Acyclic 1,2-/1,3-Mixed Pentols. Synthesis and General Trends in Bichromophoric Exciton Coupled Circular Dichroic Spectra

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Abstract: The synthesis of all eight configurational isomers of acyclic 1,2,3,4,6-pentols belonging to the 2R enantiomeric series is described. The 1-anthroyl-2,3,4,6-p-methoxycinnamates of these pentols give rise to unique exciton coupled circular dichroic spectra in the range of 220-380 nm. Comparisons with the CD of corresponding bichromophoric derivatives of the lower homologous tetrals, 1-anthroyl-2,3,4-p-methoxycinnamates led to a predictable general trend in which only minor differences result from 1,3-syn extensions whereas major differences result from 1,3-anti extensions.

INTRODUCTION

There exists no general microgram scale method for determining the absolute and relative configurations of acyclic 1,2-polyols, 1,3-polyols (skipped polyols) and mixed 1,2-/1,3-mixed polyols. These moieties exist as such in a large number of natural products, e.g., hopanoids, or in numerous antibiotics, particularly the polyene microlides; in the antibiotics, the polyol moieties can be isolated by a combination of hydrolysis, ozonolysis, periodate oxidation, etc. We have recently been developing bichromophoric exciton coupled circular dichroic methods for microscale configurational assignments of different types of acyclic 1,2- and 1,3-polyols and aminopolyols containing terminal primary hydroxyl or amino groups. In this bichromophoric method, two selectively introduced chromophores couple to give rise to “fingerprint” CD curve, which can be reproduced by summation of all interacting basis set pairs; this pairwise additivity principle was first fully demonstrated with glycopyranoside derivatives. In the case of 1,2-acyclic polyols derived from sugars, the terminal hydroxyl and remaining hydroxyls groups are derivatized as anthroates and p-methoxycinnamates, respectively, to give a CD library of triols, tetrals and pentals. The method was further extended to aminobacteriohopanes which carry acyclic side-chain moieties consisting of aminotetros and pentals. The bichromophoric approach has also been extended, together with a CD library, to 1,3-polyols with a terminal 1,2-diol group, i.e., 1,2,4-triols, 1,2,4,6-tetrals and 1,2,4,6,8-pentals. Both in 1,2-polyol and 1,3-polyols, a general trend is seen which makes it possible to predict the CD of unknown cases; this is particularly facile with the skipped polyols.

Two general reiterative NMR and/or CD methods for 1,3-polyol absolute configurational assignments that can be extended to longer systems including a difference CD approach has been described. An NMR
method for relative configurational assignments of 1,3-polyols has also been described. However, they depend on multistep transformations not suited for microscale manipulations, or have limited applicabilities.

None of the methods, including the coupled CD methods described above, are applicable to mixed 1,2-/1,3-polyol systems which have been found recently in new hopanoids; furthermore, these moieties exist in masked forms in polyene macrolides, e.g., primycin, myxovirescin, octacomycin, pentamycin. In order to facilitate microscale structural studies of such compounds, we describe the synthesis and CD of mixed polyols, which is followed by an application.

RESULTS AND DISCUSSION

Synthesis of ω-Monoanthroate Per-p-methoxycinnamates

Skipped pentol peracylates 2 and 3. These were prepared from corresponding acyclic pentols 4 and 5, respectively (Scheme 1).

![Scheme 1](image)

Allylic tetrol peraclylates 13-16. Propanal acetonide 6 (Scheme 2), obtained from (D)-mannitol, was diastereoselectively converted into 3α and 3β alcohols 7 and 8 by the procedure developed by Dondoni. Acetonides 7 and 8, upon treatment with allylmagnesium bromide gave diastereomeric pairs 9/10 and 11/12, respectively, each pair of which was separated by repeated silica gel chromatography using 10-11% ether/hexane mixture as eluate. Since pairs 9/10 and 11/12 could not be differentiated by NMR, the stereochemistry was determined from the CD data (Figure 3, see later on in the text). Diastereomers 9-12 were converted into the corresponding bichromophoric derivatives 13-16 (Scheme 2) by desilylation, acetonide cleavage, anthroylation of primary hydroxyl with 9-anthroyltetrazole and percinamoylation of the three secondary hydroxyls with p-methoxycinnamoylimidazole. The assignment of absolute configuration was
Scheme 2. a) CH₂=CHCH₂MgBr, THF, -30°C, 15 min., then 0°C, 45 min.; b) 1.0 M tetrabutylammonium fluoride in THF, rt., 5.5 h, 70%; c) MeOH, CH₃COCI, rt., 2 h; d) 9-anthroyl tetrazole, DBU, MeCN, 8 h, 53%; e) p-methoxycinnamoyl imidazole, DBU, MeCN, 4 h, 88%.

achieved by comparison of the CD of 13-16 with those of authentic ethyl tetrois (13r-16r) measured in acetonitrile and in methylcyclohexane.

Mixed pentol derivatives 37-44. A three step conversion of acetones 9-12 (Scheme 3) afforded aldehydes 25-28 as precursors of the skipped and mixed 1,2-1,3-pentols. Thus silyl derivatives 9-12 were first desilylated to diol acetones 17-20 and then converted into bisacetones 21-24. The latter upon ozonolysis yielded bisacetone aldehydes 25-28. Treatment of aldehydes 25-28 with allylmagnesium bromide at -30°C afforded, respectively, the 1,3-syn- and 1,3-anti- hydroxyl extended pairs, 29/30, 31/32, 33/34 and 35/36. All pairs were separated into respective diastereomers by silica gel chromatography, except for the pair 33/34, which was separated after chromophoric derivatization.

The pentol bisacetones 29 and 30, 31 and 32, and 35 and 36 were converted into bichromophoric derivatives, 37 and 38, 39 and 40, and 43 and 44, respectively, where the primary hydroxyl groups were anthroylated and secondary hydroxyl groups were cinnamoylated (Scheme 4). In the case of the inseparable diastereomeric pair 33/34, the mixture was first subjected to chromophoric derivatization and then base-line separated into diastereomers 41 and 42 by 3μ-silica HPLC column and 2% THF/CH₂Cl₂.

The syn versus anti extension at C-6 was determined by NMR as follows (Figure 1). The 1H-NMR J constants of 5-H and the extent of 7-H's chemical shifts difference in the three diastereomeric pentol
Scheme 3. a) 1.0 M tetrabutylammonium fluoride in THF, rt., 5.5 h, 70%; b) p-TsOH, CH3OC(CH3)2OCH3, 3.5 h, 83%; c) O3, Ph3P, -78°C, 93%; d) CH2=CHCH2MgBr, THF, -30°C, 15 min., then 0°C, 45 min.
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Scheme 4. a) MeOH, CH$_3$COCl, rt., 2 h; b) 9-anthroyl tetrazole, DBU, MeCN, 8 h, 53%; c) p-methoxy-cinnamoyl imidazole, DBU, MeCN, 4 h, 88%.

Figure 1. Conformations 35a and 36a and NMR data of 1,3-syn- and 1,3-anti- extended bisacetonides 35 and 36, respectively.

bisacetonides 29/30, 31/32, and 35/36 led to the C-6 stereochemical assignments. This is exemplified by the pair 35a (syn) and 36a (anti). The upfield 5-H signal of homoallylic alcohol 35 at 1.71 ppm exhibits two large vicinal coupling constants, $J_{4,5}$ 11.3 and $J_{5,6}$ 9.0, in addition to $J_{gem}$ 13.9 Hz; the two 7-H appears as a single 2H multiplet centered at 2.25 ppm. In contrast, the upfield 5-H of 36a at 1.77 ppm has $J_{4,5}$ 11.0 and $J_{5,6}$ 2.6, in addition to the $J_{gem}$ 13.7 Hz; the 7-H's appear as two multiplets at 2.20 and 2.30 ppm. This difference can be rationalized by the fact that in the syn-extended 35a, the C-7 homoallylic group adopts a quasi equatorial conformation with respect to the intramolecular H-bonded ring; this leads to a large $J_{5,6}$ of 9.0 Hz. In the anti-extended 36a, the H-bonded ring causes C-7 to assume a quasi axial orientation, and hence 6-H becomes quasi equatorial, leading to the small $J_{5,6}$ of 2.6 Hz. This is corroborated by the observation of an NOE between the 1.77 ppm 5-H and the 3.90 ppm 6-H signals. The 7-methylene protons in 35a has a greater degree of freedom to rotate around C(6)-C(7) in comparison to the 7-methylene in 36a, thus giving rise to the difference in the two 7-H signals mentioned above. Similar trends were observed in the pairs 29/30 and 31/32.
General Trends in CD

CD of skipped pentol derivatives 2 and 3. The CD curves of these derivatives are compared with the lower homologous tetrol derivative 17a in two solvents, the nonpolar methylcyclohexane and the more polar acetonitrile (Figure 2). It was noted earlier that bisacylates which are in 1,3-syn relation do not couple. This was accounted for by the fact that acyclic 1,3-bisacylates adopt the planar zig-zag form as their most stable conformation, and that the related electric transition moments of the acylates are parallel and hence exhibit no exciton coupling. This trend is clearly seen in the present 1,3-syn extension of tetrol derivative 1 to pentol derivative 2, where the CD curves are similar. The positive Cotton effect (CE) at ca. 252 nm reflects the 2β-configuration, while the negative couplet centered at 300 nm is due to the 4,6-dicinnamate moiety which constitutes a counter-clockwise twist.

Figure 2. CD spectra of 1,3-skipped tetrol and pentol bichromophoric derivatives 1 (dashed), 2, and 3 (solid) in methylcyclohexane and acetonitrile.

In the case of 1,3-anti extensions, 1→3, the terminal and penultimate acylates are gauche-oriented and hence this extension reflects the coupling corresponding to their screw sense. Namely, in 3, the projection angle of the acylates at C-6 and C-8 is counter-clockwise or negative (by definition), which in turn gives rise to a negative contribution to the split (bisignate) CD curve. This trend is clearly seen in the higher pentol derivative as well. Thus, the CD of the anti-extended pentol derivative 3, except for the positive CE at 250 nm diagnostic of the 2β-configuration, is different from that of the lower homolog, i.e., intensity of the 300 nm negative couplet of 1 is greatly reduced because of the positive screw sense of the 6,8-acylates.
Figure 3. CD spectra of bichromophoric derivatives of allylic tetrol 13-16 (solid) and reference ethyl tetrol 13r-16r (dashed) in methylcyclohexane and acetonitrile.
Configurational assignments of 1,2-tetrol derivatives 13-16. Comparisons of the CD of bichromophoric anthroate/methoxycinnamate derivatives of 1,2-acyclic polyols with corresponding reference curves are occasionally not straightforward (Figure 3). In such cases the following general process should be taken: measure CD in both the nonpolar methylcyclohexane and the more polar acetonitrile, and then draw conclusions from the solvent showing greater similarity.

This is exemplified in the xylo- and lyxo derivatives 15/15r ("r" for reference) and 16/16r, respectively. It was noted earlier5,6 that the CD of homologous 1,2-polyol bichromophoric derivatives followed clearer systematic trends when measured in methylcyclohexane than in acetonitrile. It was therefore unexpected that the CDs of the xylo and lyxo series, allylic-15/ethyl-15r and allylic-16/ethyl-16r showed better agreement in acetonitrile than in methylcyclohexane; the reason for this is unclear. Thus it is recommended that the CDs in both solvents should be compared.

Table 1. CD (λ_{ext} nm/Δε) Data of Bichromophoric Derivatives of Acyclic Polyols with 2β-Configuration in Methylcyclohexane and Acetonitrile.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compd</th>
<th>CD [λ_{ext} (Δε)] in C₆H₁₁CH₃</th>
<th>CD [λ_{ext} (Δε)] in CH₃CN</th>
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<tr>
<td>1</td>
<td>1</td>
<td>254(+16.4), 278(+18.2), 316(-32.6)</td>
<td>252(+24.9), 280(+27.2), 318(-49.9)</td>
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<td>2</td>
<td>2</td>
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<tr>
<td>3</td>
<td>3</td>
<td>254(+18.8), 280(+6.2), 319(-12.8)</td>
<td>252(+22.3), 282(+10.7), 323(-16.5)</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
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<td>252(+38.2), 287(-16.3), 327(+8.0)</td>
</tr>
<tr>
<td>5</td>
<td>13r</td>
<td>250(21.9), 282(-18.3), 315(+8.4)</td>
<td>253(+41), 287(-9), 322(+10)</td>
</tr>
<tr>
<td>6</td>
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<td>252(+11.2), 288(+12.1), 323(-15.9)</td>
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<tr>
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<td>253(+18), 287(+6), 322(-26)</td>
</tr>
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<td>252(+10.3), 286(+2.0), 322(-6.3)</td>
</tr>
<tr>
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<td>16</td>
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<td>252(+2.0), 295(+3.2), 316(+5.4)</td>
<td>257(-3.0), 279(-5.3), 318(+16.0)</td>
</tr>
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Figure 4. CD spectra of bichromophoric derivatives of allylic tetrol 13-16 (dashed) and 1,2-/1,3-mixed pentol 37-44 (solid) in methylcyclohexane and acetonitrile.
Figure 4. (continued).
CD of mixed pentol derivatives 37-44. The italicized comments mentioned above, i.e., measurements in two solvents, apply here as well when comparing the spectra with their lower homologs. The CD spectra of eight diastereomers 37-44, measured in methylcyclohexane and in acetonitrile, are compared with the four parent tetroi derivatives 13-16 on Table 1 and Figure 4. The following trend emerges from this comparison.

i) 1,3-syn extension: The CD spectra of 1,3-syn extended mixed pentol derivatives 37, 39, 41 and 43 closely resemble those of parent tetrols 13-16. The 1,3-syn extensions exert only a weak effect arising from 1,3-interactions in the pairwise additivity interactions. However, the curves do not necessarily show similarity in both solvents. As mentioned earlier, because of the inherent conformational flexibility of these acyclic compounds with lipophilic acylate branches, configurational correlations are more reliable upon comparisons of CD measured in both the nonpolar methylcyclohexane and the more polar acetonitrile. For example, the CDs of syn-extended 37 and "ribo" 13 are similar in methylcyclohexane (MC) but not in acetonitrile (AN). On the other hand, for a similar syn-extended 41, the CD is similar to the reference precursor 15 in AN but not in MC.

ii) 1,3-anti extension: In contrast to syn-extensions, the CDs of 1,3-anti extended mixed pentol derivatives 38, 40, 42, and 44 differ significantly, but in a predictable pattern, from those of parent tetrols 13-16. Without exception, the 1,3-anti extension contributes a strong exciton split CE, the sign of which reflects the screw sense between the newly introduced 1,3-extension.

iii) the 252 nm Cotton effect (CE): The sign of the anthroate CE at 252 nm is primarily dependent upon the C-2 configuration. A clear positive CE at 252 nm (positive shorter wavelength counterpart of a negative couplet) is diagnostic for a 2β-configuration and for an anticlock-wise twist between 1-anthroate/2-cinnamate transition moments. This CD band is distinctly positive in 2β,3α 1,2-type polyols, e.g. in "ribo" 13, “arabino” 14, as well as in the 1,3-extended mixed polyols compounds 37-40 prepared in this study. The uniformly positive sign is due to fact that both 1-anthroate/2β-methoxycinnamate and 1-anthroate/3α-methoxycinnamate both exhibit positive 252 bands. The intensity of this band is solvent dependent and is generally stronger in AN than in MC, e.g., 37 and 38.

In contrast, in the 2β,3β mixed polyols 15, 16, 41-44, the 252 nm CE is variable, ranging from weakly positive to weakly negative; this is because the 1-anthroate/3β-methoxycinnamate moiety has a negative CE in this region. The 252 nm CE represents the shorter wavelength wing of a split CD which is generally much more intense than the longer wavelength wing; however, the reason for this difference in intensities of the two wings is currently under study.

CONCLUSION

CD curves of all eight diastereomers 37-44 with mixed 1,2- and 1,3-acylate functions are characteristic and give rise to predictable trends for each stereochemical pattern. These reference curves and general trends can be used for configurational assignments of other 1,2- and 1,3-mixed polyols of the same type. The microscale application of the results described above to the determination of absolute configuration of two new bacteriohopanepentols isolated from cyanobacterium Nostoc PCC 6720 is described in the following paper.
EXPERIMENTAL SECTION

**General.** Solvents used for reactions were reagent grade. Anhydrous solvents were freshly distilled (THF from Na/benzophenone; CH2Cl2 and acetonitrile from CaH2). Unless otherwise stated, reagents were obtained from commercial sources and were used as such. Moisture sensitive reactions were carried out in oven-dried glassware under argon. Thin-layer chromatography (TLC), Analtech Silica Gel GH LF plates (250 μm thickness), was used for monitoring reactions.

ICN silica gel (32-63 mesh) was employed for flash chromatography. HPLC purifications were performed using either Rainin or waters HPLC system equipped with a Rainin Dynamax model UV-D detector or diode array detector, respectively. Solvents used for chromatographic separation were HPLC grade.

All 1H NMR spectra were measured in CDCl3 on a Varian VXR 400 and are reported in parts per million (δ) relative to CHCl3 (7.24 ppm) as internal reference, with coupling constants (J) reported in Hertz (Hz). Low-resolution and high-resolution FAB mass spectra were measured on a JEOL JMS-DX 303 HF mass spectrometer using glycerol matrix and Xe ionizing gas. CI mass spectra were measured on a NERMAG R10-10 spectrometer with NH3 as ionizing gas. UV-VIS and CD spectra were recorded in methylcyclohexane and acetonitrile (spectroscopic grade) solutions on a Perkin-Elmer Lambda 4B UV/VIS spectrophotometer and JASCO J-720 spectropolarimeter, respectively. Smoothing (Discrete Fourier Transform procedure) and other manipulations of CD spectra were carried out with in house developed software.

Representative procedure for preparation of bichromophoric derivatizatives of polyols (Method A): (2S,4S,6R,8R)- and (2S,4S,6R,8S)-1-O-anthroyl-2,4,6,8-tetra-(O-p-methoxycinnamoyl)-nonane-1,2,4,6,8-pentols (2) and (3).

i) Anthroylation: To 4 (or 5) (5 mg, 24.3 mmol) in acetonitrile (0.5 ml) was added 9-anthroyltetrazole (13.3 mg, 48.5 mmol) and DBU (7 μl, 48.5 mmol). The reaction mixture was stirred at room temperature for 8 h and concentrated. The yellow residue was purified by silica gel flash chromatography (8% MeOH/CH2Cl2) to give 5.0 mg of pentol-1-anthroate in 50% yield.

ii) Cinnamoylation: To 1-anthroate of 4 (or 5) (5 mg, 12.2 mmol) in acetonitrile (0.5 ml) was added p-methoxycinnamoyl imidazole (22.6 mg, 97.6 mmol) and DBU (11 μl, 73.2 mmol). The reaction mixture was stirred at room temperature for 4 h. After removal of solvent, the residue was purified by silica gel flash chromatography (30% EtOAc/Hexane) to give 11.3 mg of 2 (or 3) in 88% yield. FAB-HRMS for C64H60O14, calcd 1052.3980, found 1052.3990 for 2 and 1052.3960 for 3.

Representative procedure for Grignard addition (Method B): (2R,3S,4S)- and (2R,3S,4R)-1,2-O-isopropylidene-3-tert-butyldimethylsilyl-6-heptene-1,2,3,4-tetrols (9) and (10). To a solution of aldehyde 7 (428 mg, 1.56 mmol) in CH2Cl2 (8 ml) at -30°C was added 1.0 M THF solution of allylmagnesium bromide (1.72 ml). The mixture was maintained at -30°C for 45 min. and then at 0°C for 15 min.. It was diluted with CH2Cl2 (20 ml), the organic phase was washed with water (10 ml x 2), brine (20 ml), dried over Na2SO4 and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel. The two diastereomers 9 (230 mg, 47%) and 10 (220 mg, 46%) were isolated in pure form upon elution with 10 and 11% ether/hexane, respectively.
Acyclic 1,2-/1,3-mixed pentols

(9) \(^1^H\)-NMR δ 0.08 (S, 3H, Si-Me), 0.09 (S, 3H, Si-Me), 0.87 (S, 9H, Si-t-Bu), 1.32 (S, 3H, Me), 1.37 (S, 3H, Me), 2.20 (m, 1H, H-5), 2.30 (m, 1H, H-5'), 3.73 (m, 1H, H-4), 3.78 (m, 1H, H-3), 3.80 (m, 1H, H-1), 4.00 (dd, 1H, J = 8.0, 6.1 Hz, H-1'), 4.10 (m, 1H, H-2), 5.08 (m, 2H, H-7, 7'), 5.84 (m, 1H, H-6); CI-MS (NH₃) m/z 317 (m+1)^+, 334 (M+18)^+.

(10) \(^1^H\)-NMR δ 0.08 (S, 3H, Si-Me), 0.09 (S, 3H, Si-Me), 0.87 (S, 9H, Si-t-Bu), 1.32 (S, 3H, Me), 1.39 (S, 3H, Me), 2.20 (m, 1H, H-5), 2.30 (m, 1H, H-5'), 3.61 (m, 1H, H-4), 3.74 (dd, 1H, J = 6.4, 2.8 Hz, H-3), 3.78 (dd, 1H, J = 7.8, 6.4 Hz, H-1), 4.02 (dd, 1H, J = 8.0, 6.3 Hz, H-1'), 4.10 (m, 1H, H-2), 5.08 (m, 2H, H-7, 7'), 5.86 (m, 1H, H-6); CI-MS (NH₃) m/z 317 (m+1)^+, 334 (M+18)^+.

(2R,3R,4S)- and (2R,3R,4R)-1,2-O-isopropylidene-3-tert-butyldimethylsilyl-6-heptene-1,2,3,4-tetrols (11) and (12). The two compounds were prepared from allylmagnesium bromide addition to aldehyde 8 by the procedure described in method B. They were purified by flash chromatography. Compound 11 was eluted with 10-11% and compound 12 with 11-13% ether/hexane (87% overall yield of 1:1 mixture of 11 and 12).

(11) \(^1^H\)-NMR δ 0.09 (S, 3H, Si-Me), 0.12 (S, 3H, Si-Me), 0.90 (S, 9H, Si-t-Bu), 1.32 (S, 3H, Me), 1.39 (S, 3H, Me), 2.25 (m, 1H, H-5), 2.45 (m, 1H, H-5'), 3.69-3.76 (m, 2H, H-3, 4), 3.95 (dd, 1H, J = 8.4, 6.6 Hz, H-1), 4.06 (dd, 1H, J = 8.4, 6.3 Hz, H-1'), 4.19 (m, 1H, H-2), 5.16 (m, 2H, H-7, 7'), 5.85 (m, 1H, H-6); CI-MS (NH₃) m/z 317 (m+1)^+, 334 (M+18)^+.

(12) \(^1^H\)-NMR δ 0.08 (S, 3H, Si-Me), 0.09 (S, 3H, Si-Me), 0.88 (S, 9H, Si-t-Bu), 1.33 (S, 3H, Me), 1.41 (S, 3H, Me), 2.20 (m, 1H, H-5), 2.37 (m, 1H, H-5'), 3.61-3.68 (m, 2H, H-3, 4), 3.81 (dd, 1H, J = 8.3, 7.9 Hz, H-1), 3.98 (dd, 1H, J = 8.4, 6.6 Hz, H-1'), 4.19 (m, 1H, H-2), 5.11 (m, 2H, H-7, 7'), 5.85 (m, 1H, H-6); CI-MS (NH₃) m/z 317 (m+1)^+, 334 (M+18)^+.

(2R,3S,4S)-1,2-O-isopropylidene-6-heptene-1,2,3,4-tetrols (17). Compound 9 (130 mg, 0.41mmol) was stirred in 1.0 M solution of tetrabutylammonium fluoride in THF (0.85 mol) for 5.5 h. The solvent was removed under reduced pressure and the residue was column chromatographed (silica gel, 50% ether/hexane) to afford tetrol acetonide 17, 70% yield.

Tetrol acetonides 18-20 were prepared from 10-12, respectively, by using the same desilylation procedure.

Bichromophoric derivatization of 17-20 to 13-16 (Method C): (2R,3S,4S)-1-O-anthroyl-2,3,4-tri-(O-p-methoxycinnamoyl)-heptene-1,2,3,4-tetrol (13).

i) Acetonide cleavage: To a methanolic solution (0.5 ml) of tetrol acetonide 17 (2.5 mg) was added 2-3 drops of acetyl chloride. The mixture was stirred for 2 h. The solvent was removed under reduced pressure and the residue was dried over night in vacuo. The tetrol thus obtained was subjected to anthroylation without further purification.

ii) Anthroylation: The tetrol obtained from earlier step was monoanthroylated according to method A (i). The monoanthroate derivative was purified over a short silica gel column (5% MeOH/ether) to afford tetrol acetonide 17, 70% yield.

Tetrol acetonides 18-20 were prepared from 10-12, respectively, by using the same desilylation procedure.
Bichromophoric derivatives 14, 15, 16 were prepared from the corresponding compounds 10, 11, 12 respectively, by using the above procedure for 13 (method C).

(2R,3S,4R)-1-O-anthroyl-2,3,4-tri-(O-p-methoxycinnamoyl)-heptene-1,2,3,4-tetrol (14). HPLC (3μ YMC silica gel, 25% ethyl acetate/hexane); FAB-MS 846 (M+); FAB-HRMS for C52H46O11Na, calcd 869.2938, found 869.2969.

(2R,3R,4S)-1-O-anthroyl-2,3,4-tri-(O-p-methoxycinnamoyl)-heptene-1,2,3,4-tetrol (15). HPLC (3μ YMC silica gel, 25% ethyl acetate/hexane); FAB-MS 846 (M+); FAB-HRMS for C52H46O11, calcd 846.3040, found 846.3021.

(2R,3R,4R)-1-O-anthroyl-2,3,4-tri-(O-p-methoxycinnamoyl)-heptene-1,2,3,4-tetrol (16). HPLC (3μ YMC silica gel, 25% ethyl acetate/hexane); FAB-MS 846 (M+); FAB-HRMS for C52H46O11Na, calcd 869.2949, found 869.2949.

(2R,3S,4S)-1,2,3,4-bis(O-isopropylidene)-6-heptene-1,2,3,4-tetrol (21). p-Toluenesulfonic acid (2 mg) was added to a stirred solution of compound 17 (0.247 mmol) in 2,2-dimethoxypropane (2 ml). The mixture was stirred at ambient temperature for 3.5 h. The solvent was removed and the residue was chromatographed over a short silica column (11% ether/hexane) to afford the tetrol diacetonide 21 (83%); CI-MS (NH3) 243 (M+1) +, 260 (M+18) +.

Tetrol diacetonides 22-24 were synthesized from 18-20, respectively, using the same procedure.

(2R,3S,4R)-1,2,3,4-bis(O-isopropylidene)-6-heptene-1,2,3,4-tetrol (22). Purification by silica gel chromatography (11% ether/hexane) afforded 22 (81%); CI-MS 243 (M+1)+, 260 (M+18)+.

(2R,3S,4S)-1,2,3,4-bis(O-isopropylidene)-6-heptene-1,2,3,4-tetrol (23). Purification by silica gel chromatography (10% ether/hexane) yielded 23 (82%); CI-MS (NH3) 243 (M+1)+, 260 (M+18)+.

(2R,3R,4R)-1,2,3,4-bis(O-isopropylidene)-6-heptene-1,2,3,4-tetrol (24). Purification by silica gel chromatography (12% ether/hexane) gave 24 (82%); CI-MS (NH3) 243 (M+1)+, 260 (M+18)+.

(2R,3S,4S)-1,2,3,4-bis(O-isopropylidene)-6-hexanal-1,2,3,4-tetrol (25). Into a solution of compound 21 (8.5 mg, 0.035 mmol) in CH2Cl2 : MeOH (4 : 1, 12 ml) maintained at -78°C was bubbled O3 for 2-3 min until the solution turned deep blue. Then triphenylphosphine was added (46 mg, 0.18 mmol) and the mixture was stirred for 10 min. at -78°C and 45 min. at 0°C. The mixture was concentrated under reduced pressure. Purification (silica gel column, 10% ether/hexane) afforded compound 25 (93%); CI-MS (NH3) 245 (M+1)+, 262 (M+18)+.

Ozonolysis of compounds 22-24 under the same conditions yielded aldehydes 26-28, respectively.
(2R,3S,4R)-1,2:3,4-bis(O-isopropylidene)-6-hexanal-1,2,3,4-tetrol (26). Chromatography over silica gel (15% ether/hexane) afforded 26 (88%); CI-MS (NH$_3$) 245 (M+I)$^+$, 262 (M+18)$^+$. 

(2R,3R,4S)-1,2:3,4-bis(O-isopropylidene)-6-hexanal-1,2,3,4-tetrol (27). Silica gel chromatography (10% ether/hexane) gave 27 (87%); CI-MS (NH$_3$) 245 (M+I)$^+$, 262 (M+18)$^+$. 

(2R,3R,4R)-1,2:3,4-bis(O-isopropylidene)-6-hexanal-1,2,3,4-tetrol (28). Purification on silica gel (12% ether/hexane) yielded 28 (85%); CI-MS (NH$_3$) 245 (M+I)$^+$, 262 (M+18)$^+$. 

Grignard addition of allylmagnesiumbromide to the aldehydes 25-28. Pentols diacetonides 29-36 were synthesized from the corresponding aldehydes 25-28 by Grignard reaction with allylmagnesiumbromide according to the procedure described earlier (method B). Each aldehyde yields a mixture of two diastereomeric pentol diacetonides in almost equal amounts.

(2R,3S,4S,6S)- and (2R,3S,4S,6R)-1,2:3,4-bis(O-isopropylidene)-8-nonene-1,2,3,4,6-pentols (29) and (30). Compound 25 (8 mg, 0.032 mmol) gave a mixture of 29 and 30 after the Grignard reaction. The two isomers were separated on silica gel column with 17% ether/hexane (42% each).

(29). $^1$H-NMR $\delta$ 1.32 (S, 6H, 2-Me), 1.37 (S, 3H, Me), 1.40 (S, 3H, Me), 1.70 (ddd, 1H, $J = 14.3, 9.4, 9.2$ Hz, H-5a), 1.91 (ddd, 1H, $J = 14.0, 3.5, 2.9$ Hz, H-5e), 2.27 (m, 2H, H-7, 7'), 3.88 (m, 1H, H-1), 3.90 (m, 1H, H-6), 3.96 (m, 1H, H-1'), 4.05 (m, 1H, H-2), 4.09 (dd, 1H, $J = 8.1, 5.9$ Hz, H-3), 4.38 (ddd, 1H, $J = 9.8, 5.4, 4.3$ Hz, H-4), 5.10 (m, 2H, H-9, 9'), 5.80 (m, 1H, H-8); CI-MS (NH$_3$) m/z 287 (m+1)$^+$, 304 (m+18)$^+$.

(30). $^1$H-NMR $\delta$ 1.31 (S, 3H, Me), 1.34 (S, 3H, Me), 1.37 (S, 3H, Me), 1.38 (S, 3H, Me), 1.88 (m, 2H, H-5a, e), 2.28 (bm, 2H, H-7, 7'), 3.81 (m, 1H, H-6), 3.90 (dd, 1H, $J = 8.2, 5.5$ Hz, H-1), 4.03 (m, 2H, H-1', 3), 4.11 (m, 1H, H-2), 4.41 (m, 1H, H-4), 5.10 (m, 2H, H-9, 9'), 5.82 (m, 1H, H-8); CI-MS (NH$_3$) m/z 287 (m+1)$^+$, 304 (m+18)$^+$.

(2R,3S,4R,6R)- and (2R,3S,4R,6S)-1,2:3,4-bis(O-isopropylidene)-8-nonene-1,2,3,4,6-pentols (31) and (32). Separation of these two diastereomers was achieved by silica gel chromatography, compound 31 and 32 being eluted with 21% and 24% ether/hexane, respectively (40% each).

(31). $^1$H-NMR $\delta$ 1.32 (3H, S, Me), 1.34 (S, 3H, Me), 1.37 (S, 3H, Me), 1.38 (S, 3H, Me), 1.63 (ddd, 1H, $J = 14.3, 9.6, 9.6$ Hz, H-5a), 1.94 (ddd, 1H, $J = 14.3, 2.9, 2.9$ Hz, H-5e), 2.26 (m, 2H, H-7, 7'), 3.56 (dd, 1H, $J = 8.0, 7.9$ Hz, H-3), 3.91 (bm, 1H, H-6), 3.94 (dd, 1H, $J = 8.4, 4.8$ Hz, H-1), 4.00 (ddd, 1H, $J = 8.4, 6.0, 4.8$ Hz, H-2), 3.96 (m, 1H, H-1), 4.05 (m, 1H, H-2), 4.12 (dd, 1H, $J = 8.4, 6.0$ Hz, H-1'), 5.07 (m, 2H, H-9, 9'), 5.83 (m, 1H, H-8); CI-MS (NH$_3$) m/z 287 (m+1)$^+$, 304 (m+18)$^+$.

(32). $^1$H-NMR $\delta$ 1.32 (3H, S, Me), 1.34 (S, 3H, Me), 1.38 (S, 6H, 2-Me), 1.78 (ddd, 1H, $J = 14.5, 7.5, 2.7$ Hz, H-5e), 1.90 (ddd, 1H, $J = 14.3, 9.0, 3.9$ Hz, H-5a), 2.27 (bm, 2H, H-7, 7'), 3.60 (m, 1H, H-3), 3.91 (bm, 1H, H-6), 3.92 (dd, 1H, $J = 8.4, 5.1$ Hz, H-1), 4.01 (m, 1H, H-2), 4.11 (dd, 1H, $J = 8.4, 6.1$ Hz, H-1'), 4.16 (ddd, 1H, $J = 7.6, 7.5, 3.9$ Hz, H-4), 5.06 (m, 2H, H-9, 9'), 5.80 (m, 1H, H-8); CI-MS (NH$_3$) m/z 287 (m+1)$^+$, 304 (m+18)$^+$. 

Acyclic 1,2-/1,3-mixed pentols 2773
(2R,3R,4S,6S)- and (2R,3R,4S,6R)-1,2,3,4-bis(O-isopropylidene)-8-nonene-1,2,3,4,6-pentols (33) and (34). Compounds 33 and 34 could not be separated even after repeated column chromatography over silica gel (84%). This mixture was therefore separated after bichromophoric derivatization (see below).

(2R,3R,4R,6R)- and (2R,3R,4R,6S)-1,2,3,4-bis(O-isopropylidene)-8-nonene-1,2,3,4,6-pentols (35) and (36). These two diastereomers were easily separated on silica gel column, compound 35 and 36 being eluted with 30% and 38% ether/hexane, respectively (84%).

Bichromophoric derivatization of pentol diacetonides 29-36 to 37-44. Bichromophoric derivatives 37-40, 43, and 44 were prepared from the pentol diacetonides 29-32, 35, and 36 by acetonide cleavage, anthroylation and cinnamolytion (method C). The products were purified over silica gel column (4% MeOH/ether) in 40-45% overall yield. A small fraction of the flash chromatography purified samples were further purified by HPLC for CD and high-resolution FAB mass spectra. In the case of the diastereomeric pair 33 and 34, the mixture was subjected to acetonide cleavage and bichromophoric derivatization. The resultant derivatives 41, 42 were separated by HPLC.

(2R,3S,4S,6S)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (37). HPLC (5μ alltech silica gel, 26% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C_{64}H_{58}O_{14}, calcd 1050.3830, found 1050.3853.

(2R,3S,4R,6R)-anthry-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-2,3,4,6-pentol (38). HPLC (5μ alltech silica gel, 31% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C_{64}H_{58}O_{14}, calcd 1050.3830, found 1050.3857.

(2R,3S,4R,6R)-anthry-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-2,3,4,6-pentol (39). HPLC (3μ YMc silica gel, 28% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C_{64}H_{58}O_{14}, calcd 1050.3830, found 1050.3870.
(2R,3S,4R,6S)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (40). HPLC (5 μ alltech silica gel, 26% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C₆₄H₅₈O₁₄, calcd 1050.3830, found 1050.3845.

(2R,3R,4S,6S)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (41). HPLC (3 μ YMC silica gel, 2% THF/CH₂Cl₂, retention time of 6.234 min); FAB-MS 1050 (M+); FAB-HRMS for C₆₄H₅₈O₁₄, calcd 1050.3830, found 1050.3837.

(2R,3R,4S,6R)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (42). HPLC (5 μ YMC silica gel, 27% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C₆₄H₅₈O₁₄, calcd 1050.3830, found 1050.3860.

(2R,3R,4R,6R)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (43). HPLC (5 μ alltech silica gel, 27% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C₆₄H₅₈O₁₄, calcd 1050.3830, found 1050.3830.

(2R,3R,4S,6S)-1-O-anthroyl-2,3,4,6-tetra-(O-p-methoxycinnamoyl)-8-nonene-1,2,3,4,6-pentol (44). HPLC (5 μ alltech silica gel, 25% ethyl acetate/hexane); FAB-MS 1050 (M+); FAB-HRMS for C₆₄H₅₈O₁₄, calcd 1050.3830, found 1050.3842.

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