

Tobacco Chemistry. 65*. Two New 7,8-Epoxycebranoids from Tobacco

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Two new diterpenoids have been isolated from tobacco. They have been identified as the (1*S*,2*E*,4*S*,6*R*,7*R*,8*R*,11*E*)- and (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diols *1* and *2* by synthesis and X-ray analysis. The conformation about the 5,6 bond in some 7,8-epoxycebranoids is discussed, as is the biogenesis of the two new compounds.

The cuticular wax of the leaf and flower of most tobacco varieties contains substantial amounts of macrocyclic diterpenoids of the cebranane class. The (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*)-2,7,11-cembratriene-4,6-diols (*3*, *4*) are the major components, and are the postulated precursors of the majority of the other tobacco cebranoids. We now report the isolation from green leaves and flowers of tobacco of two new compounds (*1*, *2*), which are plausible metabolites of the 4*S*,6*R*-diol *3*.²

Results

Structure determination. It was concluded from the ¹H NMR spectrum that the first new compound (*1*), C₂₀H₃₄O₃, possesses five methyl groups, of which two form part of an isopropyl substituent, two are attached to fully substituted oxygen-carrying carbon atoms and one is vinylic. Of the two double bonds, one is 1,2-di- and one is trisubstituted. The three oxygen atoms present in *1* are accommodated by a 1,2 epoxide group [¹³C NMR signals at δ 61.1 (s) and 63.4 (d), see Table 1], a secondary and a tertiary hydroxyl group [OH absorption in the IR spectrum; ¹³C NMR signals at δ 71.9 (d) and 74.8 (s)]. These results are consonant with *1* being a carbomonocyclic diterpene.

*For Part 64, see Ref. 1.

To formulate the partial structures A–C, ¹H-¹H and ¹H-¹³C chemical shift correlation spectroscopy^{3–5} was used. Although these can be linked in two alternative ways, a 7,8-epoxy-2,11-cembradiene-4,6-diol structure seemed most likely from a biogenetic point of view. This assignment was readily verified by regioselective epoxidation of the 7,8 double bond in the 4*S*,6*R* diol *3*, using *t*-butyl hydroperoxide and vanadyl acetylacetonate. Two isomeric products were obtained, the least polar of which was identical to compound *1*. The most polar product proved to be indistinguishable from the second new tobacco constituent (*2*). These results are consistent with 1*S*,2*E*,4*S*,6*R*,11*E* stereochemistries in both *1* and *2*, but leave the configurations of C-7 and C-8 to be accounted for. X-ray analyses of epoxides *1* and *2* using a direct phase determination procedure were therefore undertaken.

Epoxide *1* crystallized in the tetragonal space group P4₃. The crystal data, obtained on a computer-controlled Stoe diffractometer, were: *a* = 9.7665, *b* = 9.7665, *c* = 20.5908 Å, *Z* = 4. With anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for all but one of the hydrogen atoms the structure was refined to an *R* value of 0.075.⁶ A stereoscopic view, which summarizes the X-ray results and demonstrates that *1* is (1*S*,2*E*,4*S*,6*R*,7*R*,8*R*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol, is shown in Fig. 1.

Epoxide 2 crystallized as a monohydrate in the monoclinic space group $P2_1$ with $a = 9.8080$, $b = 8.0190$, $c = 13.7549$ Å, $\beta = 105.729^\circ$, $Z = 2$. The structure, shown in Fig. 2, was refined to an R value of 0.055 with anisotropic thermal parameters assigned to all non-hydrogen atoms and isotropic thermal parameters to all hydrogen atoms.⁶ The analysis showed epoxide 2 to be (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cem-bradiene-4,6-diol.

Conformation about the 5,6 bond. As is demonstrated in Figs. 1 and 2 by the position of the 6*R* hydroxyl group, the conformation about the 5,6 bond is significantly different in 1 and 2. This can also be illustrated as in Scheme 1 by the Newman projections made with the aid of the X-ray crystallographic data. Thus, epoxide 1 exists as conformer A, in which the dihedral angle between the *pro-R* hydrogen at C-5 and H-6 is 77° and that

between the *pro-S* hydrogen at C-5 and H-6 is 41° . Epoxide 2 has conformation B, in which the corresponding angles are 83° and 160° .

It also follows from the crystallographic study that the hydroxyl groups at C-4 and C-6 are intramolecularly hydrogen-bonded to each other in epoxide 1, the distance between acceptor and donor being 2.706 Å. In epoxide 2, on the other hand, intramolecular hydrogen bonding is found between the hydroxyl hydrogen at C-6 and the epoxide oxygen (2.922 Å). The water molecule is situated so as to participate in hydrogen bonds with the hydroxyl group at C-4 in two molecules, and with the hydroxyl group at C-6 and the epoxide group in a third molecule of 2.

A detailed analysis of the ^1H NMR spectrum of epoxide 1 was made using ^1H - ^1H shift correlation spectroscopy and spin simulation studies. It was found that the two hydrogens at C-5, resonating at δ 1.97 and 2.25, show vicinal couplings (3J) to

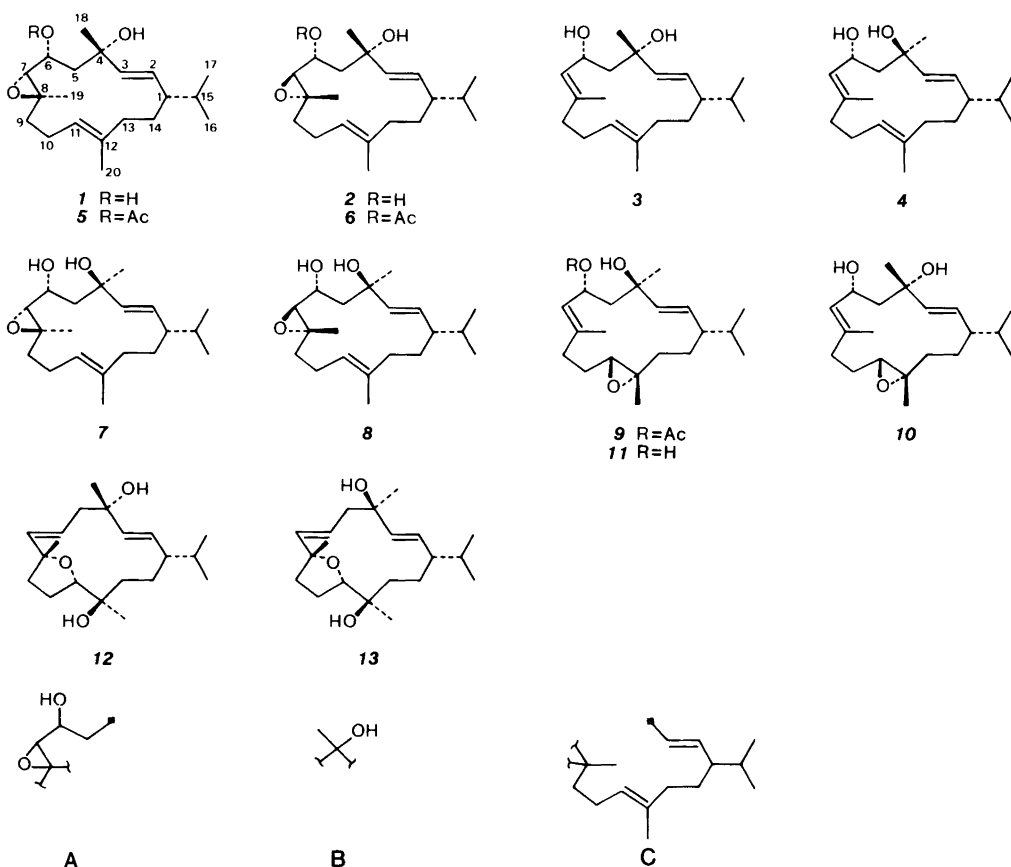


Table 1. ^{13}C NMR chemical shift values and assignments for compounds 1, 2 and 5-8.^a

| Com- pound | Carbon | | | | | | | | | | | | | | | | | | | |
|----------------|--------|-------|-------|------|------|------|------|------|------|------|-------|-------|------|------|------|------|------|------|------|------|
| | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | C-7 | C-8 | C-9 | C-10 | C-11 | C-12 | C-13 | C-14 | C-15 | C-16 | C-17 | C-18 | C-19 | C-20 |
| 1 | 43.7 | 128.9 | 138.6 | 74.8 | 42.6 | 71.9 | 63.4 | 61.1 | 39.8 | 23.6 | 125.1 | 133.5 | 36.6 | 28.1 | 34.1 | 19.2 | 19.9 | 32.3 | 15.7 | 13.7 |
| 2 | 46.8 | 129.0 | 137.5 | 72.4 | 49.5 | 67.2 | 68.2 | 63.2 | 36.7 | 22.5 | 124.1 | 135.0 | 36.4 | 28.1 | 32.7 | 19.7 | 20.7 | 29.1 | 17.9 | 14.7 |
| 5 ^c | 44.1 | 128.7 | 138.7 | 73.6 | 41.7 | 72.5 | 61.8 | 61.5 | 39.5 | 23.5 | 124.8 | 133.9 | 36.8 | 28.4 | 34.1 | 19.1 | 20.0 | 31.7 | 16.0 | 13.6 |
| 6 ^d | 46.5 | 128.7 | 137.3 | 72.2 | 48.6 | 66.1 | 68.6 | 62.6 | 36.4 | 22.7 | 123.8 | 135.1 | 36.4 | 27.9 | 32.7 | 19.6 | 20.7 | 28.1 | 17.4 | 14.5 |
| 7 | 46.0 | 131.4 | 136.9 | 70.7 | 48.1 | 64.4 | 66.0 | 61.4 | 38.2 | 22.9 | 124.5 | 134.1 | 37.0 | 27.5 | 33.0 | 19.6 | 20.1 | 28.5 | 17.3 | 14.4 |
| 8 | 46.6 | 131.3 | 136.9 | 71.5 | 50.0 | 64.9 | 68.9 | 63.4 | 36.7 | 22.9 | 123.5 | 135.2 | 36.0 | 28.3 | 32.2 | 19.9 | 20.4 | 28.7 | 17.4 | 14.6 |

^a δ values in CDCl_3 relative to TMS. ^bThe spectrum was recorded under WALTZ-16 conditions. ¹⁰ $^{\circ}\text{OCOCH}_3$, 169.2; $^{\circ}\text{OCOCH}_3$, 21.2. ^c $^{\circ}\text{OCOCH}_3$, 170.1; $^{\circ}\text{OCOCH}_3$, 21.1.

H-6 of 1.0 and 6.8 Hz, respectively (Table 2). These coupling constants accord with the dihedral angles in A,⁷ and as a result, the downfield and upfield H-5 signals are assigned to the *pro-R* and *pro-S* hydrogens, respectively. Moreover, since the coupling constants of the hydrogen atoms at C-9, C-10 and C-11 are in harmony with the dihedral angles found in the crystalline state (see Experimental), it is suggested that the conformation of 1 is retained in solution. As indicated by the ^1H and ^{13}C NMR data, this conformation is also preserved when 1 is converted to the monoacetate 5.

Since the ^1H NMR spectrum was not amenable to analysis due to severe overlap, epoxide 2 was acetylated. The corresponding monoacetate 6, which was judged from relevant ^{13}C NMR results to be conformationally similar to 2, gave a ^1H NMR spectrum (C_6D_6) displaying the H-5 signals at δ 1.91 and 2.03 with couplings to H-6 of 5.3 and 3.7 Hz, respectively. These values are somewhat at variance with those conforming with the pertinent dihedral angles in B, suggesting that the conversion of 2 from the crystalline state to solution is associated with some conformational change. This result was not unexpected, however, since epoxide 2 crystallized as a monohydrate.

In view of previous findings for other cembrane alcohols and acetates,⁸ it was also of interest to include a study of the influence of the stereochemistry at C-4 on the conformation of the 7,8 epoxides. To this end, the 4*R*,6*R* diol 4 was converted to the corresponding 7,8 epoxides 7 and 8. These were assigned 7*R*,8*R* and 7*S*,8*S* stereochemistries, respectively, from a comparison of the chemical shift values of their C-7 and C-8 signals with those of the corresponding signals for 1 and 2 (Table 1).

It can be seen from Table 2 that the chemical shift values and coupling constants of the H-5 signals of 7 differ significantly from those of 1 but are reminiscent of those previously reported for the 11,12 epoxide 9.⁸ These results revealed that the conformation of 1 does alter on reversal of the configuration at C-4 and that 7, like 9, rather exists as a conformer of type C (Scheme 1).⁸

A contrasting situation prevails with the 7*S*,8*S* epoxides. The data listed in Table 2 for 8 are sufficiently close to those found for 6 to suggest that 2, 6 and 8 are conformationally similar with respect to the 5,6 bond. It may well be that intra-

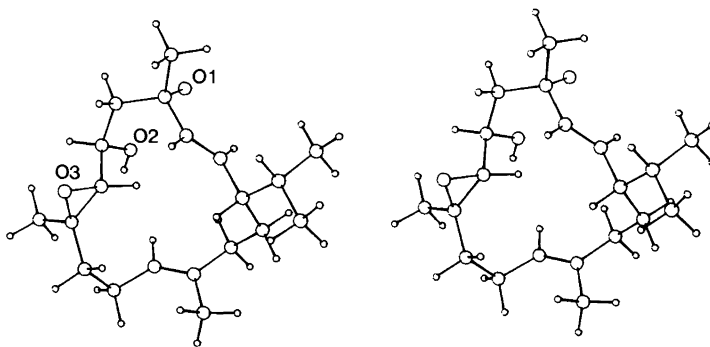


Fig. 1. A stereoscopic view of (1*S*,2*E*,4*S*,6*R*,7*R*,8*R*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol (1).

molecular hydrogen bonding is a contributing factor to this conformational behaviour. Thus, it is obvious that reversal of the configuration at C-4 in 1 (to 7) with retention of a conformation of type A about the 5,6 bond would increase the distance between the interacting hydroxyl groups at C-4 and C-6 significantly. In the case of the 7*S*,8*S* epoxides 2 and 8, which exist as conformers of type B, hydrogen bonds are developed between the hydroxyl group at C-6 and the epoxide, leaving no major influence to the hydroxyl group at C-4.

Biogenesis. Compounds 1 and 2, which are the only 7,8-epoxy cembranoids so far encountered in tobacco, are present in minute quantities only. It seems therefore that the metabolic pathway involving epoxidation of the 7,8 double bond in the 4,6 diols 3 and 4 is of minor importance. The major epoxidation reaction occurs with the 11,12 double bond, the resulting 11*S*,12*S* epoxides 10 and 11 as well as some of their rearrangement products, e.g. the 8*R*,11*S* epoxides 12 and 13 being present in fair amounts not only in cured tobacco but also in the green leaves and flowers.²

Experimental

With the exception of optical rotations, which were recorded on a Perkin-Elmer 241 polarimeter, the instruments specified in Ref. 9 were used.

An extract (100 g) obtained by immersing green leaves of *Nicotiana tabacum* (Coker) in chloroform was initially separated into 6 fractions, A (19.6 g), B (13.2 g), C (4.6 g), D (24.6 g), E (15.9 g) and F (2.6 g), by flash chromatography over silica gel using a gradient of hexane/ethyl acetate/methanol as the eluent. Fraction C was separated further by flash chromatography over silica gel (hexane/ethyl acetate gradient) and HPLC using a column packed with Spherisorb[®] 5 nitrile to give 1.3 mg of (1*S*,2*E*,4*S*,6*R*,7*R*,8*R*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol (1).

A chloroform extract (83 g) of flowers of *Nicotiana tabacum* (Basma) was separated into 5 fractions, A (12.7 g), B (4.7 g), C (8.0 g), D (30 g) and E (3.6 g) by flash chromatography (silica gel; hexane/ethyl acetate/methanol). Part of fraction C (6.2 g) was separated further into 8 frac-

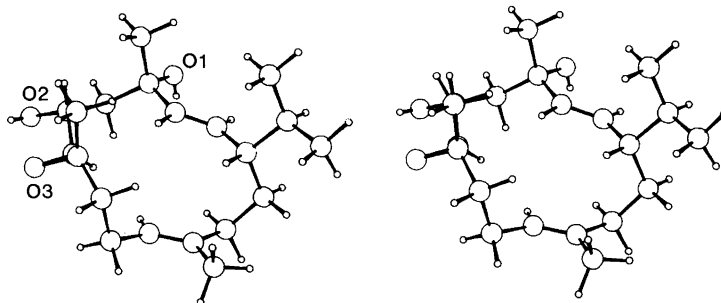
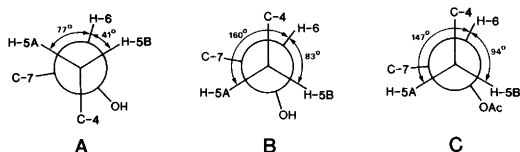


Fig. 2. A stereoscopic view of (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol (2).



Scheme 1. Conformation about the 5,6 bond in 1 (A), 2 (B) and 9 (C).

tions, C1–C8, using a Prep Pak®-500/C₁₈ cartridge and methanol/water (65:35) as the eluent. Repeated HPLC of fraction C3 (272 mg) using columns packed with Lichrosorb® 5 diol and Spherisorb® 5 nitrile led to the isolation of 3.7 mg of (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol (2).

Compound 1 had m.p. 121–122°C; $[\alpha]_D +0.8^\circ$ (c 0.8, CHCl₃); (Found: M⁺ 322.2543. Calc. for C₂₀H₃₄O₃: 322.2508); IR (CCl₄): 3608 and 3364 cm⁻¹; ¹H NMR (CDCl₃): δ 0.83 (d, *J* = 6.9 Hz)/0.86 (d, *J* = 6.8 Hz) (H-16/H-17), 1.05 (ddd, *J* = 3.9, -12.7 and 12.8 Hz, H-9a), 1.30 (s, H-18), 1.39 (s, H-19), 1.53 (broad s, H-20), 1.91 (dddd, *J* = 3.7, 5.0, 12.8 and -14.7 Hz, H-10a), 1.97 (dd, *J* = 1.0 and -15.0 Hz, H-5a), 2.10 (ddd, *J* = 3.7, 4.3 and -12.7 Hz, H-9b), 2.25 (dd, *J* = 6.8 and -15.0 Hz, H-5b), 2.34 (dddd, *J* = 3.9, 4.3, 10.5 and -14.7 Hz, H-10b), 3.37 (d, *J* = 9.2 Hz, H-7), 3.75 (ddd, *J* = 1.0, 6.8 and 9.2 Hz, H-6), 5.43 (dd, *J* = 5.0 and 10.5 Hz, H-11), 5.53 (dd, *J* = 7.7 and 15.8 Hz, H-2) and 5.68 (d, *J* = 15.8 Hz, H-3); MS [*m/z* (%), composition]: 322 (M, 0.2), 304 (0.4, C₂₀H₃₂O₂), 286 (0.2, C₂₀H₃₀O), 261 (0.8, C₁₇H₂₅O₂ and C₁₈H₂₉O), 243 (0.7, C₁₇H₂₃O), 233 (0.9, C₁₆H₂₅O), 205 (1, C₁₄H₂₁O and C₁₅H₂₅), 137 (10, C₁₀H₁₇ and C₉H₁₃O), 123 (16, C₉H₁₅ and C₈H₁₁O), 109 (15, C₈H₁₃ and C₇H₉O), 95 (22, C₇H₁₁ and C₆H₇O), 81 (32, C₆H₉ and C₅H₅O), 69 (28, C₅H₉ and C₄H₅O), 55 (30, C₄H₇ and C₃H₃O) and 43 (100).

Dihedral angles (X-ray results): H-9a, C-9, C-10, H-10a: -175.1°; H-9a, C-9, C-10, H-10b: 66.0°; H-9b, C-9, C-10, H-10a: 65.6°; H-9b, C-9, C-10, H-10b: -53.3°; H-10a, C-10, C-11, H-11: 31.2°; H-10b, C-10, C-11, H-11: 150.5°.

The compound (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol (2) had m.p. 45–47 and 67°C; $[\alpha]_D +67^\circ$ (c 0.88, CHCl₃); (Found: [M-18]⁺ 304.2370. Calc. for C₂₀H₃₂O₂: 304.2402); IR (CCl₄): 3586 and 3467 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* = 6.7 Hz)/0.86 (d, *J* = 6.6 Hz) (H-16/H-17), 1.33 (s, H-19), 1.36 (s,

H-18), 1.53 (broad s, H-20), 3.03 (d, *J* = 8.1 Hz, H-7), 3.59 (m, H-6), 5.09 (broad t, *J* = 6.0 Hz, H-11), 5.36 (d, *J* = 15.3 Hz, H-3) and 5.43 (dd, *J* = 8.4 and 15.3 Hz, H-2); MS [*m/z* (%), composition]: 304 (M-18, 0.2), 286 (0.1), 261 (0.3, C₁₇H₂₅O₂), 243 (0.3), 221 (1, C₁₅H₂₅O and C₁₄H₂₁O₂), 203 (1, C₁₁H₂₃O₃), 139 (8, C₉H₁₅O and C₈H₁₁O₂), 123 (12, C₉H₁₅ and C₈H₁₁O), 109 (13, C₈H₁₃ and C₇H₉O), 95 (21, C₇H₁₁ and C₆H₇O), 81 (27, C₆H₉ and C₅H₅O), 69 (22, C₅H₉ and C₄H₅O), 55 (25, C₄H₇ and C₃H₃O) and 43 (100).

Epoxidation of (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*)-2,7,11-cembratriene-4,6-diol (3). To a solution of 98.3 mg of 3 and a catalytic amount of vanadyl acetylacetonate in 5 ml of benzene, kept at 0°C, was added a solution of 100 μl of *t*-butyl hydroperoxide in 3 ml of benzene. After 3 h at room temperature, the reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic phase was washed with a saturated aqueous solution of ferrous sulfate, then water and finally dried. The solvent was removed under reduced pressure and the residue separated by flash chromatography over silica gel using a hexane/ethyl acetate gradient into 23 mg of (1*S*,2*E*,4*S*,6*R*,7*R*,8*R*,11*E*)-7,8-epoxy-2,11-cembradiene-4,6-diol and 72 mg of (1*S*,2*E*,4*S*,6*R*,7*S*,8*S*,11*E*)-7,8-epoxy-2,11-cem-

Table 2. Chemical shift values (δ) and coupling constants (*J* in Hz) for the H-5a, H-5b, H-6 and H-7 signals in the ¹H NMR spectra of compounds 1 and 5–9.

| Compound | H-5a | H-5b | H-6 | H-7 |
|----------------|--|--|---------------------------------------|------|
| 1 | 1.97 <i>J</i> _{5a,6} = 1.0 | 2.25 <i>J</i> _{5b,6} = 6.8 | 3.75 <i>J</i> _{6,7} = 9.2 | 3.37 |
| 5 | 1.98 <i>J</i> _{5a,6} = 0.9 | 2.31 <i>J</i> _{5b,6} = 7.0 | 4.86 <i>J</i> _{6,7} = 9.1 | 3.44 |
| 6 ^a | 1.91 <i>J</i> _{5a,6} = 5.3 | 2.03 <i>J</i> _{5b,6} = 3.7 | 5.27 <i>J</i> _{6,7} = 8.9 | 2.86 |
| 7 | 1.91 <i>J</i> _{5a,6} = 9.3 | 2.10 <i>J</i> _{5b,6} = 1.5 | 4.53 <i>J</i> _{6,7} = 4.4 | 3.05 |
| 8 | 1.89 <i>J</i> _{5a,6} = 4.9 | 2.11 <i>J</i> _{5b,6} = 3.6 | 4.00 <i>J</i> _{6,7} = 7.9 | 2.84 |
| 9 | 1.90 <i>J</i> _{5a,6} = 8.7 | 2.03 <i>J</i> _{5b,6} = 1.6 | 5.80 <i>J</i> _{6,7} = 9.9 | 5.32 |

^aRun in C₆D₆.

bradiene-4,6-diol, whose physical and spectral data were identical with those of 1 and 2, respectively.

Acetylation of the (1S,2E,4S,6R,7R,8R,11E)- and (1S,2E,4S,6R,7S,8S,11E)-7,8-epoxy-2,11-cembradiene-4,6-diols (1, 2). Acetylation using acetic anhydride/pyridine converted 1 and 2 into the (1S,2E,4S,6R,7R,8R,11E)- and (1S,2E,4S,6R,7S,8S,11E)-6-acetoxy-7,8-epoxy-2,11-cembradiene-4-ols 5 and 6, respectively.

Compound 5 was an oil; IR (CCl₄): 3601, 3484, 1756, 1740, 1240 and 1220 cm⁻¹; ¹H NMR (CDCl₃): δ 0.83 (d, *J* = 6.9 Hz)/0.87 (d, *J* = 6.8 Hz) (H-16/H-17), 1.27 (s)/1.29 (s) (H-18/H-19), 1.54 (broad s, H-20), 2.12 (s, -OCOCH₃), 3.44 (d, *J* = 9.1 Hz, H-7), 4.86 (ddd, *J* = 0.9, 7.0 and 9.1 Hz, H-6), 5.28 (m, H-11), 5.50 (dd, *J* = 7.9 and 15.8 Hz, H-2) and 5.68 (dd, *J* = 0.6 and 15.8 Hz, H-3); MS [*m/z* (%): 364 (M, 0.1), 346 (0.1), 321 (0.2), 305 (2), 286 (1), 271 (0.5), 261 (1), 243 (3), 215 (1), 203 (3), 135 (9), 123 (13), 109 (15), 95 (20), 81 (28), 69 (21), 55 (20) and 43 (100).

Compound 6 was also an oil; IR (CCl₄): 3610, 3511, 1740 and 1237 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* = 6.9 Hz)/0.86 (d, *J* = 6.6 Hz) (H-16/H-17), 1.32 (s)/1.42 (s) (H-18/H-19), 1.53 (broad s, H-20), 2.09 (s, -OCOCH₃), 2.94 (d, *J* = 8.9 Hz, H-7), 4.99 (m, H-6), 5.06 (m, H-11), 5.38 (dd, *J* = 8.0 and 15.3 Hz, H-2) and 5.43 (d, *J* = 15.3 Hz, H-3); MS [*m/z* (%): 364 (M, 0.1), 346 (0.2), 304 (0.6), 286 (0.9), 271 (0.6), 261 (1), 243 (3), 215 (1), 203 (3), 135 (8), 123 (11), 109 (12), 95 (19), 81 (26), 69 (23), 55 (21) and 43 (100).

Epoxidation of (1S,2E,4R,6R,7E,11E)-2,7,11-cembratriene-4,6-diol (4). To a solution of 96.8 mg of 4 and a catalytic amount of vanadyl acetylacetonate in 5 ml of benzene, kept at 0°C, was added a solution of 100 μl of *t*-butyl hydroperoxide in 3 ml of benzene. After 3 h at room temperature, the reaction mixture was worked up and separated by flash chromatography over silica gel (hexane/ethyl acetate 70:30) into 34 mg of (1S,2E,4R,6R,7R,8R,11E)-7,8-epoxy-2,11-cembradiene-4,6-diol (7) and 67 mg of (1S,2E,4R,6R,7S,8S,11E)-7,8-epoxy-2,11-cembradiene-4,6-diol (8).

Compound 7 was an oil and had [α]_D -2.7° (c 0.62, CHCl₃); IR (CCl₄): 3613 and 3453 cm⁻¹; ¹H NMR (CDCl₃): δ 0.83 (d, *J* = 6.8 Hz)/0.86 (d, *J* = 6.8 Hz) (H-16/H-17), 1.47 (s, H-18), 1.51 (s,

H-19), 1.53 (s, H-20), 3.05 (d, *J* = 4.4 Hz, H-7), 4.53 (ddd, *J* = 1.5, 4.4 and 9.3 Hz, H-6), 5.00 (m, H-11), 5.35 (dd, *J* = 8.6 and 15.7 Hz, H-2) and 5.57 (d, *J* = 15.7 Hz, H-3); MS [*m/z* (%): 322 (M, 0.1), 304 (1), 286 (0.3), 261 (1), 243 (1), 223 (3), 203 (2), 189 (3), 163 (4), 137 (12), 123 (22), 109 (21), 95 (28), 81 (38), 69 (33), 55 (30) and 43 (100).

Compound 8 was also an oil and had [α]_D +58° (c 0.87, CHCl₃); IR (CCl₄): 3589 and 3437 cm⁻¹; ¹H NMR (CDCl₃): δ 0.82 (d, *J* = 6.8 Hz)/0.86 (d, *J* = 6.7 Hz) (H-16/H-17), 1.36 (s, H-19), 1.45 (s, H-18), 1.53 (s, H-20), 2.84 (d, *J* = 7.9 Hz, H-7), 4.00 (ddd, *J* = 3.6, 4.9 and 7.9 Hz, H-6), 5.03 (m, H-11), 5.27 (dd, *J* = 9.1 and 15.7 Hz, H-2) and 5.49 (d, *J* = 15.7 Hz, H-3); MS [*m/z* (%): 322 (M, 0.3), 304 (1), 286 (0.3), 261 (1), 243 (1), 223 (2), 203 (2), 189 (3), 161 (4), 137 (12), 123 (22), 109 (21), 95 (29), 81 (40), 69 (31), 55 (28) and 43 (100).

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