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CHEMISTRY OF AYURVEDIC CRUDE DRUGS — VII[a]

GUGGULU (RESIN FROM *COMMIPHORA MUKUL*)—6

ABSOLUTE STEREOCHEMISTRY OF GUGGULTETROLS[b,c,d]

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Abstract — With a view to elucidating the stereochemistry of guggultetrols, components of saponified *Commiphora mukul* resin, D-*lyxo*-, L-*ribo*-, and L-*xylo*-octadecane-1,2,3,4-tetrols have been synthesised by two different routes. One method starts with D-glyceraldehyde, while the second route is based on the appropriate pentose. The absolute configuration of the natural product guggultetrol-18, has been deduced as D-*xylo* (2*S*, 3*S*, 4*R*-configuration) by direct comparison with synthetic compounds. This work also serves to establish the chirality of guggultetrol-20.

In an earlier publication[1], we described the isolation of a crystalline material from saponified Commiphora mukul (Hook. ex Stocks) Engl. (Syn. Balsamodendron mukul Hook. ex Stocks) resin, and this was characterised as a mixture of octadecane-1,2,3,4-tetrol (~50%), nonadecane-1,2,3,4-tetrol (~7%) and eicosane-1,2,3,4-tetrol (~40%) with minor amounts of other components, possibly lower (C_{16},C_{17}) and higher (C_{21},C_{22}) homologous tetrols. These compounds constitute a new class of naturally occurring lipids, and we wish to propose the generic name guggultetrol for this group.[2] Through derivatization and preparative GLC, the two major constituents with eighteen (guggultetrol-18) and twenty carbon atoms (guggultetrol-20) were obtained in a state of purity. Though, the gross structures of these compounds were readily established as 1 and 2 respectively, their configurations were not defined. Of the four theoretical possible configurations (relative), the arabino-configuration can be ruled out, as guggultetrol-20 with m.p. 85-87°[3] is clearly

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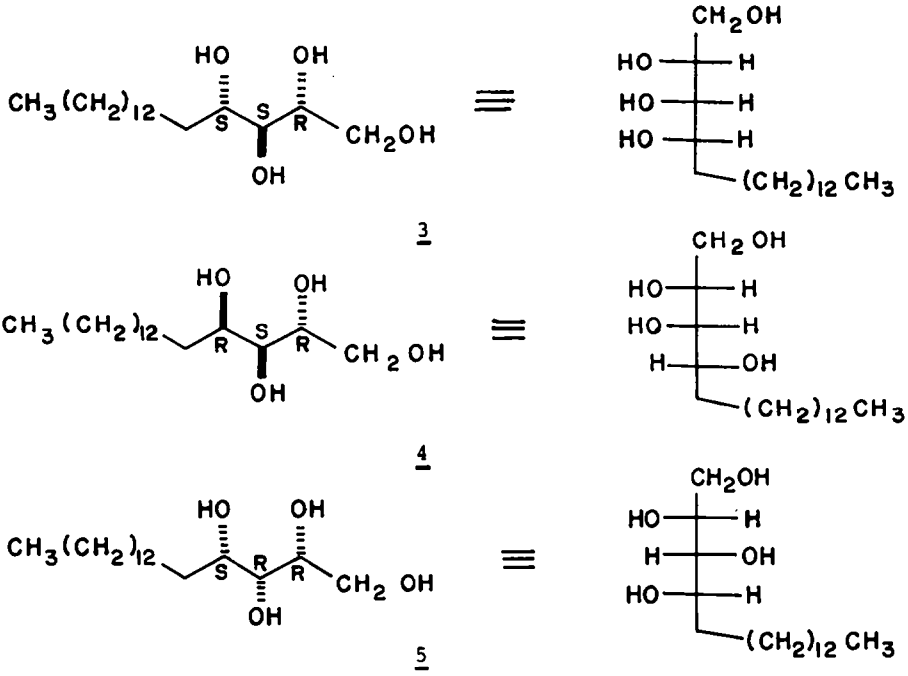
[b] MRC Communication No. 57
[c] Abstracted from the Ph.D Thesis of Vijay Kumar, M.S. University, Baroda (1984)
[d] Presented at Indian Institute of Science Platinum Jubilee Symposium on Recent Trends in Organic Chemistry, July 20-23, 1984, Bangalore.

different from the known[4,5] synthetic L-arabino-1,2,3,4-tetrahydroxyeicosane (or its enantiomer) which has a reported m.p. of 116-119°. The present work was carried out to establish absolute stereochemistry of guggultetrols through synthesis. As a result of these investigations, synthesis of L-ribo-(3), D-lyxo-(4), and L-xylo-octadecane-1,2,3,4-tetrols (5) have been achieved and are reported hereunder. Comparison of synthetic tetrols with the naturally occurring guggultetrol—18 helped establish the absolute configuration of natural product as 2S,3S, 4R i.e. D-xylo (23).[7]

$CH_3(CH_2)_n\ CHOH\cdot CHOH\cdot CHOH\cdot CH_2OH$

1 : n = 13

2 : n = 15



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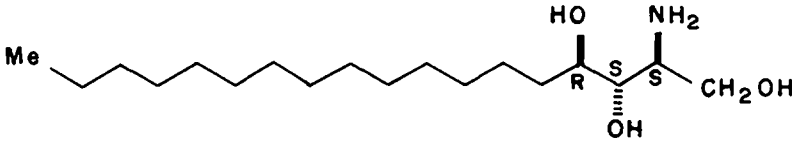
L-Ribo-octadecane-1,2,3,4-tetrol (3)

Closely related to the guggultetrols are the biologically important phytosphingosines (C_{18} and C_{20}), widely distributed in the plant sphingolipids and certain animal tissues, and possessing well-defined 2S,3S,4R-configuration, e.g.D-(+)-ribo-2-amino-1,3,4-trihydroxyoctadecane (6).[9,10] As a first approximation, it was conjectured that the guggultetrols may be similarly configurated, and hence

synthesis of ribo-guggultetrol-18 became the immediate objective. Synthesis of L-ribo-tetrol, rather than that of its antipode, was undertaken purely because of ready availability of starting materials.



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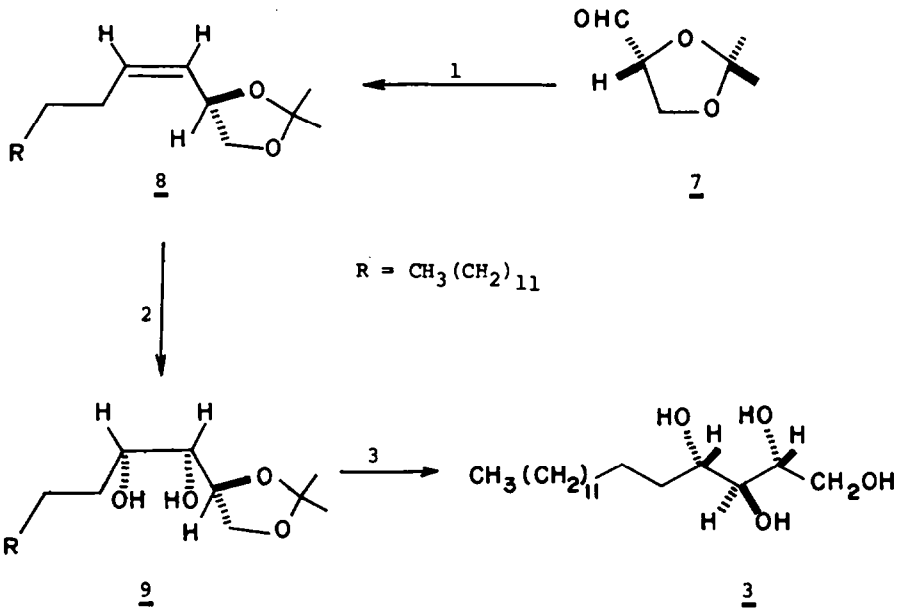
First, an expedient synthesis of the required ribo-octadecane-1,2,3,4-tetrol was devised taking advantage of the empirical rule of Kishi,[11] according to which osmylation of a cis-olefin such as 8 (preferred conformation) would result in formation of ribo-tetrol as the predominant product (addition of OsO_4 to the face of the olefinic bond opposite to the allylic hydroxyl or alkoxy group). To this end, olefin 8 (R= $C_{12}H_{25}$; Fig. 1) was first synthesised from 2,3-O-isopropylidene-D-glyceraldehyde (7), readily available by glycol cleavage of 1,2:5,6-di-O-isopropylidene-D-mannitol.[12] Aldehyde 7 was reacted with ylid from pentadecyltriphenylphosphonium bromide[13] under salt-free Wittig reaction[14] conditions to furnish essentially a single olefin in over 40% yield (based on D-mannitol diacetonide). From its method of preparation the product was expected to be Z-configurated (8),[15,16] and this was confirmed by hydrolysing it to the corresponding diol (m.p. 58-59°), checking its IR spectrum (no absorption in 950-1000 cm^{-1}, where trans 1,2-disubstituted olefins display an intense absorption band[17]), reconverting the crystalline material into the acetonide and comparing its spectral characteristics with the original product. Osmylation of 8 (R = $C_{12}H_{25}$) was effected with OsO_4 (catalytic) and sodium chlorate [18] and the crude cis-hydroxylation product (9) hydrolysed ($HClO_4$ aq) to furnish, after chromatography, only one crystalline tetrol, which was expected to be L-ribo-octadecane-1,2,3,4-tetrol (3). That this indeed was so, was confirmed by its straightforward synthesis from D-ribose as outlined below.

Synthesis of 3 from D-ribose is outlined in Fig. 2. In this and the related other syntheses described later, the sugars were suitably protected, as free or partially protected sugars give anomalous Wittig reaction products.[14a] The desired protected sugars were obtained by first trapping the pentose aldehyde form as dithioacetals[19] and then, protecting the free hydroxyls as acetonides, which are known to be stable to Wittig reaction conditions.[20] Specifically, D-ribose diethyldithioacetal (10)[21] was converted to the known mixture of 2,3:4,5- (11) and 2,5:3,4-di-O-isopropylidene-D-ribose diethyldithioacetal (12), though by a different process. Earlier workers[22] carried out this conversion using acetone and anhydrous $CuSO_4$ (36 hr), however we find that the reaction can be carried out much more



Reagents: 1. $C_{15}H_{31}\overset{+}{P}\phi_3\bar{B}r$, PhLi, Et_2O

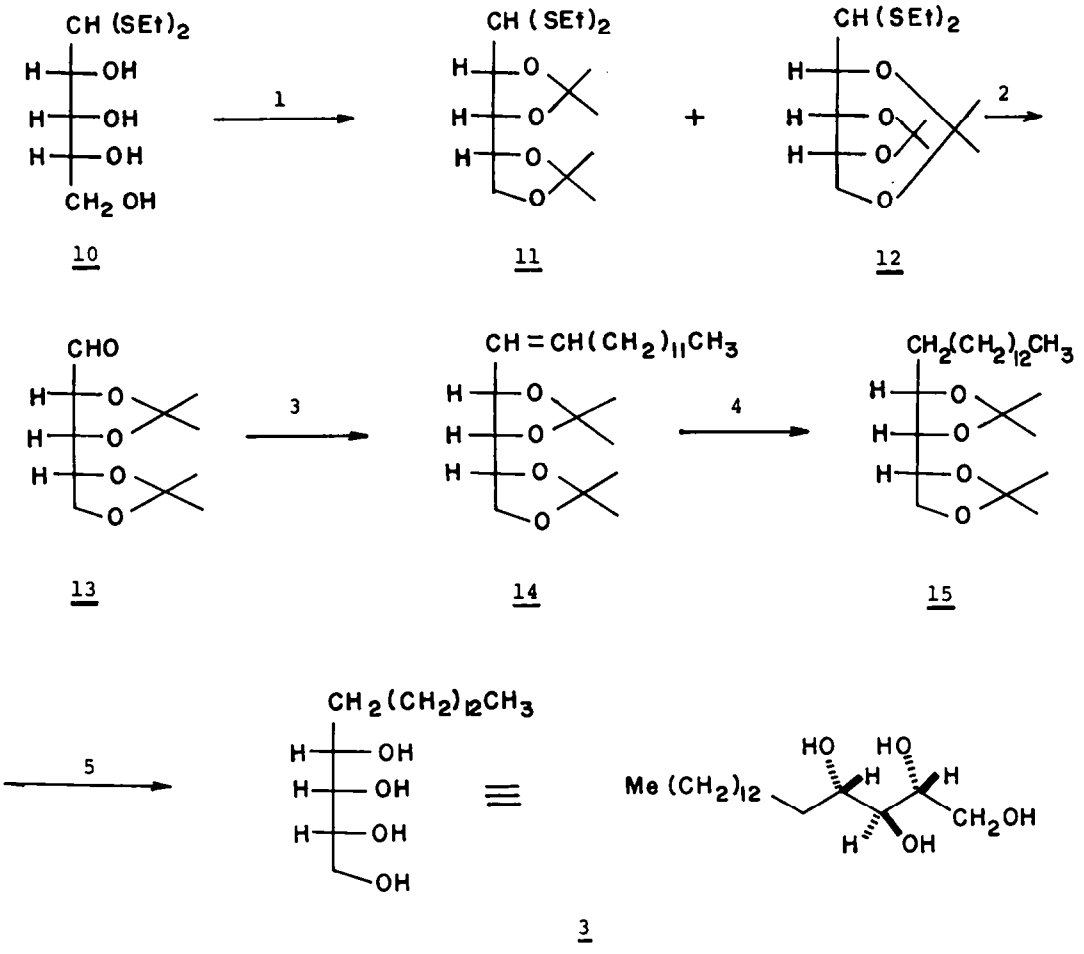
2. OsO_4, $NaClO_3$, THF

3. $HClO_4$aq, dioxane-H_2O

Fig. 1. Synthesis of L-ribo-octdecane-1,2,3,4-tetrol from D-glyceraldehyde acetonide

expeditiously (1 hr) and in superior yields by ferric chloride catalysis.[23] This product (11/12 ≈ 3/2) on treatment with mercuric chloride and cadmium carbonate in aqueous acetonitrile furnished the desired aldehyde mixture[24] (13 and the corresponding 2,5:3,4-di-O-isopropylidene isomer; in Fig. 2 only 2,3:4,5-isomer is shown for this and subsequent steps for sake of brevity). This product on reaction with ylid from tridecyltriphenylphosphonium bromide furnished the olefin mixture 14 (+ its isomer) in over 60% yield. On catalytic hydrogenation this material gave a product (15 + its isomer), which on hydrolysis yielded the required L-ribo-1,2,3,4-octadecanetetrol (2R, 3S, 4S-configuration) (3). This product was fully identical (m.p., IR, PMR) with the material obtained via D-glyceraldehyde route.

This compound was found to be different from the natural product (vide infra).



10 11 12 13 14 15 3

Reagents: 1. Acetone, $FeCl_3$

2. $HgCl_2$, $CdCO_3$, CH_3CN-H_2O

3. $C_{13}H_{27}\overset{+}{P}\phi_3\bar{B}r$, PhLi, THF

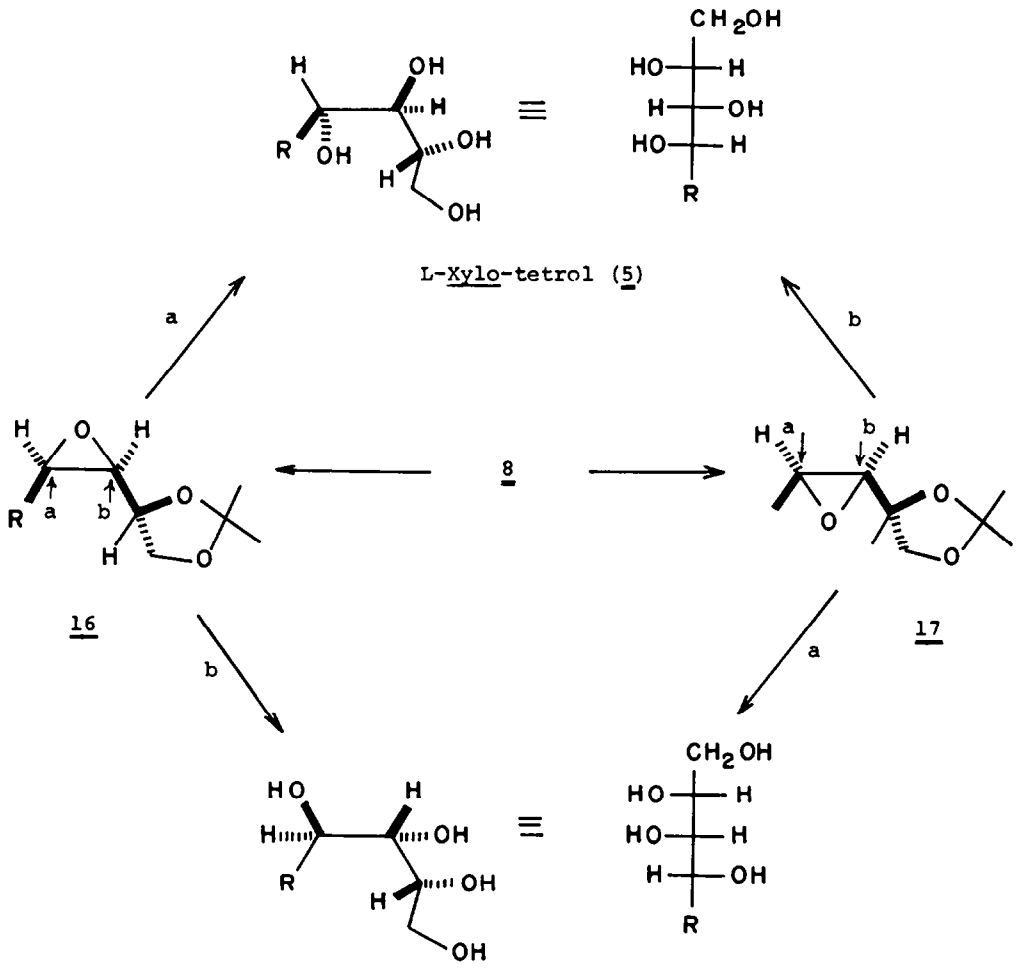
4. 10% Pd-C, H_2, EtOH. 5. $HClO_4$ aq, dioxane-H_2O

Fig. 2. Synthesis of L-ribo-octadecane-1,2,3,4-tetrol from D-ribose

D-Lyxo-octadecane-1,2,3,4-tetrol (4) and L-xylo-octadecane-1,2,3,4-tetrol (5)

Since guggultetrol-18 (1) does not have the ribo-configuration, it becomes necessary to consider other possibilities. An analysis (Fig. 3) of product development from trans-hydroxylation of the already synthesised cis-olefin (8) revealed that two distinct isomers, namely lyxo- and xylo - should result from such a reaction. Though, it became clear that it would be difficult[25] to predict which of the processes depicted in Fig. 3 will be favoured, and that unambiguous synthesis

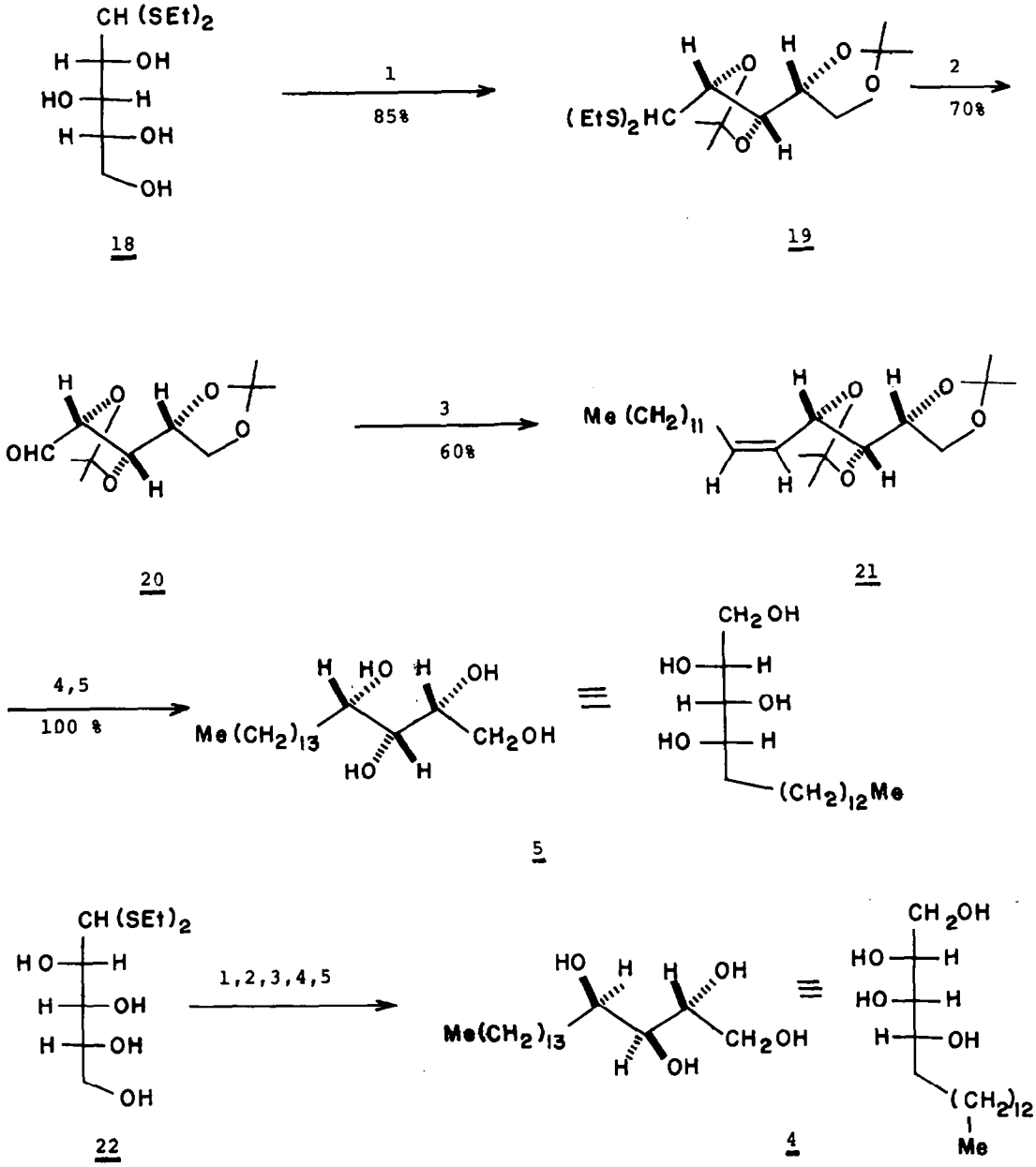
will still be necessary, it was decided to explore this reaction as it promised to provide a simple access to two other isomers from an intermediate used earlier for ribo-tetrol. In practice, exposure of 8 (R = $C_{12}H_{25}$) to performic acid in formic acid, followed by saponification gave a product, which on fractional crystallisation yielded two compounds: m.p. 81-83° (~30%) and m.p. 138-140° (~15%). The major product was found to be identical, except for its sign of optical rotation, with guggultetrol-18. By an unambiguous synthesis, described in the sequel, the main compound was characterised as L-xylo-octadecane-1,2,3,4-tetrol (5), whence the compound with m.p. 138-140° should be the D-lyxo isomer (4). That this indeed was so was established by its synthesis from D-arabinose, discussed later.



(a,b represent two possible modes for trans-glycol development)

Fig. 3. Product development from trans-hydroxylation of cis-olefin (8)

Synthesis of L-xylo-octadecane-1,2,3,4-tetrol (5) was carried out exactly on the lines already described for the ribo-isomer (3), and is depicted in Fig. 4. D-xylose diethyldithioacetal (18),[26] on exposure to acetone in presence of catalytic amounts of ferric chloride, furnished the known[27] 2,3: 4,5-di-O-isopropylidene-D-xylose diethyldithioacetal (19) in over 85% yield. This was converted into the



Reagents: see Fig. 2

Fig. 4. Synthesis of L-xylo-octadecane-1,2,3,4-tetrol (5) and D-lyxo-octadecane-1,2,3,4-tetrol (4)

corresponding aldehyde (20) as already described for 13. Wittig condensation furnished olefin 21, which on hydrogenation, followed by aq. acid-hydrolysis gave the required L-xylo-tetrol (5).

Synthesis of D-lyxo-octadecane-1,2,3,4-tetrol (4) was carried out starting with D-arabinose diethyldithioacetal (22)[28] and proceeding through the sequence described above for 5 (Fig. 4)

Guggultetrols

It has already been mentioned that guggultetrol-18 is enantiomeric with L-xylo-octadecane-1,2,3,4-tetrol (5). The relevant data (m.p., $[\alpha]_D$, IR) permitting this assignment, is summarised in Table 1 and Fig. 1. Based on comparison of IR and ^{1}H-NMR spectra of guggultetrol-18 and guggultetrol-20 and their derived acetonides, it had been concluded earlier[1] that both of these tetrols must have the same configurations at the chiral centres. Thus, these naturally occurring tetrols are

Table 1. Physical characteristics of guggultetrol-18 and synthetic 1,2,3,4-octadecanetetrols

No	Compound	m.p.	$[\alpha]_D^{25^\circ}$ (C)
1	Guggultetrol-18	80-82°	+11.4° (c 0.34%)
2	L-Xylo-octadecane-1,2,3,4-tetrol (5)	81-83°	-5.7° (c 0.42%)
3	L-Ribo-octadecane-1,2,3,4-tetrol (3)	101-103°	-8.9° (c 0.4%)
4	D-Lyxo-octadecane-1,2,3,4-tetrol (4)	138-140°	+5.1° (c 0.1%)

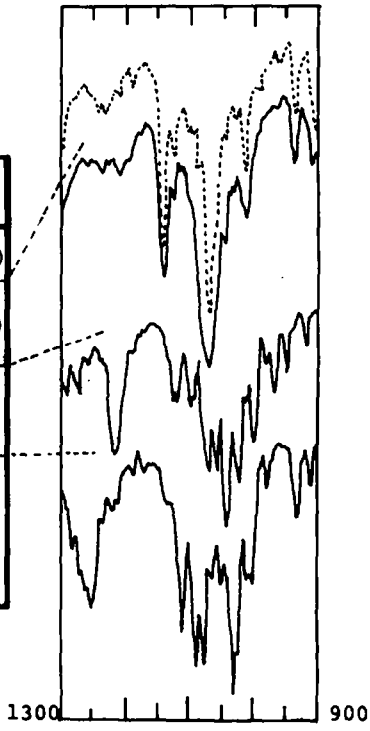
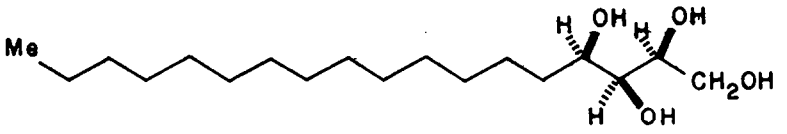


Fig. 5. Infrared absorption (900 to 1300 cm^{-1}) characteristics of guggultetrol-18 and synthetic 1,2,3,4-octadecanetetrols

assigned structures D-xylo-guggultetrol-18 (23) and D-xylo-guggultetrol-20 (24) respectively.

It may be noted that tetrols with differing configurations (3,4,5) display distinct patterns in the IR spectra in the 900 to 1300 cm^{-1} region (Fig.5), and



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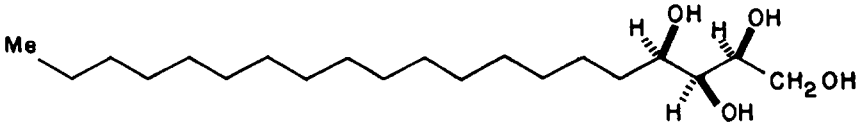

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this is of clear diagnostic value. The ^{1}H-NMR spectra (90 MHz) of the tetrols or their derived acetonides are not distinct enough in the C$\underline{H}$–O region for identification purposes.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p 60-80°. All solvent extracts were finally washed with brine and dried (Na_2SO_4). Silica gel for chromatography (-100, + 200 mesh) was washed with hot water till sulphate-free, dried and activated at 125-130° for 6 hr and standardized.[29] Alumina for column chromatography (-100, + 250 mesh) was water-washed, dried, activated at ~400°(8-10 hr) and then standardized.[30] TLC was carried out on silica gel layers (0.25 mm) containing 15% gypsum and activated at 110-115° (2 hr); visualization: iodine vapours.

The following instruments were used for spectral/analytical data: Schmidt + Haensch electronic polarimeter model Polatronic 1; Perkin-Elmer model 781 Infrared Spectrophotometer; Perkin-Elmer model R32 (90 MHz) NMR spectrometer; Varian Mat CH7 Mass Spectrometer (70 eV, direct inlet system); Fewlett-Packard 5712A and 7624A Gas Chromatographs (Al columns, 180 cm x 0.6 cm; support 60-80 mesh Chromosorb W; carrier gas, H_2). All ^{1}H-NMR were recorded in CCl_4 (unless stated to the contrary) with TMS as internal reference; signals are reported in ppm (δ); while citing ^{1}H-NMR data, following abbreviations have been used: s(singlet), t(triplet), q(quartet), m(multiplet), b(broad). While summarising mass spectral data, besides the molecular ion, nine most abundant ions (m/z) are reported with their relative intensities.

n-Pentadecyltriphenylphosphonium bromide

n-Pentadecyl bromide (15.7 g, 0.054 mole) and triphenylphosphine (14.7 g, 0.056 mole) were refluxed in acetonitrile (200 ml) for 12 hr. Solvent was removed from a steam-bath, under vacuum. The residue was cooled (~10°), triturated with dry ether (100 ml) to get a white solid, which was collected by filtration, washed with dry ether (25 ml x 2) and dried, m.p. 89-90°, yield 24.5g (80%) (Lit.[13], m.p. 92°)

(2S)-1,2-O-Isopropylidene-octadec-3(Z)-ene-1,2-diol (8)

To a stirred suspension of pentadecyltriphenylphosphonium bromide (11.06g, 0.02 mole) in dry ether (120 ml), an ether soln of phenyl lithium (20 ml of 1 molar soln; 1.68 g of ϕLi, 0.02 mole) was introduced dropwise (10 min) at room temp. (~25°). The resulting deep red reaction mixture was refluxed for 10 min, cooled to ~10° and filtered (N_2, anhydrous conditions) to remove Li salts. To this red soln, (2R)-2,3-O-isopropylidene-glyceraldehyde (7; prepared 12b from 2.6 g of 1,2:5,6-di-O-isopropylidene-D-mannitol by cleavage with 4.4g of lead tetraacetate in 80 ml dry benzene) was added dropwise. The resulting colourless reaction mixture was refluxed (N_2, 6 hr), freed of solvent, diluted with water (200 ml) and extracted with light petroleum (100 ml x 3). The combined extracts were washed with water and dried, and the solvent removed. The product was chromatographed on SiO_2-gel/IIB (64 cm x 1.7 cm), while monitoring with TLC (solvent: 20% ether in hexane). After rejecting the initial light petroleum eluates (50 ml x 5), the same solvent (10 ml x4) and light petroleum containing 10% EtOAc (10 ml x 10) eluted the required product, which was distilled: b.p. 185-190°(bath)/0.1 mm, $\{\alpha\}_D$ + 10°(EtOH, c 0.2%), yield 3.0 g. IR (neat): 1660, 1472, 1385, 1375, 1255, 1220, 1162, 1065 and 865 cm^{-1}. ^1H NMR:Me (3H, t, 0.89 ppm, J = 7.5 Hz), CH_2 and Me_2C-O (30H, bs, 1.26 ppm), OCH_2 (1H, t, 3.36 ppm, J_1 = 8Hz; 1H, dd, 3.92ppm, J_1 = 8Hz, J_2 = 6Hz), OCH (1H, m, 4.7 ppm), C = CH (2H, m, 5.4 ppm). Mass: m/z 324 (M^+, 8%), 97 (100%), 95 (88%), 81 (84%), 83(83%), 55 (80%), 109 (60%), 309 (43%), 123 (37%), 266 (27%). (Found: C,77.25; H,12.02.$C_{21}H_{40}O_2$ requires: C, 77.72; H, 12.42%).

(2S)-Octadec-3(Z)-ene-1,2-diol

To a stirred soln of 8 (2.5 g) in dioxane (50 ml), $HClO_4$ aq (10%, 10 ml) was added and the stirring continued for 5 hr at room temp. (~25°). The reaction mixture was diluted with water (100 ml), extracted with EtOAc (100 ml x 3), washed with water (50 ml x 3) and worked up as usual to get a solid (2.2 g), m.p.52-54°. This was twice recrystallized from CH_3CN to get crystals (1.98 g), m.p. 58-59°. IR (KBr): 3320, 2910, 2845, 1630, 1464, 1312, 1088, 1065, 1020, 872 and 710 cm^{-1}. ^1H-NMR ($CDCl_3$): Me (3H, bt, 0.90 ppm), CH_2 (24H, s, 1.28 ppm); OCH_2 (2H,bm, 3.48 ppm); OCH (1H, bm, 4.50 ppm); C=CH (2H, bm, 5.42 ppm). Mass: m/z 57 (100%), 55 (69%),

95(62%), 81(62%), 83(44%), 67(44%), 109(29%), 253(9%), 236(5%), 137(2%). (Found: C, 75.28; H, 12.12. $C_{18}H_{36}O_2$ requires: C, 75.99; H, 12.76%)

This material (1.8 g) in dry acetone (180 ml) was treated with anhyd. $FeCl_3$ (0.6 g) at 0-5°, and the soln stirred at 25° for 1 hr. After diluting with K_2CO_3 aq (10%, 20 ml), acetone was distilled off, the product taken up in $CHCl_3$ (20 ml x 3), washed with water (20 ml x 3), dried, and freed of solvent to get the isopropylidene derivative 8 (1.9 g).

Cis-hydroxylation of 8: isolation of L-ribo-octadecane-1,2,3,4-tetrol (3)

To a stirred soln of olefin 8 (324 mg, 0.001 mole) and OsO_4 (88 mg, 0.00023 mole) in aq tetrahydrofuran (20%, 10 ml), aq sodium chlorate (0.16 g in 2 ml water, 0.0013 mole) was introduced dropwise at 25° (5 min) and the stirring continued for 3 hr. The reaction mixture was next diluted with water (20 ml), extracted with EtOAc (20 ml x 3), washed with water (20 ml x 3), dried and freed of solvent to get a viscous liquid (320 mg). This was treated (25°) with aq $HClO_4$ (10%, 2 ml) in dioxane (10 ml) for 1 hr, and worked up as above to get a product (300 mg), which was chromatographed on SiO_2 gel/IIB (35 cm x 1.6 cm) with TLC monitoring (solvent: 20% MeOH in EtOAc). The first eluates (EtOAc; 25 ml x 6) gave a viscous liquid (200 mg), while the next EtOAc eluates (25 ml x 6) furnished a solid (60 mg) which was crystallized from EtOH to give needles, m.p. 101-103°, $[\alpha]_D$-8.9° (EtOH, c 0.44%), and characterized as 3. IR (KBr): 3420, 3350, 2920, 2850, 1465, 1215, 1068, 1053, 1040, 1020, 998, 962, 945, 885 cm^{-1}. ^{1}H-NMR (DMSO-d_6): Me (3H, bt, 0.90 ppm); CH_2 (26H, s, 1.28 ppm); OCH_2 (2H, b, 3.5 ppm); OCH (2H, d, 4.2 ppm; 1H, b, 4.4 ppm). Mass: m/z 55(100%), 73 (73%), 256(59%), 97 (44%), 129 (27%), 98 (25%), 111(20%), 264 (19%), 213 (13%), 284 (12%). (Found: C, 67.43; H, 11.96. $C_{18}H_{38}O_4$ requires: C, 67.88; H, 12.03%)

Trans-hydroxylation of 8 : isolation of D-lyxo- and L-xylo-octadecane-1,2,3,4-tetrol (4,5)

To a stirred soln of 8 (972 mg, 0.003 mole) in aq HCOOH (85%, 1.8 ml) at ~10°, aq H_2O_2 (30%, 0.5 ml, 0.0044 mole) was added and the mixture stirred at room temp. (~25°) for 12 hr. Formic acid, water were removed at ~40° under vacuum, the residue cooled and 1 ml of ice-cold 50% aq NaOH added. After heating the reaction mixture at 40-45° for 1 hr, it was diluted with water (10 ml), product taken up in EtOAc (10 ml x 4), washed with water, dried, and freed of solvent to get a sticky mass (850 mg). This was taken up in EtOH (6 ml) and kept at 25° for 12 hr, when fine needles (130 mg, m.p. 136-137°), characterized as D-lyxo-octadecane-1,2,3,4-tetrol (4), separated out. Cooling of mother liquor to ~15° (24 hr) gave another solid (330 mg, m.p. ~80°), identified as L-xylo-octadecane-1,2,3,4-tetrol (5).

D-Lyxo-octadecane-1,2,3,4-tetrol (4). Recrystallised from EtOH, m.p. 138-140°, $\{\alpha\}_D$ + 5.1° (c 0.1%). IR (KBr): 3350, 3245, 2920, 2840, 1460, 1406, 1255, 1110, 1090, 1077, 1030, 930, 906, 873, 850 cm^{-1}. Mass: m/z 74(100%), 69 (42%),83(20%), 67(21%), 81 (19%), 95(16%), 109(8%), 123(4%), 269(2%), 258(2%). (Found: C, 67.46; H, 11.93. $C_{18}H_{38}O_4$ requires: C, 67.88; H, 12.03%).

L-Xylo-octadecane-1,2,3,4-tetrol (5). Recrystallised from EtOH, m.p. 81-83°, $\{\alpha\}_D$-5.7°(EtOH, c 0.42%). IR (KBr): 3420, 3320, 2910, 2840, 1465, 1138, 1068, 1010, 932, 905, 860, 840, 820, 795 cm^{-1}. ^{1}H-NMR (DMSO-d_6): Me (3H, bt,0.90 ppm); CH_2 (26H, s, 1.28 ppm); OCH_2 (2H, b, 3.45 ppm); OCH (1H, bt, 3.75 ppm; 1H, m, 3.94 ppm; 1H, m, 4.25 ppm). Mass: m/z 319 (M + 1^+, 1%), 74(100%), 56 (72%), 57 (54%), 55(54%), 69(34%), 67(18%), 81(14%), 95(12%), 85(8%). (Found: C, 67.48; H, 11.80. $C_{18}H_{38}O_4$ requires: C, 67.88; H, 12.03%).

Pentoses diethyldithioacetals

These were prepared according to known procedures. Their mass spectra have been recorded.

D-Ribose diethyldithioacetal (10)[21], m.p. 82-83°, $\{\alpha\}_D$-39° (H_2O, c 0.5%). Mass: m/z 256 (M^+, 8%), 135(100%), 105(42%), 75(38%), 73(29%), 61(27%), 107(23%), 177(15%), 184(4%), 185(4%).

D-xylose diethyldithioacetal (18)[26], m.p. 63-65°,$\{\alpha\}_D$-30° (H_2O, c 0.5%). Mass: m/z 256 (M^+, 20%), 135(100%), 105(63%), 107(43%), 61(43%), 75(35%),59(25%), 73(17%), 177(8%), 185(6%).

D-Arabinose diethyldithioacetal (22)[28], m.p. 125-125°, $\{\alpha\}_D$-11° (MeOH, c 0.5%).

Pentoses diethyldithioacetal bisacetonides

General procedure is described. To a stirred soln of the dithioacetal (1 g) in dry acetone (100 ml) at 0-5°, anhyd. $FeCl_3$ (300 mg) was added, and the reaction mixture stirred at room temp. (~30°) for 1 hr. To this aq K_2CO_3 (10%, 10 ml) was added and acetone removed from a water bath, and the product taken up in $CHCl_3$ (10 ml x 3), washed with water, dried, freed of solvent and the material (~1.3 g) chromatographed on Al_2O_3 (18 cm x 1.7 cm). Light petroleum (250 ml x 8) eluted the desired product, purity of which was checked by GLC. (10% SE-30 column; temp, 200°).

2,3:4,5- and 2,5:3,4-O- Bisisopropylidene-D-ribose diethyldithioacetals (11, 12)[22], liquid, $\{\alpha\}_D$-55° ($CHCl_3$, c 0.8%), yield 80%, GLC purity 98% (RRT, 1:1.02). Mass: m/z 336 (M^+, 38%), 143(100%), 135(96%), 217(84%), 57(44%),159(30%), 101(30%), 275(9%), 263(7%), 177(7%).

2,3:4,5-O-Bisisopropylidene-D-xylose diethyldithioacetal (19)[27], liquid, $[\alpha]_D$-50° (C_6H_6, c 0.3%), yield 85%, GLC purity 98%. Mass: m/z 336 (M^+, 21%), 135(100%), 101(63%), 143(60%), 159(26%), 201(20%), 275(4%), 321(3%), 263(3%).

2,3:4,5-O-Bisisopropylidene-D-arabinose diethyldithioacetal[31], liquid, $[\alpha]_D$ + 80° (MeOH, c 1.4%), yield 92%, GLC purity 98%. ^{1}H-NMR: Me (18H, m, 1.36 ppm), CH_2 (4H, m, 2.7 ppm), OCH_2, OCH (5H, m, 3.96 ppm), SCH (1H, b, 4.15 ppm).

Bisisopropylidene-aldehydo-pentoses

To a soln of the bis-isopropylidene-pentose diethyldithioacetal (336 mg) in aq. CH_3CN (20%, 21 ml), cadmium carbonate (1.7 g) was added, and while stirring a soln of mercuric chloride (1.7 g in 7 ml of 20% aq. CH_3CN) was introduced (5 min) at room temp (~30°). After stirring for 6 hr, the precipitated salts were filtered off, the filtrate diluted with 1% aq K_2CO_3 (15 ml), and extracted with $CHCl_3$ (15 ml x 3). The combined extracts were washed with water, dried and freed of solvent to get the crude product, which was distilled.

2,3:4,5- and 2,5:3,4-O-Bisisopropylidene-aldehydo-D-ribose (13 and isomer)[24] liquid, b.p. 70-75°(bath)/0.1 mm, $[\alpha]_D$-30° ($CHCl_3$, c 0.6%), yield 85%. ^{1}H-NMR: OCH_2, OCH (5H, bm, 3.75-4.75 ppm), HC=O (1H, d, 9.62 ppm, J = 2Hz). Mass: m/z 215 (M^+-15, 8%), 43(100%), 59(37%), 101(18%), 85(18%), 57(16%), 115(11%), 143(9%), 157(6%), 171(5%).

2,3:4,5-O-Bisisopropylidene-aldehydo-D-xylose (20)[27a], liquid, b.p. 75-80°(bath)/0.1 mm, $[\alpha]_D$-28° (EtOH, c 3.1%), yield 70% (GLC purity, 98%; SE-30, 170°). ^{1}H-NMR: OCH_2, OCH (5H, m, 3.75-4.4 ppm), HC=O (1H, d, 9.70 ppm, J = 2Hz). Mass: m/z 215 (M^+-15, 85%), 101(100%), 55(65%), 85(62%), 59(54%), 201(48%), 143(25%), 115(15%), 155(13%), 129(6%).

2,3:4,5-O-Bisisopropylidene-aldehydo-D-arabinose[32], liquid, b.p. 65-70°(bath)/0.1 mm, $[\alpha]_D$-16°($CHCl_3$, c 4.5%), yield 70% (GLC purity, 98%; SE-30, 170°). ^{1}H-NMR: OCH_2, OCH (4H, m, 4.0 ppm; 1H, m, 4.26 ppm), HC=O (1H, d, 9.66 ppm, J = ~1Hz). Mass: m/z 215 (M^+-15, 29%), 43(100%), 101(37%), 85(36%), 59(35%), 143(31%), 57(30%), 69(26%), 73(20%), 201(11%).

Wittig condensation with tridecyltriphenylphosphonium bromide

To a stirred soln of tridecyltriphenylphosphonium bromide[4] (372 mg, 0.71 mmole) in dry THF (5 ml) at room temp (~30°), an ether soln of phenyllithium (0.75 ml of 1 molar soln, 0.73 mmole) was added. The resulting red soln was refluxed for 10 min, cooled (10-15°), and freshly prepared bisisopropylidene-aldehydo-pentose (0.16 g, 0.69 mmole) in THF (2 ml) introduced, and the reaction mixture refluxed for 6 hr. Usual work-up (see 8) gave a product which was chromatographed on Al_2O_3/IIB

(14.5 cm x 1.7 cm) with TLC monitoring (solvent: 25% ether in light petroleum). After rejecting light petroleum eluate (50 ml x 1), product was eluted with 25% benzene in light petroleum (~15 ml x 20). Removal of solvent furnished the required Wittig product.

1,2:3,4- and 1,4:2,3-O-Bisisopropylidene-L-ribo-octadec-5-ene-1,2,3,4-tetrol (14) and isomer), viscous liquid, $\{\alpha\}_D$-91° (EtOH, c 0.25%), yield 60%. IR (neat): 1245, 1218, 1165, 1125, 1070, 1045, 875, 855 cm^{-1}. ^{1}H-NMR: OCH_2, OCH (5H, bm, 3.5-4.4 ppm), C=CH (2H, m, 5.45 ppm). Mass: m/z 396 (M^+, 2%), 101(100%), 97 (68%), 59(47%), 266(36%), 251(25%), 237(25%), 83(25%), 114(16%), 381(10%). (Found: C, 72.38; H, 10.69. $C_{24}H_{44}O_4$ requires: C, 72.68; H, 11.18%).

1,2:3,4-O-Bisisopropylidene-L-xylo-octadec-5-ene-1,2,3,4-tetrol (21), viscous liquid, $\{\alpha\}_D$-30.5° (EtOH, c, 0.28%), yield 60%. IR (CCl_4): 1265, 1220, 1162, 1105,1070, 1030, 885 $cm.^{-1}$ ^{1}H-NMR: OCH_2 (1H, dd, 3.45 ppm, J_1=8Hz, J_2=2Hz; 1H, m, 3.98 ppm), OCH (2H, m, 3.89 ppm; 1H, t, 4.7 ppm, J = 8Hz), C=CH (2H, m, 5.5 ppm). Mass: m/z 396 (M^+, 6%), 101(100%), 91(68%), 266(54%), 59(44%), 105(37%), 251(25%), 237(25%), 157(25%), 381(24%). (Found: C, 73.11; H, 10.76. $C_{24}H_{44}O_4$ requires: C, 72.68; H, 11.18%).

1,2:3,4-O-Bisisopropylidene-D-lyxo-octadec-5-ene-1,2,3,4-tetrol, viscous liquid, $\{\alpha\}_D$-35°(EtOH, c 0.25%), yield 60%. IR(CCl_4): 1265, 1220, 1160, 1065, 1025, 885, 855 cm^{-1}. ^{1}H-NMR: OCH_2 (1H, t, 3.55 ppm, J = 8Hz; 1H, m, ~4.0 ppm), OCH (2H, m, ~4.0 ppm; 1H, t, 4.56 ppm, J = 8Hz), C=CH (2H, m, 5.4 ppm). (Found: C,72.34; H,10.70.$C_{24}H_{44}O_4$ requires: C, 72.68; H, 11.18%).

Bisisopropylidene-octadecane-1,2,3,4-tetrols

The above olefins (150 mg) in EtOH (10 ml) were hydrogenated at room temp.(25°) and pressure in presence of 10% Pd-C, until no more H_2 was absorbed. Usual work-up yielded the required products.

1,2:3,4- and 1,4:2,3-O-Bisisopropylidene-L-ribo-octadecane-1,2,3,4-tetrol (15 and isomer), viscous liquid, yield ~100%. IR (CCl_4): 1255, 1225, 1162, 1075, 1020,885cm^{-} ^{1}H-NMR: OCH_2, OCH (5H, m, 3.45-4.1 ppm). Mass: m/z 398 (M^+, 1.5%), 297(100%), 101(77%), 59(71%), 383(61%), 57(42%), 69(35%), 343(9%), 143(9%), 157(7%) (Found: C, 72.42; H, 11.25. $C_{24}H_{46}O_4$ requires: C, 72.31; H, 11.63%).

1,2:3,4-O-Bisisopropylidene-L-xylo-octadecane-1,2,3,4-tetrol, viscous liquid, yield ~100%. IR(CCl_4): 1265, 1220, 1165, 1080, 1020 cm^{-1}. ^{1}H-NMR: OCH_2, OCH (1H, dd,

3.50 ppm; 4H, m, 3.8-4.1 ppm). Mass: m/z 398 (M^+, 5%), 297(100%), 383(95%), 101(32%), 59(30%), 325(24%), 265(18%), 95(18%), 323(16%), 83(16%). (Found: C, 72.26; H, 11.07. $C_{24}H_{46}O_4$ requires: C, 72.31; H, 11.63%).

1,2:3,4-O-Bisisopropylidene-D-lyxo-octadecane-1,2,3,4-tetrol, viscous liquid, yield ~100%. IR(CCl_4): 1245, 1215, 1160, 1065, 1020, 855 cm^{-1}. ^{1}H-NMR: OCH_2, OCH (1H, m, 3.40 ppm; 4H, m, 3.7-4.1 ppm). Mass: m/z 398 (M^+, 3%), 383(100%), 297(100%), 101 (56%), 59(53%), 69(21%), 157(13%), 109(10%), 143(8%), 265(7%). (Found: C, 72.38; H, 11.19. $C_{24}H_{46}O_4$ requires: C, 72.31; H, 11.63%).

Octadecane-1,2,3,4-tetrols (3,5,4)

The above bisisopropylidene-octadecanetetrols (100 mg) in dioxane (10 ml) containing 10% aq $HClO_4$ (3 ml) was stirred at room temp (~25°) for 2 hr, diluted with water (100 ml), and the product taken up in EtOAc (25 ml x 3). The extract was washed with water, dried and freed of solvent to furnish the appropriate tetrol, which was crystallised from EtOH. These products were identical in all respects with the products obtained by the D-glyceraldehyde route.

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2 The name guggultetrol is reserved for long-chain linear aliphatic tetrols with hydroxyl functions at C-1, C-2, C-3, and C-4 positions. A numerical suffix indicating the number of carbon atoms and a prefix depicting the absolute stereochemistry, suffice to completely describe such a compound. Thus, the C_{18}-tetrol to which xylo-configuration has now been assigned will be: D-xylo-guggultetrol-18 or 2S, 3S,4R-guggultetrol-18. Work is on hand to check distribution of these compounds in the plant kingdom.

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