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SYNTHESIS AND PROPERTIES OF SOME STEREOISOMERIC LONG-CHAIN 1,2,3,4-TETROLS

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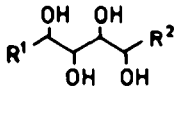
Abstract - Syntheses of 1,2S,3R,4R, 1,2S,3R,4S, 1,2R,3S,4R, and 1,2S,3S,4R-icosanetetrol, as well as of 1,2S,3S,4R-octadecanetetrol, are described, all based upon Wittig reactions of 1,2,3-protected pentodialdo-1,4-furanoses, serving as "chiral templates", with pentadecyl (or tridecyl) triphenylphosphorane, followed by catalytic hydrogenation, hydrolysis, and reduction. The tetrols, all forming liquid crystals on heating, are characterized spectroscopically and as their O-tetraacetates. The latter serve admirably for GLC-separation and -characterization of all non-enantiomeric tetrols. From the sign of rotation and GLC-comparison with the synthetic O-tetraacetates it follows that the 1,2,3,4-octadecanetetrol and 1,2,3,4-icosanetetrol, reported several years ago as the predominant members of a homologous series of tetrols derived from the gum-resin of *Commiphora mukul*, possess the 2S,3S,4R-configuration ('D-xylo').

Acyclic, vicinal tetrols **1**, occasionally encountered as natural products, pose a biosynthetic problem, linked, by necessity, to that of their stereochemistry.



1

2: $R^1 = Me[CH_2]_2$; $R^2 = [CH_2]_3NCS$

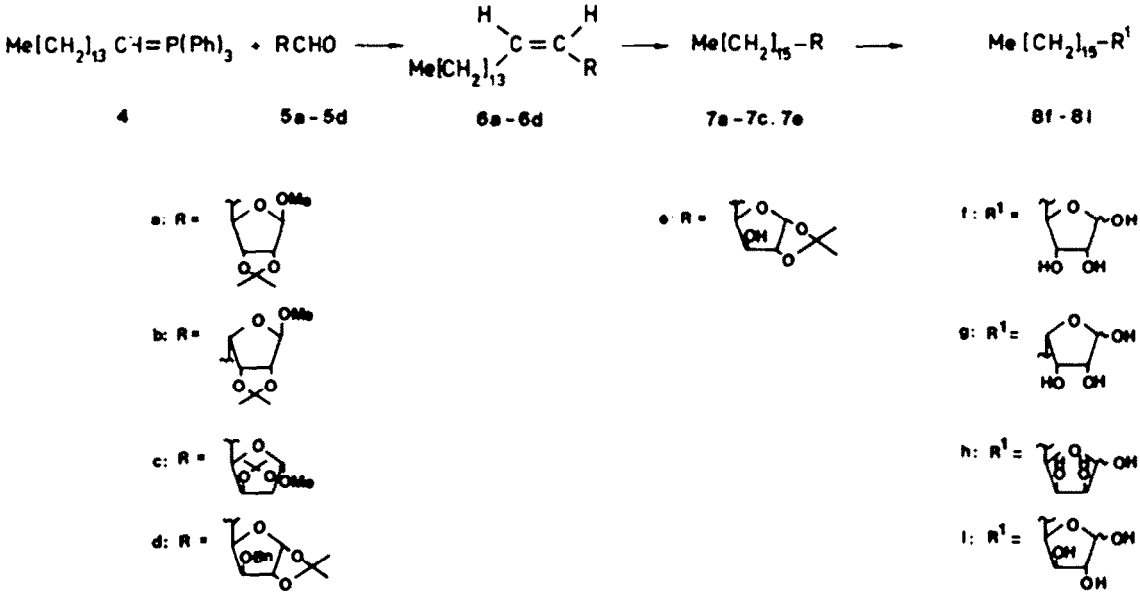
3: $R^1 = H$; $R^2 = [CH_2]_nMe$

The finding several years ago of an isothiocyanate with the stereochemically non-specified structure **2**, deriving from a glucosinolate in *Capparis grandis* L.,[1] prompted our interest in other acyclic, vicinal tetrols of natural derivation. Particularly intriguing to us was a series of homologous, straight-chain 1,2,3,4-tetrols [**3**, n=11-17(vastly dominated by n=13 and 15)], described in 1973 by Sukh Dev and colleagues as constituents of the alkali-hydrolyzed, neutral fraction of an extract of the well-known gum-resin ('guggulu'), exuded by the tropical tree *Commiphora mukul*.[2] Coherent GLC-data were quoted in support of identical though unknown stereochemistry throughout the series of homologues, the predominant two of which, **3** (n=13 and 15), were individually characterized.[2] The melting point (85-87°) of the C_{20}-tetrol precluded its identity with 1,2S,3S,4S-icosanetetrol ('L-arabino') (m.p. 116-119°)[3] (or its enantiomer), the sole reported, non-racemic stereoisomer of the C_{18}- and C_{20}- tetrol series. On this background we set out to synthesize

and characterize 1,2S,3R,4R-('D-ribo'), 1,2R,3S,4R-('D-lyxo'), and 1,2S,3S,4R-('D-xylo')-icosanetetrol one of which must necessarily be identical with or enantiomerically related to the C_{20}-tetrol of natural derivation.

RESULTS AND DISCUSSION

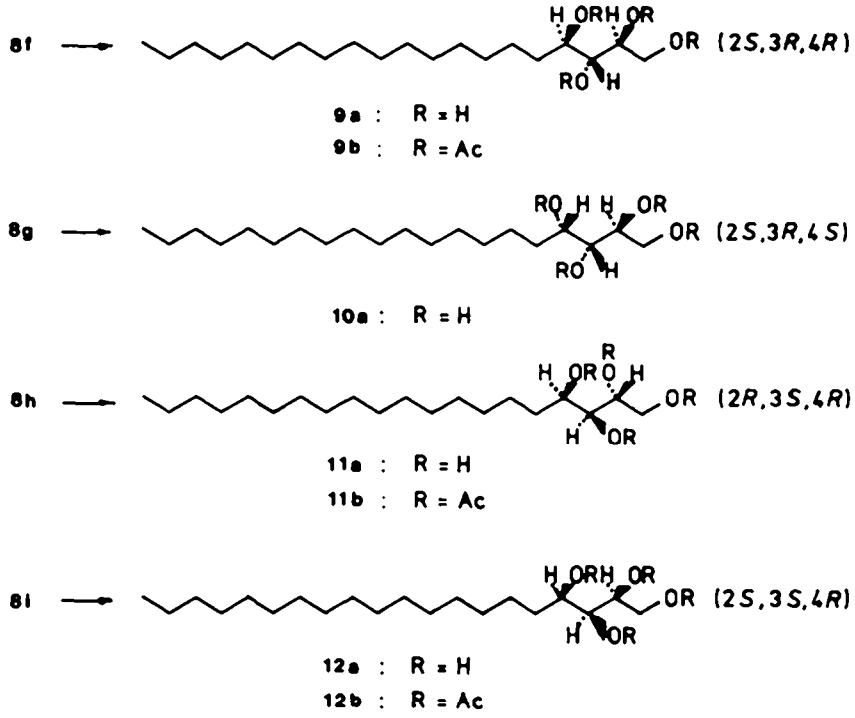
Wittig-reaction mediated chain elongation of suitably protected aldopentose derivatives lies close at hand for assembling the desired icosanetetrols. In order to circumvent the undesired formation of C-glycosides, a complicating feature in the reaction of furanoses (and pyranoses) with non-stabilized alkylidenephosphoranes, 1,2,3-protected pentodialdo-1,4-furanoses were selected as sources of the C_1-C_5 moieties of the icosanetetrols, a strategy not unlike that employed by Gigg and Warren in their synthesis of the 1,2S,3S,4S-isomer.[3] The requisite pentadecyltriphenylphosphorane 4, affording the remaining fifteen carbon atoms, was generated *in situ* from the corresponding phosphonium bromide, obtained from triphenylphosphine and pentadecyl bromide.[4] The latter was conveniently produced from palmitic acid by the photoassisted Cristol-Firth-Hunsdiecker reaction introduced by Meyers and Fleming.[5] The synthetic sequences leading to the stereoisomeric icosanetetrols are outlined in Schemes 1 and 2.



SCHEME 1

Oxidation of the readily accessible methyl 2,3-O-isopropylidene-β-D-ribofuranoside (Scheme 3) to methyl 2,3-O-isopropylidene-β-D-ribo-pentodialdo-1,4-furanoside 5a has been effected previously with Sarett's reagent,[6] or, alternatively, by the Pfitzner-Moffatt method.[7] Whereas a slightly modified version of the Sarett oxidation[8] served well in our hands to produce the aldehyde 5a in satisfactory yield and purity, oxidation under the mild conditions introduced by Swern for the Pfitzner-Moffatt oxidation [DMSO/$(COCl)_2$/TEA][9] resulted in a good yield of a nearly 1:1-mixture of 5a and the unknown methyl 2,3-O-isopropylidene-α-L-lyxo-pentodialdo-1,4-furanoside 5b, separable by chromatography. The observed

4-epimerisation was found to be slower at the product level, 5a→5b, and hence may take place chiefly through the vinyloxysulphonium ion 14 (Scheme 3). We are here faced with yet another addition to the several reported cases of analogous, base-induced epimerisations in fused, five-membered tetrahydrofurans.[10]

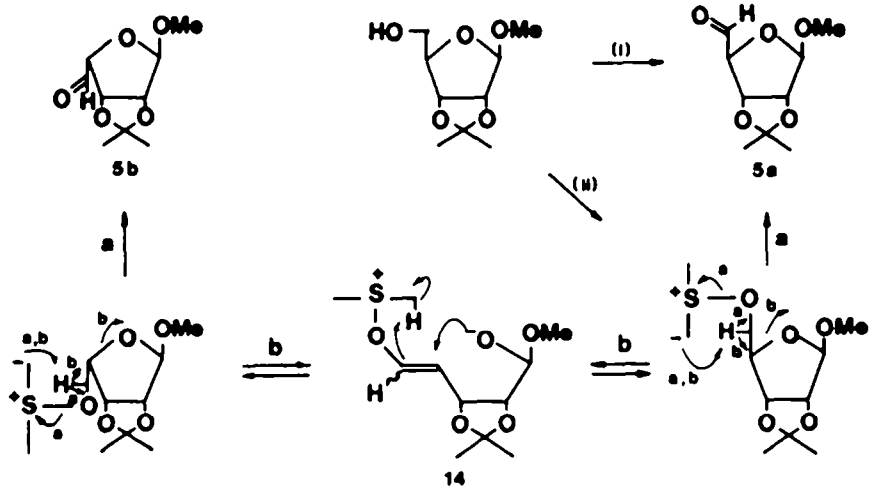


SCHEME 2

The Wittig reaction of the ylide 4 with the aldehyde 5a (Scheme 1) was conducted in THF with DMSO as a co-solvent, conditions recommended by Sonnet[11] for the stereoselective production of (Z)-olefins from non-stabilised alkylidenephosphoranes. The reaction, conducted under these conditions, afforded methyl (Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-β-D-ribo-icosofuranoside 6a as the sole product. Mixtures of the epimeric aldehydes 5a and 5b yielded equally composed mixtures of the Wittig products 6a and 6b, more conveniently separated by chromatography than the parent aldehydes. Upon catalytic hydrogenation, 6a was converted into the saturated methyl hexadecadeoxyicosofuranoside 7a which, on acid hydrolysis, afforded the hexadecadeoxy-D-ribo-icosofuranose 8f as a mixture of anomers. Reduction of the sugar with $NaBH_4$ proceeded unexceptionally to give the 1,2S,3R,4R-icosanetetrol ('D-ribo') 9a (Scheme 2). This, as well as the other tetrols discussed in the present paper, form liquid crystals on heating. Apparent melting points, representing transitions from ordered, three-dimensional to ordered, two-dimensional states, are followed by true melting points ('Klärungspunkte') at considerably higher temperatures (see Experimental).

A similar sequence of reactions, starting from the methyl 2,3-O-isopropylidene-α-L-lyxo-pentodialdo-1,4-furanoside 5b discussed above, led, through 6b, 7b, and the hexadecadeoxy-L-lyxo-icosofuranose 8g, to 1,2S,3R,4S-icosanetetrol ('L-lyxo')

10a (Scheme 2). Its enantiomer was synthesized by a similar series of conversions, starting with a Wittig reaction between 4 and the known methyl 2,3-O-isopropylidene-α-D-lyxo-pentodialdo-1,4-furanoside 5c, produced from 2,3:5,6-bis-O-isopropylidene-D-mannofuranose according to the procedure of Tronchet *et al.*,[12] and proceeding *via* the methyl hexadecadeoxy-8-D-lyxo-icosofuranosides 6c and 7c, and the hexadecadeoxy-D-lyxo-icosofuranose anomers 8h, to the 1,2R,3S,4R-icosanetetrol 11a (Scheme 2). The racemic modification of the tetrol, obtained by mixing equal quantities of the enantiomers 10a and 11a in solution, exhibited exactly the same behaviour on melting as the enantiomers. Again, no deviations were noted in its solid-phase (KBr) IR-spectrum from that of the enantiomers, a result at variance with the observation by Sukh Dev and colleagues[2] that published IR-spectra (in Nujol) of stereoisomeric, racemic C_{18}- and C_{19}-tetrols[13] were of no help in identifying the naturally derived C_{18}- and C_{20}-tetrols.



(i)$CrO_3 \cdot 2Py/CH_2Cl_2$;(ii)1.DMSO/$(COCl)_2/CH_2Cl_2$;2.Et_3N.

SCHEME 3

3-O-Benzyl-1,2-O-isopropylidene-α-D-xylo-pentodialdo-1,4-furanose 5d, requested for the synthesis of the 1,2S,3S,4R-icosanetetrol 12a, was prepared according to Horton and Swanson[14] by periodate cleavage of 3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-furanose which was, in its turn, obtained from 1,2:5,6-bis-O-isopropylidene-α-D-glucofuranose and purified *via* 3-O-benzyl-5,6-di-O-acetyl-1,2-O-isopropylidene-α-D-glucofuranose as previously reported.[15] On reaction with the Wittig reagent 4, the aldehyde 5d afforded the protected (Z)-5,6-dehydro-hexadecadeoxy-D-xylo-icosofuranose 6d. Catalytic hydrogenation of the latter, accompanied by hydrogenolysis, brought about its conversion to the furanose derivative 7e, which on acid hydrolysis afforded the hexadecadeoxy-D-xylo-icosofuranose 8i, finally reduced to give the desired 1,2S,3S,4R-icosanetetrol 12a ('D-xylo') (Scheme 2).

For further characterization the synthetic icosanetetrols 9a, 11a, and 12a were converted into their O-tetraacetates 9b, 11b, and 12b (Scheme 2). PMR,

^{13}C-NMR, and mass spectra were recorded for these and the parent tetrols. Generally, variations in spectroscopical characteristics were small and of limited diagnostic use within the groups of isomers. Whereas attempts at separation of the pertrimethylsilylated tetrol isomers by GLC were only partly successful, complete separation of the O-acetates 9b, 11b, and 12b was achieved by GLC on an efficient capillary column system (see Experimental) (Fig. 1). A second tracing in Fig. 1 depicts the GLC characteristics of a series of O-acetates, produced by acetylation of a mixture of homologous tetrols isolated from Commiphora mukul and kindly placed at our disposal by Dr. Sukh Dev. The reported dextro-rotation of the naturally derived C_{20}-tetrol[2], and an observed coincidence in retention time of its O-tetraacetate with that of 12b (Fig. 1), together provide proof of the naturally derived tetrol being 1,2S,3S,4R-icosanetetrol (12a)('D-xylo').

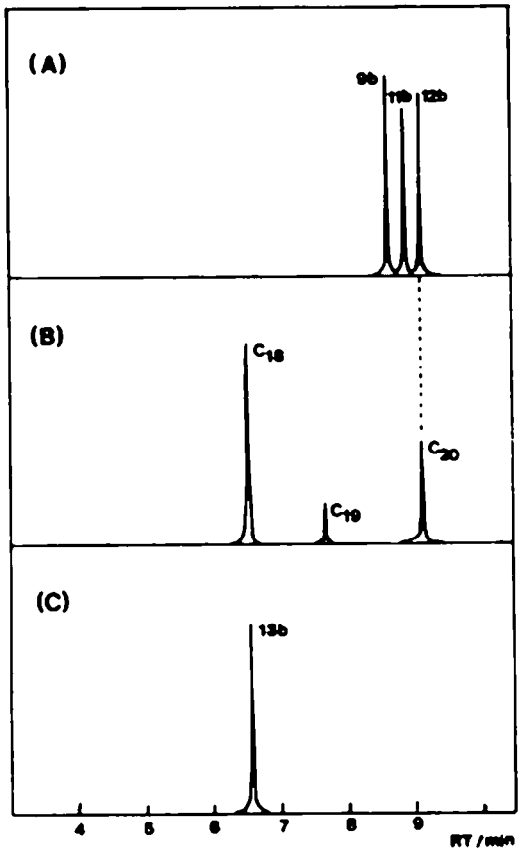
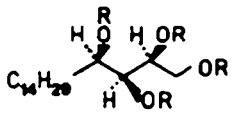


FIGURE 1. GLC profiles of: (A) A mixture of the synthetic 1,2(S),3(R),4(R)-(9b), 1,2(R),3(S),4(R)-(11b), and 1,2(S),3(S),4(R)-(12b) tetra-O-acetyl-icosanetetrols; retention times (RT) in min.: 8.63,8.87, and 9.08, respectively. (B) Tetra-O-acetyl-tetrols from acetylation of the tetrol mixture of natural derivation;[2] RT for C_{20}-acetate: 9.08, for C_{18}-acetate: 6.62. No line splitting or widening observed on 'spiking' with 12b and 13b. (C) 1,2(S),3(S),4(R)-Tetra-O-acetyl-octadecanetetrol 13b, RT: 6.62.

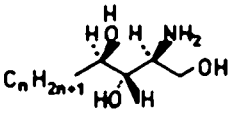
In order to verify the suggested identity in configuration of the C_{18}- and C_{20}-tetrols,[2] 1,2S,3S,4R-octadecanetetrol 13a was synthesized by a sequence of reactions identical to that employed for the synthesis of 12a, yet departing from tridecyl-triphenylphosphorane[16] rather than from 4. The reported dextro-rotation of the naturally derived octadecanetetrol,[2] and the observed GLC-coincidence (Fig. 1) between its O-tetraacetate and 13b, prepared by acetylation of the synthetic octadecanetetrol, together suggest that the C_{18}-tetrol of natural provenance is indeed 1,2S,3S,4R-octadecanetetrol 13a.*

*In the course of the present work we learnt, through correspondence with Dr. Sukh Dev, that he and his colleagues had synthesized various C_{18}-tetrols and independently established the configuration of the naturally derived C_{18}-isomer as xylo.

The acquired knowledge about the stereochemistry of the long-chain tetrols deriving from a higher plant provides a helpful requisite for unveiling their biosynthetic origin including a possible biological relationship to the long-known phytosphingosines with their well-established 2S,3S,4R-2-amino-1,3,4-alkanetriol structures (15).



13a : R = H
13b : R = Ac



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EXPERIMENTAL

General. M.ps. were determined in capillary tubes or on a Reichert m.p. microscope (mmp) and are uncorrected. ^{13}C-NMR spectra (at 125 MHz) and PMR spectra (at 500 MHz) were measured on a Bruker HX 500; 90 MHz PMR spectra on a Bruker HX 90 E spectrometer, all, when not otherwise indicated, in $CDCl_3$, with TMS as an internal standard. Optical rotations were determined in 1 dm micro cells on a Perkin-Elmer 141 polarimeter. IR-spectra were run in KBr on a Perkin-Elmer 421 instrument. Mass spectra were recorded using a VG Micromass 7070 instrument, equipped with a VG 2035 data system, operating at 70 eV or in the chemical ionization mode with isobutane as the reactant gas. GLC analyses were performed on a Sigma 1 gas chromatograph fitted with a fused silica capillary column (0.3 mm i.d., length 50 m) containing a crosslinked silicon SE 54 film (film thickness 0.52 µM); carrier gas: H_2; flow rate: 40 cmsec^{-1}; split injection (1:30) with injection port temperature, 280°; isothermal operation at 280°. Microanalyses were performed at the LEO company by Mr. G. Cornali and his staff.

Methyl 2,3-O-isopropylidene-β-D-ribo-pentodialdo-1,4-furanoside 5a. Methyl 2,3-O-isopropylidene-β-D-ribofuranoside[17] was oxidized with chromium trioxide: pyridine (1:2)[8] in dichloromethane, following the detailed instructions of Moorman and Borchardt,[8] to give, after chromatography, a 60% yield of pure, crystalline aldehyde, m.p. 59-60° [lit.[6] 60-61°].

Alternatively, the transformation was accomplished by an adoption of the Swern procedure for oxidizing alcohols[9]: oxalyl chloride (1.0 ml; 11 mmol) in CH_2Cl_2 (25 ml) was cooled to -60° ($CHCl_3$: Dry Ice); DMSO (1.7 ml; 22 mmol), in CH_2Cl_2 (5 ml), was added under stirring at such a rate that the temp. did not exceed -50°, followed by methyl 2,3-O-isopropylidene-β-D-ribofuranoside[17] (2.04 g, 10 mmol), dissolved in CH_2Cl_2 (10 ml) and added in the course of 5 min. After an additional 15 min, triethylamine (7.0 ml, 50 mmol) was introduced and the stirred solution was allowed to come to room temp. Ten min later, water (50 ml) was added. The organic phase, supplemented with two CH_2Cl_2-extracts, was washed with brine, dried, and concentrated to a syrup (85%) which, according to PMR-analysis, consisted of a nearly 1:1 ratio of two aldehydes. Separation of these by flash chromatography (hexane:ether, 1:2) gave a crystalline aldehyde, shown to be the ribo-aldehyde 5a described above, and a non-crystalline aldehyde identified as methyl 2,3-O-isopropylidene-α-L-lyxo-pentodialdo-1,4-furanoside 5b by means of its PMR-spectrum: (90 MHz) δ 1,29 (3H,s), 1.44 (3H,s), 3.36 (3H,s), 4.36 (1H,d,4-H), 4.58 (1H,d,2-H), 5.05 (1H,m,3-H), 5.06 (1H,s,1-H), and 9.65 (1H,s,5-H), identical to that of the known, independently prepared enantiomer 5c (vide infra). In a second oxidation experiment, in which the reaction mixture was stirred at 20° for 1.5 h before working-up, the 5a:5b - ratio increased to 4:1.

Pentadecyltriphenylphosphonium bromide 4. Palmitic acid was quantitatively converted into pentadecyl bromide as described by Meyers and Fleming.[5] Reaction of the bromide with triphenylphosphine, according to Cunningham and Gigg,[4] afforded pentadecyltriphenylphosphonium bromide as colourless crystals, m.p. 91°

(lit.[4] 92°) (from acetone:ether).

Methyl (Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-β-D-ribo-icosofuranoside 6a, and methyl (Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-α-L-lyxo-icosofuranoside 6b. A slurry of pentadecyltriphenylphosphonium bromide (10 g, 18 mmol) in THF (33 ml) was prepared under argon and cooled to -10°. n-BuLi (21.5 ml, 1.6 M in hexane) was injected at such a rate that the temperature did not exceed 0°. After 5 min, DMSO (17 ml) was added, causing a colourless solid to precipitate. The ribo:lyxo-aldehyde mixture (4:1) described above (3.35 g, 17 mmol), dissolved in THF (17 ml), was then injected and the mixture was stirred for 2 h at 20°. Water (170 ml) was added, and the mixture was extracted with 3x100 ml of hexane. After drying and evaporation, hexane (50 ml) was added and traces of insoluble triphenylphosphine oxide was removed by filtration. The residue was subjected to flash chromatography in hexane:ether (20:1) to give the oily D-ribo-(1.7 g), L-lyxo-(0.5 g), and mixed (0.6 g) Wittig products.

The D-ribo product 6a: $[\alpha]_D^{20}$ - 14.8° (c 1.0, $CHCl_3$). PMR-spectrum: (500 MHz) δ 0.89 (3H,t,20-H), 1.24 (22H,br.s.,9→19-H), 1.31 (3H,s) and 1.51 (3H,s) gem. Me's, 1.39 (2H,m,8-H), 2.15 (2H,m,7-H), 3.33 (3H,s,OMe), 4.59 (1H,d,2-H), 4.66 (1H,d,3-H), 4.99 (1H,d,4-H), 5.00 (1H,s,1-H), 5.48 (1H,dd,5-H,$J_{5,6}$ 11,$J_{4,5}$ 8), and 5.60 (1H,m, 6-H). (Found: C,72.84;H,11.24. Calc. for $C_{24}H_{44}O_4$: C,72.68;H,11.18).

The L-lyxo product 6b: $[\alpha]_D^{20}$ - 6.4° (c 1.0, $CHCl_3$). PMR-spectrum: (500 MHz) δ 0.88 (3H,t,20-H), 1.24 (22H,br.s.,9→19-H), 1.31 (3H,s) and 1.48 (3H,s) gem. Me's, 1,38 (2H,m,8-H), 2.13 (2H,m,7-H), 3.36 (3H,s,OMe), 4.60 (1H,d,2-H), 4.64 (1H,dd, 3-H), 4.74 (1H,dd,4-H), 4.91 (1H,s,1-H) 5.65 (1H,dd,5-H,$J_{5,6}$ 11,$J_{4,5}$ 7), and 5.75 (1H,m,6-H). (Found: C,72.98;H,11.27. Calc. for $C_{24}H_{44}O_4$: C,72.68;H,11.18).

Methyl 5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-β-D-ribo-icosofuranoside 7a. The D-ribo-product 6a (1.1 g) was dissolved in EtOAc (30 ml), PtO_2 (100 mg) was added, and the suspension was shaken in a H_2-atmosphere (1 at) until the up-take had ceased. After filtration through Celite, the solution was evaporated and the residue was recrystallized from methanol to give 7a as colourless scales, m.p. 42-44°, $[\alpha]_D^{20}$ - 29.3° (c 1.1,$CHCl_3$); PMR-spectrum: (90 MHz) δ 0.89 (3H,t,20-H), 1.24 (~30H,br.s.,5→19-H), 1.31 (3H,s) and 1.49 (3H,s) gem. Me's, 3.31 (3H,s,OMe), 4.11 (1H,t,4-H), 4.47 (1H,d,3-H), 4.58 (1H,d,2-H) and 4.92 (1H,s,1-H). (Found: C,72.26;H,11.66. Calc. for $C_{24}H_{46}O_4$: C,72.31;H,11.63).

5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-Hexadecadeoxy-D-ribo-icosofuranose 8f. The isopropylidene-ribofuranoside 7a (900 mg) was kept in a mixture of dioxane (70 ml) and 1 M HCl (23 ml) at 60° for 4 h. After neutralization (with 2 M NaOH), the solvents were removed in vacuo and the residue was washed with water. Recrystallization from methanol gave the sugar 8f as colourless needles (66%), forming liquid crystals on heating (mmp. 80°→120°). $[\alpha]_D^{20}$ + 1.5° (10 min) → -7.4° (18 h) (c 0.9, pyridine). (Found: C,69.54;H,11.54. Calc. for $C_{20}H_{40}O_4$: C,69.72;H,11.70).

1,2(S),3(R),4(R)-Icosanetetrol 9a. Sodium borohydride (375 mg, 9.9 mmol) was added to a solution of the sugar 8f (410 mg, 1.1 mmol) in MeOH (60 ml) and stirred at room temp. for 3.5 h. The solution was neutralized with acetic acid, concentrated to a small volume, and repeatedly dissolved in MeOH and evaporated. The residue was washed with water and recrystallized from MeOH to give colourless crystals of 9a (85%), mmp. (liquid crystals) 106°→159°; $[\alpha]_D^{20}$ + 6.8° (c, 0.6, pyridine). MS m/z (%): 74 (100), 43 (27), 56 (20), 57 (20), 55 (18), 41 (15), 69 (14), 83 (12), 73 (10), and 97 (10); (CI): 347 (M+1), 329, 311, 293, 285. (Found: C,69.17;H,12.41. Calc. for $C_{20}H_{42}O_4$: C,69.32;H,12.22).

1,2(S),3(R),4(R)-Tetra-O-acetyl-icosanetetrol 9b. The tetrol 9a (150 mg) was dissolved in pyridine (10 ml), acetic anhydride (0.7 ml) was added, and the solution was left standing at 20° for 48 h. Water was added, and the mixture concentrated. An analytical specimen was produced as a colourless oil by chromatography on silica gel (hexane:ethyl acetate, 85:15). $[\alpha]_D^{20}$ + 3.3° (c 1.2,$CHCl_3$). PMR-spectrum: (500 MHz) δ 0.90 (3H,t,20-H), ~ 1.30 (28H,br.s.,6→19-H), 1.64 (2H,m,5-H), 2.10-2.18 (12H,4s,4xMeCO-), 4.15 (1H,dd,1-H_A), 4.38 (1H,dd,1-H_B), 5.06 (1H,dd,4-H), 5.22 (1H,m,3-(or 4-)H), 5.27 (1H,m,4-(or 3-)H). ^{13}C-NMR: δ 13.9 (C-20), 20.5-20.8 (4xMeCO-), 22.5 (C-19), 25.1 (C-18), 29.1-29.6 (C-6→C-17), 31.8 (C-5), 62.0 (C-1), 69.4 (C-4), 71.6 (C-2,orC-3), 71.8 (C-3,orC-2), and 169.5-170.5 (4xMeCO-). (Found: C,65.37;H,9.75. Calc. for $C_{28}H_{50}O_8$: C,65.34;H,9.79).

Methyl 5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-α-L-lyxo-icosofuranoside 7b. The L-lyxo Wittig product 6b was subjected to catalytic hydrogenation with PtO_2 in ethyl acetate and worked up as described above for the D-ribo-epimer to give (in 94% yield) the saturated furanoside 7b as colourless crystals (from methanol), m.p. 33-36°, $[\alpha]_D^{20}$ - 38.8° (c 1.0,$CHCl_3$). PMR-spectrum (90 MHz) δ 0.88 (3H,t,20-H), ~1.3 (~30H,br.s.,5→19-H), 1.32 (3H,s) and 1.45 (3H,s) gem. Me's, 3.30 (3H,s,OMe), 3.87 (1H,dt,4-H), 4.49 (1H,d,2-H), 4.59 (1H,dd,3-H), and 4.83 (1H,s,1-H). (Found: C,72.33;H,11.70. Calc. for $C_{24}H_{46}O_4$: C,72.31;H,11.63).

5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-Hexadecadeoxy-L-lyxo-icosofuranose

8g. The methyl furanoside 7b (336 mg) was hydrolyzed in a mixture of dioxane (25 ml) and 1 M HCl (8 ml). After 8 h at 20°, the reaction was complete. After work-up as described above for the epimeric 8f, the lyxo-sugar (195 mg, 67%) was obtained as colourless crystals, mmp. (liquid crystals) 110°→122°. $[\alpha]_D^{20}$ - 13.0° (10 min)→-18.1° (20 h) (c 0.5, pyridine). (Found: C,69.56;H,11.40. Calc. for $C_{20}H_{40}O_4$:C,69.72; H,11.70).

1,2(S),3(R),4(S)-Icosanetetrol 10a. The L-lyxo-sugar 8g was reduced with sodium borohydride in methanol as described above for the 4(R)-epimer, to give the tetrol as colourless crystals (from methanol) (78%), mmp. (liquid crystals) 139°→154°. $[\alpha]_D^{20}$ - 2.1° (c 0.3, pyridine). The identity of the product followed from a comparison with the enantiomer (vide infra). (Found: C,69.28;H,12.00. Calc. for $C_{20}H_{42}O_4$:C,69.32;H,12.22).

Methyl (Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-α-D-lyxo-icosofuranoside 6c. Methyl 2,3-O-isopropylidene-α-D-lyxo-pentodialdo-1,4-furanoside 5c, prepared from D-mannose by the method of Ironchet et al.,[12] was converted into 6c exactly as described above for the α-L-lyxo-enantiomer 6b. The oily product exhibited a PMR-spectrum indistinguishable from that of 6b.

Methyl 5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-2,3-O-isopropylidene-α-D-lyxo-icosofuranoside 7c. Catalytic hydrogenation of 6c yielded the saturated furanoside 7c as colourless crystals, m.p.34-36°, $[\alpha]_D^{20}$ + 38.4° (c 1.0, $CHCl_3$). Its PMR-spectrum was identical with that of 7b reported above. (Found: C,72.38;H,11.64. Calc. for $C_{24}H_{46}O_4$:C,72.31;H,11.63).

5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-Hexadecadeoxy-D-lyxo-icosofuranose 8h. Acid hydrolysis of the furanoside 7c was performed as described above for the enantiomeric series. The D-lyxo-sugar 8h was isolated as colourless crystals, mmp. (liquid crystals) 112°→125°. $[\alpha]_D^{20}$ + 21.0° (10 min)→ + 26.4° (80 h) (c, 0.5, pyridine). (Found:C,69.40;H,11.76. Calc. for $C_{20}H_{40}O_4$:C,69.72;H,11.70).

1,2(R),3(S),4(R)-Icosanetetrol 11a. Reduction of the sugar 8h, performed as described above for the enantiomeric series, afforded the tetrol as colourless crystals (from methanol), mmp. (liquid crystals) 139°→159°, $[\alpha]_D^{20}$ + 2.5° (c 0.28, pyridine). The MS, recorded both in the electron impact and CI mode, was virtually indistinguishable from that of the 2(S),3(R),4(R)-isomer. IR:ν_{max} 3460,3350,1462, 1410,1280,1255,1110,1080,1030,1020, and 710 cm^{-1}. (Found:C,69.35;H,12.33. Calc. for $C_{20}H_{42}O_4$:C,69.32;H,12.22). On mixing equal quantities of the enantiomers 10a and 11a and recrystallization from methanol the racemic modification was obtained. Its mmp. and IR-spectrum were indistinguishable from those of the enantiomers.

1,2(R),3(S),4(R)-Tetra-O-acetyl-icosanetetrol 11b. The tetrol 11a was acetylated as described above for the 2(S),3(R),4(R)-diastereomer. The tetraacetate separated from hexane in colourless needles, m.p. 84-86°. $[\alpha]_D^{20}$ + 20.3° (c 1.0,$CHCl_3$). PMR-spectrum (500 MHz) δ 0.87 (3H,t,20-H),~ 1.25 (28H,br.s.,6→19-H), 1.50 (2H,m,5-H), 2.05-2.12 (12H,3s,4xMeCO-), 4.12 (1H,dd,1-H_A), 4.23 (1H,dd,1-H_B), 5.13 (2H,m,2-H and 4-H), and 5.28 (1H,dd,3-H). ^{13}C-NMR: δ 14.0 (C-1), 20.5-20.7 (4xMeCO), 22.5 (C-19), 25.0 (C-18), 29.2-29.5 (C-7→C-17), 30.7 (C-6), 31.8 (C-5), 61.9 (C-1), 68.4 (C-4), 70.4 (C-2, or C-3), 70.6 (C-3, or C-2), and 169.8-170.5 (4xMeCO). (Found: C,65.08;H,9.75. Calc. for $C_{28}H_{50}O_8$:C,65.34;H,9.79).

3-O-Benzyl-1,2-O-isopropylidene-α-D-xylo-pentodialdo-1,4-furanose 5d. 1,2:5,6-Diisopropylidene-D-glucofuranose was converted into the crystalline 3-O-benzyl-5,6-di-O-acetyl-1,2-O-isopropylidene-D-glucofuranose as described by Meyer and Reichstein.[13] Further elaboration of the diacetate into the aldehyde 5d followed the directions of Horton and Swanson.[14]

3-O-Benzyl-(Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecadeoxy-1,2-O-isopropylidene-α-D-xylo-icosofuranose 6d. Reaction of the aldehyde 5d with the phosphorus ylide 4, performed exactly as described above for analogous cases, yielded the Wittig product 6d in 62% yield as colourless crystals (from methanol), m.p. 30-32°, $[\alpha]_D^{20}$ - 71.5° (c 1.0,$CHCl_3$). PMR-spectrum: (90 MHz) δ 0.89 (3H,t,20-H), 1.26 (22H,br.s.,9→19-H), 1.32 (3H,s) and 1.52 (3H,s) gem. Me's, 1.41 (2H,m,8-H), 2.03 (2H,m,7-H), 3.80 (1H,d,3-H), 4.5-4.7 (2H,2xd,$PhCH_2$), 4.60 (1H,d, 2-H), 4.90 (1H,dd,4-H), 5.55-5.70 (2H,m,5-H and 6-H), 5.92 (1H,d,1-H), and 7.28 (5H,br.s.,Ph). (Found: C,76.11;H,10.22. Calc. for $C_{30}H_{48}O_4$:C,76.22;H,10.22).

5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-Hexadecadeoxy-1,2-O-isopropylidene-α-D-xylo-icosofuranose 7e. Catalytic hydrogenation of the Wittig product 6d (4.5 g) in ethyl acetate (200 ml) with 5% palladium on charcoal (900 mg) proceeded smoothly to give a gelatinous residue, converted into a crystalline product on drying (3.7 g,99%). The product separated as colourless crystals from methanol containing a few drops of water, m.p. 82-83°. $[\alpha]_D^{20}$ - 13.7° (c, 1.0,$CHCl_3$). PMR-spectrum: (90 MHz) δ 0.87 (3H,t,20-H), ~ 1.3 (30H,br.s.,5→19-H), 1.33 (3H,s) and 1.49 (3H,s) gem. Me's, 1.56 (1H,s,OH), ~ 4.05 (2H,m,3-H and 4-H), 4.48 (1H,d,2-H), and 5.88 (1H,d,1-H). (Found: C,71.76;H,11.58. Calc. for $C_{23}H_{44}O_4$: C,71.83;H,11.53).

5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-Hexadecadeoxy-D-xylo-icosofuranose 8i. Hydrolysis of the isopropylidene-derivative 7e (2.5 g) was performed in dioxane (160 ml) with 1 M HCl (40 ml) at 80° for 3 h to give the crystalline sugar 8i (87%) (from methanol), mmp. (liquid crystals) 116°→133°. $[\alpha]_D^{20}$ + 1.4° (10 min) → 0.0° (17 h). PMR-spectrum: (500 MHz) ($CDCl_3$, plus one drop of $^DCH_3OD$) δ 0.89 (3H,t,20-H), 1.27 (24H,br.s,,8→19-H), 1.58 (2H,m,6-H), 1.71 (2H,m,5-H), 3.89 (br.d.,3-H in β-anomer), 3.99 (dd,3-H in α-anomer), 4.00 (dd,2-H in α-anomer), 4.04 (d,2-H in β-anomer), 4.12 (dt,4-H in α-anomer), 4.15 (dt,4-H in β-anomer), 5.09 (s,1-H in β-anomer), and 5.41 (d,1-H in α-anomer). (Found: C,69.90;H,11.81. Calc. for $C_{20}H_{40}O_4$:C,69.72;H,11.70).

1,2(S),3(S),4(R)-Icosanetetrol 12a. Reduction of the sugar 8i with sodium borohydride yielded the crystalline tetrol (81%), (from ethanol), mmp. (liquid crystals) 87°→135°, $[\alpha]_D^{20}$ + 9.2° (c 0.28, ethanol), $[\alpha]_D^{20}$ + 8.7° (c, 0.8, pyridine). The MS was virtually identical with that of the 1,2(S),3(R),4(R)-isomer (vide supra). (Found: C,69.37;H,12.14. Calc. for $C_{20}H_{42}O_4$:C,69.32;H,12.22).

1,2(S),3(S),4(R)-Tetra-O-acetyl-icosanetetrol 12b. The tetrol 12a was acetylated in the usual way to give the tetraacetate 12b as colourless crystals (from hexane), mp. 54-56°. $[\alpha]_D^{20}$ + 2.3° (c 1.0,$CHCl_3$). PMR-spectrum: (500 MHz) δ 0.88 (3H,t,20-H), ~ 1.3 (28H,br.s.,6→19-H), 1.54 (2H,m,5-H), 2.06-2.12 (12H,4s,4xMeCO-), 4.00 (1H,dd,1-H_A), 4.40 (1H,dd,1-H_B), 5.12 (1H,q,4-H), and 5.30 (2H,m,2-H and 3-H). ^{13}C-NMR: δ 14.0 (C-20), 20.3-20.5 (4xMeCO-), 22.6 (C-19), 24.8 (C-18), 29.1-29.6 (C-7→C-17), 30.4 (C-6), 31.6 (C-5), 61.9 (C-1), 69.5 (C-4), 71.2-71.3 (C-2 and C-3), and 169.9-170.3 (4xMeCO-). (Found: C,65.45;H,9.81. Calc. for $C_{28}H_{50}O_8$: C,65.34;H,9.79).

3-O-Benzyl-(Z)-5,6-dehydro-5,6,7,8,9,10,11,12,13,14,15,16,17,18-tetradecadeoxy-1,2-O-isopropylidene-α-D-xylo-octadecofuranose. This Wittig product was synthesized exactly as described above for the higher homologue 5d, yet with tridecyltriphenylphosphonium bromide[16] serving as the ylide precursor, and was obtained as a colourless oil. $[\alpha]_D^{20}$ - 72.5° (c, 1.1, $CHCl_3$). (Found: C,75.08;H,9.88. Calc. for $C_{28}H_{44}O_4$:C,75.63;H,9.97).

5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecadeoxy-1,2-O-isopropylidene-α-D-xylo-octadecofuranose. Treatment of the above Wittig product with hydrogen and palladium on carbon in ethyl acetate afforded the saturated product as a colourless solid after drying (85%), m.p. 82-84° (from MeOH). $[\alpha]_D^{20}$ - 12.8° (c, 1.0,$CHCl_3$). (Found: C,70.68;H,11.36. Calc. for $C_{21}H_{40}O_4$: C,70.74;H,11.31).

5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecadeoxy-D-xylo-octadecofuranose. Acid hydrolysis of the isopropylidene-sugar afforded the xylo-C_{18}-sugar as colourless crystals (from methanol), mmp. (liquid crystals) 115→148°. $[\alpha]_D^{20}$ + 3.1° (10 min) → 0.0° (24 h) (c 0.9, pyridine). (Found: C,68.39;H,11.40. Calc. for $C_{18}H_{36}O_4$: C,68.32;H,11.45).

1,2(S),3(S),4(R)-Octadecanetetrol 12a. Sodium borohydride reduction of the xylo-C_{18}-sugar gave the tetrol 12a as colourless crystals, mmp. (liquid crystals) 98°→158°. $[\alpha]_D^{20}$ + 11.7° (c 0.3, ethanol), $[\alpha]_D^{20}$ + 8.9° (c 0.8, pyridine). The MS in the electron impact mode was virtually identical with those of the C-20 homologues; in the CI-mode peaks were prominent at m/z: 319(M+1),301,283,265, and 257. (Found: C,66.90;H,11.68. Calc. for $C_{18}H_{38}O_4$:C,67.89;H,12.01).

1,2(S),3(S),4(R)-Tetra-O-acetyl-octadecanetetrol 12b. Acetylation of the above C-18-tetrol afforded the tetraacetate as colourless crystals (from hexane), m.p. 49-51°. $[\alpha]_D^{20}$ + 2.1° (c 1.0, $CHCl_3$). (Found: C,64.31;H,9.53. Calc. for $C_{26}H_{46}O_4$: C,64.17;H,9.52).

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