). The filtrate was evaporated, yielding white crystals of **7** (0.62 g, 74%), which were recrystallized from hot EtOH; m.p. 178–180°; $\nu_{\text{max}}^{\text{KBr}}$ 3439 (O–H stretch), 2965 (C–H), and 1723 cm^{-1} (C=O); $^1\text{H-n.m.r.}$ (360 MHz, acetone- $d_6\text{--Me}_4\text{Si}$): see Tables I and II; also, δ 4.18 (br s, 1 H, OH) and 2.89 (br s, 1 H, OH); $J_{9,11\text{syn}}$ 1.6 Hz.

Anal. Calc. for $\text{C}_{11}\text{H}_{14}\text{O}_5$: C, 58.40; H, 6.24. Found: C, 58.23; H, 6.44.

The osmium tetroxide-catalyzed oxidation of 2 to give 8. The method of Akashi *et al.*¹⁶ was used for this procedure. Compound **2** (0.20 g, 1.0 mmol), tetraethylammonium acetate (0.52 g, 0.20 mmol), *tert*-butyl hydroperoxide (90+%; 0.22 mL, 2 mmol), and acetone (20 mL) were mixed and the resulting solution cooled in an ice bath for 10 min. A solution of osmium tetroxide (0.56 g) in *tert*-butyl alcohol (110.5 mL) and *tert*-butyl hydroperoxide (90+%; 0.55 mL) was prepared, and 0.13 mL was added to the acetone solution. The color of the solution immediately turned a light tan; it was stirred for 1 h in an ice bath, and then for 16 h at room temperature,

recooled in an ice bath, and ethyl ether (25 mL) and 10% aqueous NaHSO_3 (5 mL) were added. The mixture was stirred for 0.5 h at room temperature, and the organic layer washed with two 10-mL portions of saturated NaCl solution, and dried (anhydrous Na_2SO_4). T.l.c. with 1:1 hexane–ethyl acetate showed the presence of a major product at R_F 0.14, and two minor components, at R_F 0.41 and 0.71. However, after drying for 48 h, t.l.c. showed the disappearance of the product having R_F 0.14, and the appearance of a new spot, R_F 0.59. The ether was evaporated under diminished pressure, and the resulting yellow oil placed on a column (24 × 190 mm) of silica gel, and eluted with 1:1 hexane–ethyl acetate. The product, R_F 0.59, readily crystallized from 1:1 hexane–ethyl acetate, yielding **8** (43 mg, 19%); m.p. 183.5–184°; $\nu_{\text{max}}^{\text{KBr}}$ 2900 (C–H stretch) and 1730 cm^{-1} (C=O); ^1H -n.m.r. (360 MHz, CDCl_3 – Me_4Si): see Tables I and II; also $J_{9,11\text{syn}}$ 2.0 Hz; ^{13}C -n.m.r. (90.55 MHz, CDCl_3 – Me_4Si): δ 24.0 (C-13 $_{\text{anti}}$), 25.1 (C-13 $_{\text{syn}}$), 33.5 (C-11), 41.0 (C-10), 43.7 (C-7), 45.1 (C-4), 46.9 (C-3), 71.7 (C-6), 74.0 (C-5), 78.2 (C-1), 100.1 (C-12), 114.0 (C-8), 132.9 (C-9), and 201.3 (C-2); high-resolution e.i.-m.s.: m/z no M^+ , 251.09 ($\text{M}^+ - \text{CH}_3$, 100%),

$$\begin{array}{c} \text{O} \\ || \\ \text{---} \end{array}$$

223.10 ($\text{M}^+ - \text{CH}_3 - \text{C}^{\cdot}$, 51%), and 247.99 ($\text{M}^+ - \text{H}_2\text{O}$, 5.2%); c.i.-m.s.: m/z 267 (MH^+ , 9.4%), 251 ($\text{M}^+ - \text{CH}_3$, 10.3%), 237 ($\text{M}^+ - \text{CHO}$, 9.7%), and 209 ($\text{M}^+ - \text{C}_2\text{H}_5\text{CO}^{\cdot}$, 100%).

Anal. Calc. for $\text{C}_{14}\text{H}_{18}\text{O}_5$: C, 63.15; H, 6.81. Found: C, 63.23; H, 6.99.

1,6-Anhydro-3,4-dideoxy-2-C-tetradecyl- β -D-threo-hex-3-enopyranose (9).— To oven-dried Mg (0.14 g, 5.8 mmol) in anhydrous diethyl ether (15 mL) was slowly added a solution of 1-bromotetradecane (0.14 g, 5.0 mmol) in ethyl ether (15 mL). Initiation of the reaction was facilitated with a drop of methyl iodide. After the addition was complete, the solution was boiled on a warm-water bath for an additional 20 min, and a solution of **1** (0.56 g, 4.4 mmol) in anhydrous diethyl ether (10 mL) was slowly added to the Grignard reagent. The solution was then cooled to room temperature, and dilute H_2SO_4 was added until the aqueous layer became acidic. The aqueous layer was extracted with ether (30 mL) and the two ether layers were combined and dried (anhydrous Na_2SO_4). T.l.c. with 1:1 hexane–ethyl acetate indicated 3 major products: R_F 0.98 (octacosane, the Wurtz-coupled by-product), R_F 0.71 (**9**), and R_F 0.59 (unreacted **1**). Evaporation of the ether yielded 1.77 g of a yellow, waxy solid which was placed on a column (30 × 220 mm) of silica gel, and eluted with 1:1 hexane–ethyl acetate. Compound **9** was isolated as a white, crystalline material; this was recrystallized from hexane–ethyl acetate, to yield very fine, hair-like, white crystals (0.37 g, 24%); m.p. 60–61°; $\nu_{\text{max}}^{\text{KBr}}$ 3421 (O–H stretch), 2915, 2840 (C–H), and 1471 cm^{-1} (C=C); ^1H -n.m.r. (90 MHz, CDCl_3 – Me_4Si): δ 5.94 (dd, 1 H, H-4, $J_{4,5}$ 4.2 Hz), 5.57 (dd, 1 H, H-3, $J_{3,4}$ 9.8, $J_{1,3}$ 2.0 Hz), 5.20 (d, 1 H, H-1), 4.57 (br t, 1 H, H-5, w/2 8.0 Hz), 3.70 (m, 2 H, H-6 $_{\text{exo}}$, H-6 $_{\text{endo}}$, w/2 1.6 Hz), 2.46 (s, 1 H, OH), 1.56–1.20 (m, 26 H, CH_2 , w/2 2.0 Hz), and 0.84 (t, 3 H, CH_3).

Anal. Calc. for $\text{C}_{20}\text{H}_{36}\text{O}_3$: C, 74.03; H, 11.18. Found: C, 73.90; H, 11.38.

1,6-Anhydro-3,4-dideoxy-2-C-octadecyl- β -D-threo-hex-3-enopyranose (10). —

To oven-dried Mg (0.12 g, 5.0 mmol) in anhydrous diethyl ether (5 mL) was slowly added a solution of 1-bromo-octadecane (1.60 g, 4.8 mmol) in ethyl ether (20 mL). Initiation of the reaction was facilitated with a drop of methyl iodide. When addition was complete, the solution was boiled on a warm-water bath for 40 min, and a solution of levoglucosenone (0.60 g, 4.8 mmol) in diethyl ether (15 mL) was added to the Grignard reagent during 10 min. The mixture was then treated as before. T.l.c. with 1:1 hexane-ethyl acetate indicated the presence of two major products, R_f 0.95 (hexatriacontane, the Wurtz-coupled by-product), and R_f 0.74 (**10**). Evaporation of the ether yielded a yellow, waxy solid which was dissolved in the minimum volume of hexane, and the solution cooled to -20° . A white, waxy solid (0.20 g, 11%) that precipitated from the hexane had m.p. $67-68^\circ$; ν_{\max}^{KBr} 3424 (O-H stretch), 2915, 2850 (C-H), and 1471 cm^{-1} (C=C); $^1\text{H-n.m.r.}$ (90 MHz, $\text{CDCl}_3\text{-Me}_4\text{Si}$): δ 5.99 (dd, 1 H, H-4, $J_{4,5}$ 2.9, $J_{3,4}$ 10.6 Hz), 5.60 (dd, 1 H, H-3, $J_{1,3}$ 2.1 Hz), 5.21 (d, 1 H, H-1), 4.63 (dd, 1 H, H-5, w/2 8.0 Hz), 3.72 (m, 2 H, H-6 $_{exo}$, H-6 $_{endo}$, w/2 3.0 Hz), 2.54 (s, 1 H, OH), 1.25 (m, 34 H, CH_2 , w/2 4.0 Hz), and 0.89 (t, 3 H, CH_3).

Anal. Calc. for $\text{C}_{24}\text{H}_{44}\text{O}_3$: C, 75.74; H, 11.65. Found: C, 75.90; H, 11.72.

1,6-Anhydro-3,4-dideoxy-2-C-decyl- β -D-threo-hex-3-enopyranose (**11**). — The procedure employed was adapted from the methods of Pearce *et al.*¹⁸ Lithium wire (2.00 cm, 0.88 g, 12.7 mmol, containing 0.8% of sodium) was cut into three pieces, which were placed in THF (5 mL) under an argon atmosphere. Levoglucosenone (0.80 g, 6.3 mmol) and 1-bromodecane (0.17 g, 7.7 mmol) were dissolved in THF (3 mL), and several drops of the solution were added to the lithium. Reaction was not initiated on heating to boiling under reflux, and therefore a drop of methyl iodide was added. Upon initiation, the rest of the levoglucosenone solution was quickly added, the color of the solution changing from light yellow to brown. After addition was complete, the solution was stirred for 3 h at room temperature and then the liquid was decanted from the remaining lithium, evaporated under diminished pressure, and the crude product dissolved in diethyl ether, and the solution washed with 25mM H_2SO_4 . During this washing, a thick emulsion formed, and this was broken up by adding saturated NaCl solution. The aqueous layer was extracted with ethyl ether ($2 \times 20\text{ mL}$), and the ether solution and extracts were combined, dried (anhydrous Na_2SO_4), and evaporated, affording a yellow oil which was chromatographed on a column ($22 \times 220\text{ mm}$) of silica gel with 1:1 hexane-ethyl acetate, yielding white, crystalline **11** (0.17 g, 10%) having m.p. $50-51^\circ$; ν_{\max}^{KBr} 3424 (O-H stretch) and 2915, 2853 cm^{-1} (C-H); $^1\text{H-n.m.r.}$ (90 MHz, $\text{CDCl}_3\text{-Me}_4\text{Si}$): δ 6.00 (dd, 1 H, H-4, $J_{4,5}$ 4.6, $J_{3,4} \sim 9\text{ Hz}$), 5.60 (dd, 1 H, H-3, $J_{1,3}$ 1.7 Hz), 5.23 (br s, 1 H, H-1), 4.64 (dd, 1 H, H-5, $J_{5,6_{exo}}$ 3.9 Hz), 3.73 (m, 2 H, H-6 $_{exo}$, H-6 $_{endo}$, w 2 $\sim 3\text{ Hz}$), 9.50 (s, 2 H, OH), 1.56–1.27 (m, 18 H, CH_2 , w/2 5 Hz), and 0.87 (t, 3 H, CH_3).

Anal. Calc. for $\text{C}_{16}\text{H}_{28}\text{O}_3$: C, 71.60; H, 10.52. Found: C, 71.86; H, 10.66.

1,6-Anhydro-2-C-tetradecyl- β -D-altropyranose (**12**). — To a solution of compound **9** (0.63 g, 1.9 mmol) in 1,4-dioxane (10 mL) was added a solution of osmium tetroxide (0.51 g, 2.0 mmol) in 1,4-dioxane (13 mL). After 96 h at room temperature,

t.l.c. indicated that most of the starting material had been depleted, and 1:1 ethanol-H₂O saturated with Na₂SO₃ (20 mL) was added to the mixture. This was boiled under reflux for 2 h, the black precipitate removed by filtration, and the yellow filtrate concentrated by evaporation to a milky residue which was freeze-dried. T.l.c. with 1:1 hexane-ethyl acetate indicated the presence of some starting material (R_F 0.71) and **12** (R_F 0.09). Therefore, the mixture was placed on a column (20 × 110 mm) of silica gel and eluted with ethyl acetate, yielding **12** as a white, waxy solid (0.19 g, 27 %); m.p. 71–72 °; ν_{\max}^{KBr} 3393 (O–H stretch), 2920, 2850 (C–H), 1473 (O–H bend), and 1115 cm^{−1} (C–O); ¹H-n.m.r. (acetonitrile-*d*₃-Me₄Si): δ 5.12 (s, 1 H, H-1), 4.46 (complex d, 1 H, H-5, $J_{5,6\text{exo}}$ 5, $J_{4,5}$ 2.0, $J_{5,6\text{endo}}$ 0.9 Hz), 3.74 (dd, 1 H, H-4, $J_{3,4}$ 5 Hz), 3.68 (dd, 1 H, H-6_{endo}, $J_{6\text{endo},6\text{exo}}$ 7.7 Hz), 3.61 (dd, 1 H, H-6_{exo}), 3.58 (d, 1 H, H-3), 2.82 (br s, 3 H, OH), 1.27–1.29 (m, 26 H, CH₂), and 0.88 (t, 3 H, CH₃).

Anal. Calc. for C₂₀H₃₈O₅: C, 67.00; H, 10.68. Found: C, 66.75; H, 10.49.

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