Tobacco Chemistry. 51.* New Cembranoid Diterpenoids from Greek Tobacco

DAN BEHR,* INGER WAHLBERG,* TOSHIAKI NISHIDA,* CURT R. ENZELL,* JAN-ERIK BERGb and ANNE-MARIE PILOTTIb

* Research Department, Swedish Tobacco Company, P.O. Box 17007, S-104 62 Stockholm, Sweden and
b Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm, Sweden

The isolation of (1S,2E,4R,6R,7E,11S,12S)-11,12-epoxy-2,7-cembradiene-4,6-diol** (1), the (1S,2E,-
4R,6E,8R,11S,12E)- and (1S,2E,4S,6E,8R,11S,12E)-
8,11-epoxy-2,6,12-cembratrien-4-ols (2, 3) and
(1S,2E,4R,6E,8R,11S)-8,11-epoxy-2,6,12(20)-cembratrien-4-ol (4) from Greek tobacco is reported. Of
these 1 is a new natural product, whereas 2–4,
previously found in other tobacco varieties, are
new to Greek tobacco. The structure of 1 has been
determined by synthesis and X-ray analysis of the
corresponding mono-acetate 5. Compounds 2 and
3 have been correlated by dehydration and com-
pound 4 has been used as the starting material for a
synthesis which confirms that the structure of a
previously isolated tobacco diterpenoid is (1S,2E,-
4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-
4,12-diol (6).

The acid rearrangement of 1, a reaction which is
proposed to mimic the biogenesis of some of the
8,11- and 8,12-epoxy bridged tobacco cembranoids,
is discussed.

Recent studies have shown that depending on their
genetic origin tobacco cultivars produce cembranes,
labdanes or both.3,4 These diterpenoids, which are
present in the gummy exudate of the tobacco leaf
and flower, are prone to biodegradation thus

* For part 50 see Ref. 1.
** We have abandoned the thuberganoid nomen-
cature and adopted the nomenclature and structural
representation recommended in a recent review on
naturally occurring cembranes.5 This representation,
although advantageous in most instances, has also certain
drawbacks as is evident from the illustration of the
formation of the 8,12-epoxy bridged compounds in
Scheme 1.

RESULTS

The elemental composition, C20H34O3, and the
presence of an isopropyl group (methyl doublets at
δ 0.81 and 0.86; νmax at 1375 and 1390 cm−1) and
three methyl groups, of which one was vinylic and
and two attached to fully substituted oxygen-carrying
carbon atoms implied that the first tobacco isolate
(1) was a diterpenoid.

A secondary (one-proton multiplet at δ 4.85 in 1
and at δ 5.82 in the monoacetate 5) and a tertiary
hydroxyl group (νmax at 3620 and 3590 cm−1 in 5)
accommodated two of the oxygen atoms. The remaining
oxygen atom was evidently present as an
epoxide group extending from a methine to a fully
substituted carbon atom (doublet of doublets at δ
2.83; 13C NMR signals at δ 61.0 (d) and 59.3 (s),
cf. Table 1). Furthermore, since the 13C NMR
spectrum was consistent with the presence of a di-
and a trisubstituted double bond, it followed that
1 was carbonomonocyclic and a cembrane structure
seemed most plausible.

A spectral comparison, which showed that
fifteen signals in the 13C NMR spectrum of 1 were
of appropriate multiplicities and had chemical shift
values close to those assigned to the C-1 to C-8
and C-13 to C-19 signals for (1S,2E,4R,6R,7E,11E)-2,7,11-cembratriene-4,6-diol (7), corroborated this view and provisionally identified 1 as an 11,12-epoxy-2,7-cembradiene-4,6-diol.

This assignment was verified by chemical means. Thus, treatment of the 4,6-diol 7 with m-chloroperbenzoic acid afforded the two diastereomeric epoxides 1 and 8, the most polar of which was

![Diagram](image)

**Fig. 1.** Stereoscopic view of (1S,2E,4R,6R,7E,11S,12S)-6-acetoxy-11,12-epoxy-2,7-cembradien-4-ol (5).

identical in all respects to the new tobacco constituent. This result settled the structure and the (1S,2E,4R,6R,7E)-configuration but left the chiralities at C-11 and C-12 to be accounted for. An X-ray analysis of acetate 5 using a direct phase determination procedure was therefore undertaken.

Acetate 5 formed orthorhombic crystals of space group $P_{2_1}2_12_1$. The crystal data, obtained on a computer-controlled Philips PW 1100 diffractometer, were: $a = 21.501$ (3), $b = 12.882$ (3) and $c = 8.032$ (3) Å, $Z = 4$. The present $R$-value including anisotropic thermal parameters for all non-hydrogen atoms is 0.115, location of the hydrogen atoms and further refinement being under way. A stereoscopic view of acetate 5, which summarizes the X-ray results and demonstrates that 5 has the 11S,12S-configuration, is shown in Fig. 1.

The second isolate from Greek tobacco was identified as (1S,2E,4R,6E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (2). A compound of this structure has previously been reported as a constituent of flue-cured tobacco. However, since its physical or spectral data were not included in that report, a brief account for our structural assignment is given here.

It followed from the $^1$H and $^{13}$C NMR spectra that 2, $C_{24}H_{33}O_2$, contained an isopropyl group, two methyl groups linked to fully substituted oxygen-carrying carbon atoms, one vinylic methyl group and three double bonds, of which one was triple and two disubstituted. One of the oxygen atoms was accommodated by a hydroxyl group and the other by an ether group ($\nu_{max}$ 3600 and 3400 cm$^{-1}$; $^{13}$C NMR signals at $\delta$ 73.3 (s), 82.1 (d) and 83.0 (d)). These results inferred that 2 was a diterpenoid of the cembrane type. Moreover, a comparison of the $^{13}$C NMR spectrum of 2 with that of (1S,2E,4S,6E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (3), now isolated from Greek tobacco but previously known as a constituent of other tobacco varieties, suggested that 2 was the 4R-epimer of 3.

Conclusive evidence for this assignment was obtained by chemical means. Thus, treatment of 2 with KHSO$_4$ yielded a product, which was identical in all respects to (1S,2E,6E,8R,11S,12E)-24(18),6,12-cembratetraen-8,11-epoxide (9), the major dehydration product obtained from 3.

The isolation from Greek tobacco of the fourth compound, (1S,2E,4R,6E,8R,11S)-8,11-epoxy-2,6,12-(20)-cembratrien-4-ol (4), offered a possibility to confirm chemically the structure of another tobacco

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*5* Values in CDCl$_3$ relative to TMS. Assignment may be reversed.
constituent, which had been formulated as (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-4,12-diol (6) on the basis of spectral evidence.

Treatment of 4 with m-chloroperbenzoic acid furnished two 12,20-epoxides (10,11), which were assigned the 12R- and 12S-configurations, respectively, by a comparison of their \(^1\)H NMR spectra with those of the (1S,2E,4S,6E,8R,11S,12R)- and (1S,2E,4S,6E,8R,11S,12S)-8,11-12,20-diepoxo-2,6-cembradien-4-ols (12, 13).

Thus, the most polar epoxide of each pair, i.e.

<table>
<thead>
<tr>
<th>Isomer</th>
<th>Expected Molar Mass</th>
<th>NMR Peak at δ</th>
<th>Similarity with 4R,12S-diol</th>
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</thead>
<tbody>
<tr>
<td>11</td>
<td>589</td>
<td>2.46</td>
<td>H-20a, H-20b</td>
</tr>
<tr>
<td>10</td>
<td>589</td>
<td>2.48</td>
<td>H-20a, H-20b</td>
</tr>
<tr>
<td>12</td>
<td>589</td>
<td>2.65</td>
<td>H-20a, H-20b</td>
</tr>
<tr>
<td>13</td>
<td>589</td>
<td>2.71</td>
<td>H-20a, H-20b</td>
</tr>
</tbody>
</table>

whereas the corresponding signals for the least polar epoxides, 10 and 12, appeared as two one-proton doublets at δ 2.65 and 2.71 (J = 5 Hz) and a two-proton singlet at δ 2.68, respectively.

Reduction using LAH converted the 12S-epoxide 11 to (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-4,12-di-ol, which proved to be identical to the tobacco diol 6, and the 12R-epoxide 10 to the epimeric 4R,12S-diol 14, which has hitherto not been encountered in nature.

The 11,12-epoxide 1 is a plausible intermediate in the biogenesis of some of the 8,11- and 8,12-epoxy bridged tobacco cambranoids from the 4,6-diol 7. This hypothesis was reinforced experimentally by treatment of 1 with acid, which yielded as isolable products (1S,2E,4R,6E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (2) and (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-4,12-diol (6). A third product, as yet not known as a natural product, was also obtained. It was tentatively identified as (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-4,11-diol (15) on the basis of the following evidence.

Its \(^1\)C NMR spectrum differed from that of (1S,2E,4S,6E,8R,11S,12R)-8,12-epoxy-2,6-cembradiene-4,11-diol (16) solely with respect to the shielings of C-2 and C-18 (cf. Table 1), a result which implied that 15 is the 4R-epimer of 16. This conclusion was in harmony with their \(^1\)H NMR spectra, which displayed the signals due to the isopropyl group, the methyl groups at C-8 and C-12 and the proton attached to the hydroxyl-carrying carbon atom at virtually invariant positions but showed divergent chemical shift values for the signals assigned to the methyl group at C-4, 1.41 as against 1.35 ppm for 15 and 16, respectively. An analogous correspondence was found for the \(^1\)H NMR spectra of acetates 17 and 18.

Acid rearrangement of the (11S,12S)-epoxide 19, epimeric to 1 at C-4 and obtained together with the (11R,12R)-epoxide 20 on epoxidation of (1S,2E,4S,6R,7E,11E)-2,7,11-cembratriene-4,6-di-ol (21),

gave analogous results and lead to the isolation of (1S,2E,4S,6E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (3), (1S,2E,4S,6E,8R,11S)-8,11-epoxy-2,6,12-cembratrien-4-ol (22), (1S,2E,4S,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradiene-4,12-diol (23) and (1S,2E,4S,6E,8R,11S,12R)-8,12-epoxy-2,6-cembradiene-4,11-diol (16), all of which are tobacco constituents.8–11

*It should be pointed out that conclusive evidence of the assignments of the 6R-configurations to compounds 19–21, and 25 is, as yet, not available.

Scheme 1. Proposed mechanisms for the acid-induced rearrangements of compounds 1 and 19.

pounds may be envisaged to proceed as shown in Scheme 1.

An anti addition of water to the 11,12-epoxide group of the 4R,6R- and 4S,6S-diols 1 and 19 would produce the (1S,2E,4R,6R,7E,11S,12R)- and (1S,2E,4S,6R,7E,11S,12R)-2,7-cembradiene-4,6,11,12-tetrols (24, 25), which suffer an attack of the 11- or 12-hydroxyl group on the 7,8 double bond and a concomitant elimination of the hydroxyl group at C-6 to yield the 8R,11-epoxy bridged 4R,12R- and 4S,12R-diols 6 and 23, formal precursors of the dehydration products 2, 3, 22, or the 8R,12R-epoxy bridged 4R,11S- and 4S,11S-diols 15 and 16 respectively.

EXPERIMENTAL

With the exception of accurate mass measurements, which were carried out on a Kratos MS 50-Stereo DS 50 SM/DS 50S mass spectrometer-computer system. the instruments specified in Ref. 12 were used.

Isolation. (1S,2E,4R,6R,7E,11S,12S)-11,12-Epoxypenta-2,7-cembradiene-4,6-diol (I) was isolated from fraction A 3,13 (1S,2E,4S,5.E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (3) from fraction B 5,13 and (1S,2E,4R,6R,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (8) from fraction B 7,13 of an extract obtained from 295 kg of sun-cured Greek Nicotiana tabacum L. by column chromatography over silica gel followed by HPLC using columns packed with Partisil-PAC (Whatman) and μ-Bondapak/CN (Waters).

(1S,2E,4R,6R,7E,11S,12S)-11,12-Epoxypenta-2,7-cembradiene-4,6-diol (I, 28 mg) was an oil, [α]D +66.4° (c 1.1 CHCl3) (Found: [M – 18] + 304.2389. Calc. for C26H32O4: 304.2402): IR (film) bands at 3400, 1390 and 1375 cm⁻¹; 1H NMR (CDCl3): δ 0.81 (3 H, d, J = 6 Hz), 0.86 (3 H, d, J = 6 Hz), 1.20 (3 H, s), 1.38 (3 H, s), 1.72 (3 H, d, J = 1.3 Hz), 2.83 (1 H, dd, J = 2 and 7.5 Hz), 4.85 (1 H, dt, J = 2 and 9 Hz), 5.20 (1 H, dd, J = 7.5 and 16 Hz), 5.35 (1 H, d, J = 8 Hz) and 5.48 (1 H, d, J = 16 Hz); MS [m/z (%)]: 322 (M+, 1), 304 (7), 286 (6), 261 (9), 243 (7), 233 (3), 205 (4), 163 (18), 150 (17), 136 (54), 121 (41), 107 (43), 95 (51), 80 (70), 69 (57), 55 (58) and 43 (100).

(1S,2E,4R,6R,8R,11S,12E)-8,11-Epoxypenta-2,6,12-cembratrien-4-ol (2, 10 mg) was an oil, [α]D +63.6° (c 0.47, CHCl3) (Found: M+ 304.2398. Calc. for C26H32O2: 304.2402): IR (CHCl3) bands at 3600, 3400, 1380 and 1370 cm⁻¹; 1H NMR (CDCl3): δ 0.87 (3 H, d, J = 6.5 Hz), 0.91 (3 H, d, J = 6.5 Hz), 1.29 (3 H, s), 1.31 (3 H, s), 1.49 (3 H, broad s), 4.42 (1 H, m, W_4 = 14 Hz), 5.02 (1 H, dd, J = 8.5 and 16 Hz), 5.43 (1 H, d, J = 16 Hz), 5.65 (1 H, d, J = 16 Hz) and 4.8 – 5.6 (2 H, obscured signals); MS [m/z (%)]: 304 (M, 1), 286 (5), 261 (1), 243 (7), 228 (3), 209 (5), 179 (6), 161 (27), 160 (30), 145 (14), 126 (45), 111 (28), 93 (29), 81 (43), 71 (38), 55 (36) and 43 (100).

The least polar epoxide, (1S,2E,4R,6R,7E,11R,12R)-11,12-epoxy-2,7-cembradiene-4,6-diol (8, 4.0 mg) had m.p. 120 – 125 °C; [α]D + 18.8° (c 0.17, CHCl3) (Found: [M – 18] + 304.2411. Calc. for C26H32O2: 304.2402): IR (CHCl3) bands at 3600, 3450, 1380 and 1370 cm⁻¹; 1H NMR (CDCl3):
δ 0.83 (3 H, d, J = 6 Hz), 0.84 (3 H, d, J = 6 Hz), 1.27 (3 H, s), 1.40 (3 H, s), 1.86 (3 H, broad s), 2.68 (1 H, broad d, J = 10 Hz), 4.85 (1 H, dt, J = 3.5 and 10 Hz), 5.36 (1 H, d, J = 8 Hz), 5.44 (1 H, dd, J = 6 and 16 Hz) and 5.70 (1 H, d, J = 16 Hz); MS [m/z (%):] 304 (M - 18, 3), 286 (3), 263 (24), 243 (3), 203 (6), 163 (12), 136 (20), 121 (28), 109 (28), 95 (38), 81 (43), 71 (32), 55 (35) and 43 (100).

Preparation of (1S,2E,4R,6R,7E,11S,12S)-6-acetoxy-11,12-epoxy-2,7-cembradien-4-ol (5). Acetylation using acetic anhydride in pyridine converted 1 into (1S,2E,4R,6R,7E,11S,12S)-6-acetoxy-11,12-epoxy-2,7-cembradien-4-ol (5), which had m.p. 103–105 °C; [α]D +75.0° (c 0.22 CHCl₃); IR (CCl₄) bands at 3620, 3500, 1740 and 1720 cm⁻¹; ¹H NMR (CDCl₃): δ 0.82 (3 H, d, J = 6 Hz), 0.87 (3 H, d, J = 6 Hz), 1.21 (3 H, s), 1.37 (3 H, s), 1.88 (3 H, d, J = 1 Hz), 2.04 (3 H, s), 2.82 (1 H, dd, J = 2 and 7.5 Hz), 5.20 (1 H, dd, J = 7.5 and 16 Hz), 5.32 (1 H, m), 5.46 (1 H, d, J = 16 Hz) and 5.82 (1 H, ddd, J = 7.5 and 10 Hz); MS [m/z (%):] 304 (M - 60, 1), 286 (3), 268 (2), 243 (3), 225 (3), 215 (1), 145 (12), 132 (26), 118 (28), 106 (45), 93 (21), 81 (44), 69 (20), 55 (28) and 43 (100).

Dehydration of the (1S,2E,4S,6S,8R,11S,12E) and (1S,2E,4R,6E,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ols (3 and 2). To a solution of 10 mg of 3 in dioxane was added 20 mg of KHSO₄, and the mixture was refluxed for 6 h. Work-up and HPLC using a column packed with µ-Porasil (Waters) was used as the major component (1S,2E,4S,6R,11S,12E)-2,4(18),6,12-cembratetraen-8,11-epoxide (9, 1.6 mg), which had [α]D +12.9° (c 0.14 CHCl₃); ¹H NMR (CDCl₃): δ 0.86 (3 H, d, J = 6 Hz), 0.93 (3 H, d, J = 6 Hz), 1.31 (3 H, s), 1.50 (3 H, broad s), 2.88 (2 H, t, J = 5 Hz), 4.45 (1 H, m, Wₚ = 14 Hz), 4.82 (1 H, m), 4.99 (1 H, m), 5.1—5.5 (3 H, overlapping signals), 5.56 (1 H, d, J = 15.5 Hz) and 5.84 (1 H, d, J = 15.5 Hz); MS [m/z (%):] 286 (M, 7), 243 (8), 203 (8), 189 (18), 173 (19), 159 (18), 145 (72), 133 (24), 119 (28), 105 (42), 91 (48), 81 (67), 69 (29), 55 (100), 45 (58) and 43 (63).

Using the same procedure 2 (4 mg) was dehydrated to a compound (0.2 mg), which gave [α]D + 40° (c 0.05 CHCl₃); (Found: M⁺ 322.2548). Calc. for C₃₂H₄₈O₃: 322.2508; IR (CHCl₃) bands at 3600 and 3500 cm⁻¹. ¹H NMR (CDCl₃): δ 0.86 (3 H, d, J = 6.5 Hz), 0.90 (3 H, d, J = 6.5 Hz), 1.12 (3 H, s), 1.28 (3 H, s), 1.34 (3 H, s), 3.89 (1 H, m), 5.19 (1 H, dd, J = 8.5 and 15.5 Hz), 5.48 (1 H, d, J = 15.5 Hz) and 5.5—5.7 (2 H, overlapping signals); MS [m/z (%):] 304 (M - 18, 8), 286 (2), 261 (4), 243 (3), 217 (3), 206 (5), 177 (12), 159 (22), 133 (17), 121 (27), 109 (26), 95 (25), 81 (29), 71 (34), 55 (28) and 43 (100).

Reduction of 2.4 mg of 11 using LAH in ether gave 2.0 mg of (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradien-4,12-diol, which was identical ([α]D, IR, ¹H NMR) to tobacco diol 6.

Treatment of (1S,2E,4R,6R,7E,11S,12S)-11,12-epoxy-2,7-cembratrien-4-6-diol (1) with acid. A solution of 111 mg of 1 in 10 ml of dioxane—H₂O (2:1) and 0.5 ml of aqueous HCl (5 %) was kept at room temperature for 3 h. Work-up and chromatography over silica gel followed by HPLC using columns packed with Partisil 10 PAC (Whatman) and µ-Bondapak/CN (Waters) furnished (1S,2E,4R,6E,8R,11S,12E)-8,11-epoxy-2,6,12-cembratrien-4-ol (2.13 mg) and (1S,2E,4R,6E,8R,11S,12R)-8,11-epoxy-2,6-cembradien-4,12-diol (6, 6 mg), which were identified by direct comparison with authentic samples, and (1S,2E,4R,6E,8R,11S,12R)-8,12-epoxy-

2.6-cembra diene-4,11-diol (15), which had m.p. 179 - 184 °C; [z]_D +49.1° (c 0.33 CHCl_3) (Found: M+ 322.2519. Calc. for C_{20}H_{32}O_3: 322.2508; IR (CHCl_3) bands at 3600 and 3450 cm⁻¹; 'H NMR (CDCl_3): δ 0.86 (3 H, d, J=6 Hz), 0.90 (3 H, d, J=6 Hz), 1.18 (6 H, s), 1.41 (3 H, s), 2.33 (2 H, m), 2.67 (1 H, m), 3.50 (1 H, m), 4.8 - 5.3 (2 H, overlapping signals), 5.41 (1 H, d, J=15.5 Hz) and 5.54 (1 H, d, J=16 Hz). Irradiation at the frequency of the two-proton multiplet at δ 2.33 ppm (H-5a and H-5b) converted a signal, assigned to H-6 and centered at δ 5.15, to a doublet (J=16 Hz) and uncovered a doublet of doublets (J=5.5 and 15.5 Hz) at δ 5.06 which is due to H-2; MS [m/z (%)]: 322 (M, 1), 304 (4), 286 (26), 261 (3), 243 (3), 227 (8), 209 (4), 197 (13), 179 (7), 161 (15), 139 (17), 121 (36), 109 (27), 95 (25), 81 (27), 71 (37), 55 (19) and 43 (100).

Preparation of (1S,2E,4R,6E,8R,11S,12R)-11-acetoxy-8,12-epoxy-2,6-cembra diene-4-ol (17). Acetylation using acetic anhydride in pyridine converted 15 into (1S,2E,4R,6E,8R,11S,12R)-11-acetoxy-8,12-epoxy-2,6-cembra diene-4-ol (17) which had IR (CHCl_3) bands at 3690, 1725 and 1220 cm⁻¹. 'H NMR (CDCl_3): δ 0.85 (3 H, d, J=6.5 Hz), 0.89 (3 H, d, J=6.5 Hz), 1.08 (3 H, s), 1.18 (3 H, s), 1.40 (3 H, s), 2.11 (3 H, s), 2.33 (2 H, m), 2.74 (1 H, m), 4.80 (1 H, m), 4.9 - 5.3 (2 H, overlapping signals; pattern virtually identical to that in the spectrum of 15), 5.40 (1 H, d, J=15.5 Hz) and 5.54 (1 H, d, J=16 Hz); MS [m/z (%)]: 346 (M+18, 1), 304 (1), 286 (2), 268 (1), 243 (4), 225 (2), 159 (9), 145 (10), 119 (17), 106 (26), 93 (51), 81 (16), 71 (15), 55 (16) and 43 (100).

Preparation of the (1S,2E,4R,6R,7E,11R,12R)- and (1S,2E,4S,6R,7E,11S,12S)-11,12-epoxy-2,7-cembra diene-4,6-diols (20 and 19). Treatment of 330 mg (1.08 mmol) of (1S,2E,4R,6R,7E,11R,12R)-11,12-cembra triene-4,6-diol (21) with 220 mg (1.28 mmol) of m-chloroperbenzoic acid in CHCl_3 afforded, after work-up and chromatography, two diastereomeric 11,12-epoxides. The least polar of these, (1S,2E,4S,6R,7E,11R,12R)-11,12-epoxy-2,7-cembra diene-4,6-diol (20, 16 mg) had m.p. 105 - 107 °C; [z]_D +28.7° (c 0.62, CHCl_3) (Found: [M+ 18] + 304.386). Calc. for C_{20}H_{32}O_3: 304.2402; IR (KBr) band at 3430 cm⁻¹; 'H NMR (CDCl_3): δ 0.80 (3 H, d, J=6 Hz), 0.86 (3 H, d, J=6 Hz), 1.20 (3 H, s), 1.37 (3 H, s), 1.78 (3 H, d, J=1 Hz), 2.88 (1 H, dd, J=2.5 and 7 Hz), 4.45 (1 H, dt, J=3 and 8.5 Hz), 5.2 - 5.5 (3 H, overlapping signals); MS [m/z (%)]: 322 (M, 1), 304 (6), 286 (6), 261 (10), 243 (14), 203 (5), 177 (9), 163 (21), 136 (42), 123 (60), 109 (58), 95 (80), 81 (94), 69 (66), 55 (72) and 43 (100).

Treatment of (1S,2E,4S,6R,7E,11S,12S)-11,12-epoxy-2,7-cembra diene-4,6-diol (19) with acid. A solution of 78 mg of 19 in 5 ml of dioxane-H_2O (2:1) and 1 ml of aqueous HCl (5 %) was kept at room temperature for 6 h. Work-up and chromatography over silica gel gave a series of products of which (1S,2E,4S,6E,8R,11S,12E)-8,11-epoxy-2,6-cembra trien-4-ol (3, 2.0 mg), (1S,2E,4S,6E,8R,11S)-8,11-epoxy-2,6,12(20)-cembra trien-4-ol (22, 0.8 mg), (1S,2E,4S,6E,8R,11S,12R)-8,11-epoxy-2,6-cembra diene-4-12-diol (23, 5.4 mg) and (1S,2E,4S,6E,8R,11S,12R)-8,12-epoxy-2,6-cembra diene-4-11-diol (16, 5.4 mg) were identified by direct comparison with the corresponding authentic samples. 6 - 11

16 was an oil; [z]_D +81.9° (c 0.32, CHCl_3); IR (film) bands at 3400, 1390 and 1370 cm⁻¹; 'H NMR (CDCl_3): δ 0.86 (3 H, d, J=6 Hz), 0.89 (3 H, d, J=6 Hz), 1.16 (6 H, s), 1.35 (3 H, s), 3.03 (1 H, m), 3.54 (1 H, m), 5.12 (1 H, dd, J=8 and 16 Hz), 5.33 (1 H, d, J=16 Hz) and 5.4 - 5.5 (2 H, overlapping signals); MS [m/z (%)]: 322 (M, 1), 304 (7), 286 (2), 261 (4), 243 (3), 227 (9), 197 (14), 161 (18), 139 (17), 121 (38), 109 (27), 95 (24), 81 (33), 71 (40), 55 (22) and 43 (100).

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