

# Tobacco Chemistry. 60.\* Five New Hydroperoxycembratrienediols from Tobacco

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Five new diterpenoids of the cembrane class have been isolated from flowers of Greek tobacco and shown to be (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (*1*, *2*) and (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol (*3-5*) by spectral and chemical methods. The biogenesis of these compounds is discussed.

The cembranic diterpenoids, which are present in the gummy exudate of the leaf and flower of most tobacco varieties, include as the major components 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 (*6*, *7*). These two compounds are the postulated precursors of the majority of the other tobacco cembranoids.<sup>2</sup> We now report the isolation and biomimetic synthesis of five new cembranoids, which are likely to arise in tobacco by oxidation of the 4*S*,6*R*- and 4*R*,6*R*-diols (*6*, *7*).

**Results.** The first two compounds (*1*, *2*) gave rise to <sup>1</sup>H and <sup>13</sup>C NMR spectra consistent with the presence of an isopropyl group, a methyl group linked to a fully substituted, oxygen-carrying carbon atom, a vinylic methyl group and three double bonds. Of these, one is *E*-disubstituted, one is trisubstituted and one extends to an exocyclic methylene group. Two protons, resonating at  $\delta$  4.28 and 4.66 for *1* and at  $\delta$  4.30 and 4.68 for *2*, are evidently attached to oxygen-bearing carbon atoms. These results suggest that the new compounds (*1*, *2*) are structurally related to the 2,7,12(20)-cembratriene-4,6,11-triols, which have previously been isolated from tobacco.<sup>1,3</sup>

A comparison of the <sup>13</sup>C NMR data confirmed this and revealed that the C-1 to C-9 and C-14 to C-19 signals are present at virtually invariant positions in the spectra of *1* and (1*S*,2*E*,4*S*,6*R*,

Table 1. <sup>13</sup>C NMR chemical shifts and assignments for compounds *1-5* and *8-12*.<sup>a</sup>

Compound	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
<i>1</i>	48.7	127.9	139.7	74.2	46.2	68.5	128.5	137.5	30.2	34.6	88.1	147.1	29.6	29.0	32.2	19.2	20.8	33.1	15.9	113.5
<i>2</i>	47.6	129.8	137.0	72.3	52.1	64.7	129.8	138.7	31.3	35.0	86.2	148.6	30.2	28.6	31.9	18.8	20.5	31.6	16.6	111.8
<i>3</i>	50.7	127.9	138.4	74.2	46.7	69.4	127.9	135.2	41.0	126.9	133.9	85.0	35.8	26.5	30.2	17.9	21.6	31.6	18.3	24.4
<i>4</i>	50.8	128.1	138.5	73.9	47.0	69.3	127.6	135.4	41.1	130.0	134.0	86.4	35.5	27.4	30.2	18.0	21.6	31.8	18.1	20.9
<i>5</i>	48.3	129.4	136.7	72.0	52.1	64.9	129.4	138.3	41.7	128.0	133.6	85.0	35.9	25.9	29.8	17.9	21.2	30.4	18.2	23.2
<i>8</i>	49.0	127.4	139.8	74.1	46.5	68.5	128.5	137.8	29.8	32.9	74.8	151.6	34.6	29.3	32.2	19.2	20.8	33.4	16.0	111.2
<i>9</i>	47.6	129.7 <sup>b</sup>	137.1	72.1	51.8	64.7	129.6 <sup>b</sup>	139.1	30.3	32.5	73.4	152.4	34.9	30.3	31.9	18.7	20.6	31.4	16.6	110.3
<i>10</i>	50.8	127.3	138.3	74.3 <sup>b</sup>	47.2	69.4	128.4	134.5	40.7	124.6	138.9	74.0 <sup>b</sup>	40.1	26.5	30.1	17.8	21.8	31.6	18.0	30.0
<i>11</i>	49.9	127.6	138.4	74.4	47.1	69.2	128.0	135.7	41.0	126.1	138.1	73.9	40.2	28.0	29.8	17.9	21.6	31.7	17.9	27.1
<i>12</i>	49.3	128.8	137.2	71.9	52.3	64.8	128.8	138.9	40.9	124.8	138.0	73.8	39.7	25.9	29.6	17.6	21.5	30.4	18.2	29.8

<sup>a</sup>  $\delta$ -Values in CDCl<sub>3</sub> relative to TMS. <sup>b</sup> Assignment may be reversed.

\* For part 59 see Ref. 1.

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7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (8,<sup>3</sup> cf. Table 1). However, since the shieldings of C-11 were found to be markedly different,  $\delta$  88.1 for 1 as against  $\delta$  74.8 for 8, and since the <sup>1</sup>H NMR spectrum of 1 exhibits a broad singlet at  $\delta$  8.05,<sup>4</sup> 1 was provisionally formulated as a (1*S*,2*E*,4*S*,6*R*,7*E*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol. Analogous findings obtained by a comparison of the <sup>13</sup>C NMR spectra of 2 and (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (9)<sup>1</sup> allowed the identification of 2 as a (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol. These assignments were in harmony with the mass spectra of 1 and 2, which displayed a peak at *m/z* 320 (M-18) due to a C<sub>20</sub>H<sub>32</sub>O<sub>3</sub> ion.

The remaining three new compounds (3-5) were also hydroperoxides [broad singlets at  $\delta$  8.22, 7.33 and 7.43 in the <sup>1</sup>H NMR spectra of 3-5, respectively; <sup>13</sup>C NMR signals at  $\delta$  85.0 (3, s),  $\delta$  86.4 (4, s) and  $\delta$  85.0 (5, s)]. In contrast to hydroperoxides 1 and 2, however, compounds 3-5 contain two *E*-disubstituted and one trisubstituted double bond as well as three methyl groups, of which one is vinylic and two attached to (a) fully substituted carbon atom(s).

These results and a comparison of the <sup>13</sup>C NMR spectra with those of the (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triols (10-12)<sup>1,3</sup> led to a tentative formulation of 3 and 4 as (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diols and of 5 as a (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol.

Conclusive evidence of the structures of hydroperoxides 1-5 was obtained *via* biomimetic syntheses. These involved sensitized photo-oxygenation of the 4*S*,6*R*- and 4*R*,6*R*-diols (6, 7) and resulted, in each case, in the formation of a mixture of ene products,<sup>1</sup> which was subjected to repeated HPLC. The three major products of the 4*S*-series, which were identified as (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol by reduction to the known triols 8, 10 and 11<sup>1,3</sup> using triethyl phosphite, proved to be indistinguishable from hydroperoxides 1, 3 and 4, respectively.

The two major photo-oxygenation products of the 4*R*-series, which were correlated with triols 9 and 12 by reduction, were found to be identical to hydroperoxides 2 and 5, respectively. The latter are hence fully characterized as (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (2) and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cembratriene-4,6-

diol (5).

With the structures of these new compounds at hand, it can be inferred from the <sup>1</sup>H and <sup>13</sup>C NMR results that the conformational difference with respect to the orientation about the 5,6 bond, previously noted between triols of the 4*S*- and the 4*R*-series (e.g. 8, 10 and 11 vs. 9 and 12),<sup>1</sup> is retained among the hydroperoxides.

**Discussion.** The present results provide experimental support for the view that the 4,6,11- and 4,6,12-triols, which are fairly abundant in the cuticular wax of the tobacco leaf and flower, are formed from the 4,6-diols (6-7) through the intermediacy of hydroperoxides.<sup>1,2</sup> They do not, however, imply the exclusive operation of singlet oxygen reactions, since enzyme-catalyzed oxidations would also be expected to proceed *via* hydroperoxide intermediates.

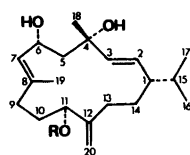
These new compounds (1-5), which are the only hydroperoxides found in tobacco so far,\* add to the small but growing group of terpenic hydroperoxides. Among these are neoconcin-diol hydroperoxide from *Laurencia snyderia*,<sup>4</sup> crispolide from *Tanacetum vulgare*<sup>5</sup> as well as 4(15),5,10(14)-germacatriene-1 $\beta$ -hydroperoxide from *Senecio glanduloso-pilosus*.<sup>6</sup>

**Experimental.** With the exception of accurate mass measurements, which were carried out on a Kratos MS 50 Stereo DS 55 SM/DS 55 S mass spectrometer-computer system and the NMR spectra, which were recorded on a Varian XL-200 spectrometer, the instruments specified in Ref. 7 were used.

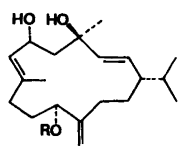
An extract (83 g) obtained by immersing flowers of Greek *Nicotiana tabacum* (Basma Drama) in chloroform, was initially separated into five fractions, A (12.7 g), B (4.7 g), C (8.0 g), D (30 g) and E (3.6 g) by flash chromatography using a column packed with silica gel and gradients of hexane-ethyl acetate-methanol as eluent.

Fraction C was further separated by flash chromatography over silica gel into five fractions C1 (250 mg), C2 (485 mg), C3 (3.0 g), C4 (3.5 g) and C5 (465 mg). Repeated HPLC of fraction C4 using columns packed with Spherisorb and Spherisorb 5 Nitrile led to the isolation of 21 mg

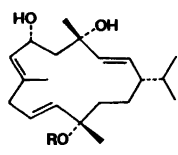
\* An analysis by TLC using ferrous thiocyanate as the spraying reagent of an extract, obtained by immersing fresh green leaves of Burley tobacco in cold chloroform (0 °C), revealed the presence of a peroxide-positive zone, whose R<sub>F</sub> value agreed with that of hydroperoxides 1-5. Moreover, since the 4,6-diols (6,7) fail to produce hydroperoxides even on prolonged exposure to triplet oxygen, it can be concluded that hydroperoxides 1-5, now isolated from flowers of Greek tobacco, are not artefacts but genuine tobacco constituents.



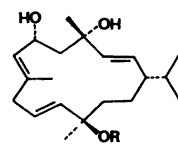
1 R=OH  
8 R=H



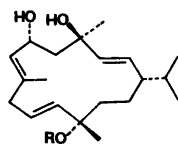
2 R=OH  
9 R=H



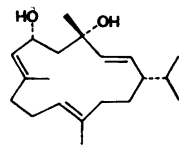
3 R=OH  
10 R=H



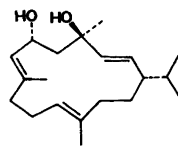
4 R=OH  
11 R=H



5 R=OH  
12 R=H



6



7

of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (1), 28 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol (3) and 5 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol (4).

Fraction C5 was further separated by HPLC using columns packed with Spherisorb and Spherisorb 5 Nitrile to give 7 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (2) and 5 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cembratriene-4,6-diol (5).

(1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-11-Hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (1) had m.p. 132–134 °C,  $[\alpha]_D^{+53}$  (c 0.47, CHCl<sub>3</sub>) (Found: [M-18]<sup>+</sup> 320.2337. Calc. for C<sub>20</sub>H<sub>32</sub>O<sub>3</sub>: 320.2352); IR (CHCl<sub>3</sub>) bands at: 3603, 3464, 3080, 1385 and 1370 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.87 (d, *J*=6.7 Hz)/0.89 (d, *J*=6.7 Hz) (H-16/H-17), 1.28 (s, H-18), 1.66 (d, *J*=1.4 Hz, H-19), 1.77 (dd, *J*=2.4 and -14.4 Hz, H-5a), 2.23 (dd, *J*=5.6 and -14.7 Hz, H-5b), 4.28 (dd, *J*=4.5 and 9.1 Hz, H-11), 4.66 (ddd, *J*=2.4, 5.6 and 9.3 Hz, H-6), 5.12 (q, *J*=1.6 Hz, H-20a), 5.15 (broad s, H-20b), 5.46 (d, *J*=15.6 Hz, H-3), 5.54 (dd, *J*=8.3 and 15.6 Hz, H-2), 5.61 (broad d, *J*=9.3 Hz, H-7) and 8.05 (broad s, OOH); MS [*m/z* (%): 320 (0.2), 302 (0.3), 259 (0.8), 243 (1), 217 (0.9), 203 (1), 135 (8), 121 (13), 109 (16), 95 (20), 81 (20), 69 (21), 55 (25) and 43 (100).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-Hydroperoxy-2,7,12(20)-cembratriene-4,6-diol (2) was an oil, which had  $[\alpha]_D^{+34}$  (c 0.54, CHCl<sub>3</sub>) (Found: [M-18]<sup>+</sup> 320.2358. Calc. for C<sub>20</sub>H<sub>32</sub>O<sub>3</sub>: 320.2352); IR (CHCl<sub>3</sub>) bands at: 3601, 3401, 3080, 1384 and 1370 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.82 (d, *J*=6.4 Hz)/0.85 (d, *J*=6.2 Hz) (H-16/H-17), 1.36 (s, H-18), 1.72 (d, *J*=1.3 Hz, H-19), 1.96 (dd, *J*=7.7 and -14.1 Hz, H-5a), 2.05 (dd, *J*=2.8 and -14.1

Hz, H-5b), 4.30 (t, *J*=6 Hz, H-11), 4.68 (ddd, *J*=2.8, 7.7 and 9.0 Hz, H-6), 5.06 (q, *J*=1.4 Hz, H-20a), 5.13 (broad s, H-20b), 5.28 (broad d, *J*=9.0 Hz, H-7), 5.37 (dd, *J*=8.3 and 15.8 Hz, H-2), 5.47 (d, *J*=15.8 Hz, H-3) and 7.90 (broad s, OOH); MS [*m/z* (%): 320 (0.2), 302 (0.5), 259 (0.8), 243 (1), 215 (1), 203 (2), 135 (8), 121 (14), 109 (16), 95 (24), 81 (24), 69 (24), 55 (27) and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-12-Hydroperoxy-2,7,10-cembratriene-4,6-diol (3) was an oil, which had  $[\alpha]_D^{+91}$  (c 0.50, CHCl<sub>3</sub>) (Found: [M-18]<sup>+</sup> 320.2345. Calc. for C<sub>20</sub>H<sub>32</sub>O<sub>3</sub>: 320.2352); IR (CHCl<sub>3</sub>) bands at: 3602, 3384, 1664, 1384 and 1369 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.82 (d, *J*=6.7 Hz)/0.86 (d, *J*=6.6 Hz) (H-16/H-17), 1.21 (s)/1.37 (s) (H-18/H-20), 1.67 (broad s, H-19), 1.73 (dd, *J*=1.8 and -14.4 Hz, H-5a), 2.20 (dd, *J*=6.2 and -14.4 Hz, H-5b), 2.65 (ddd, *J*=0.6, 7.0 and -17.6 Hz, H-9a), 2.75 (ddd, *J*=0.6, 7.0 and -17.6 Hz, H-9b), 4.76 (ddd, *J*=1.8, 6.2 and 8.4 Hz, H-6), 5.39 (dt, *J*=0.6 and 16.1 Hz, H-11), 5.41 (d, *J*=15.4 Hz, H-3), 5.56 (broad d, *J*=8.4 Hz, H-7), 5.57 (dd, *J*=8.5 and 15.4 Hz, H-2), 5.63 (dt, *J*=7.0 and 16.1 Hz, H-10) and 8.22 (broad s, OOH); MS [*m/z* (%): 320 (0.1), 302 (0.2), 287 (0.4), 259 (0.4), 243 (0.8), 219 (0.8), 203 (1), 135 (8), 121 (10), 109 (16), 95 (18), 81 (17), 71 (21), 55 (21) and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-12-Hydroperoxy-2,7,10-cembratriene-4,6-diol (4) was an oil, which had  $[\alpha]_D^{+124}$  (c 0.23, CHCl<sub>3</sub>) (Found: [M-36]<sup>+</sup> 302.2270. Calc. for C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>: 302.2246); IR (CHCl<sub>3</sub>) bands at: 3602, 3472, 1667, 1385 and 1370 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.81 (d, *J*=6.7 Hz)/0.86 (d, *J*=6.7 Hz) (H-16/H-17), 1.23 (s, H-20), 1.35 (s, H-18), 1.68 (broad s, H-19), 1.74 (dd, *J*=2.2 and -14.3 Hz, H-5a), 2.20 (dd, *J*=6.4 and -14.3 Hz, H-5b), 2.75 (dd, *J*=0.8

and 6.8 Hz, H-9a and H-9b), 4.79 (ddd,  $J=2.2$ , 6.4 and 8.6 Hz, H-6), 5.44 (d,  $J=15.4$  Hz, H-3), 5.45 (dt, 0.8 and 16.0 Hz, H-11), 5.48 (broad d,  $J=8.6$  Hz, H-7), 5.55 (dd,  $J=8.3$  and 15.4 Hz, H-2), 5.67 (dt,  $J=6.8$  and 16.0 Hz, H-10) and 7.33 (broad s, OOH); MS [ $m/z$  (%): 302 (0.1), 287 (0.6), 259 (0.5), 243 (0.8), 217 (1), 203 (1), 135 (5), 121 (9), 109 (18), 95 (18), 81 (17), 69 (18), 55 (20) and 43 (100).

(1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-Hydroperoxy-2,7,10-cembratriene-4,6-diol (5) was an oil, which had  $[\alpha]_D^{25} +64^\circ$  ( $c$  0.09,  $\text{CHCl}_3$ ) (Found:  $[\text{M}-18]^+$  320.2343. Calc. for  $\text{C}_{20}\text{H}_{32}\text{O}_3$ : 320.2352); IR ( $\text{CHCl}_3$ ) bands at 3602, 3381, 1662, 1385 and 1370  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  0.76 (d,  $J=6.6$  Hz)/0.85 (d,  $J=6.5$  Hz) (H-16/H-17), 1.36 (s)/1.37 (s) (H-18/H-20), 1.79 (d,  $J=1.3$  Hz, H-19), 1.83 (dd,  $J=9.3$  and  $-13.8$  Hz, H-5a), 2.05 (dd,  $J=2.9$  and  $-13.8$  Hz, H-5b), 2.61 (dd,  $J=7.5$  and  $-14.9$  Hz, H-9a), 2.83 (dd,  $J=6.7$  and  $-14.9$  Hz, H-9b), 4.69 (ddd,  $J=2.9$ , 8.8 and 9.3 Hz, H-6), 5.27 (broad d,  $J=8.8$  Hz, H-7), 5.35 (dd,  $J=8.3$  and 15.8 Hz, H-2), 5.45 (d,  $J=15.6$  Hz, H-11), 5.45 (d,  $J=15.8$  Hz, H-3), 5.72 (ddd,  $J=6.7$ , 7.5 and 15.6 Hz, H-10) and 7.43 (broad s, OOH); MS [ $m/z$  (%): 320 (0.1), 302 (0.2), 287 (0.2), 259 (0.4), 243 (0.7), 221 (1), 203 (1), 136 (6), 121 (11), 109 (15), 95 (20), 81 (19), 69 (21), 55 (23) and 43 (100).

*Sensitized photo-oxygenation of (1S,2E,4S,6R,7E,11E)- and (1S,2E,4R,6R,7E,11E)-2,7,11-cebratriene-4,6-diol (6, 7).* A solution of 1.1 g of 6 and 34 mg of Rose Bengal in 20 ml of methanol, in a tube cooled by a water jacket, was irradiated with a 400 W sodium high pressure lamp placed outside the tube, while oxygen was bubbled through the reaction mixture. After 1.5 h the mixture was taken to dryness and the residue filtered through alumina. Repeated HPLC using a column packed with Spherisorb 5 Nitrile allowed the isolation of 210 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cebratriene-4,6-diol (1), 140 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cebratriene-4,6-diol (3) and 12 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-12-hydroperoxy-2,7,10-cebratriene-4,6-diol (4).

A solution of 200 mg of 7 and 10 mg of Rose Bengal in 25 ml of methanol was treated with singlet oxygen for 1 h using the apparatus described above. Separation by repeated HPLC using a column packed with Spherisorb 5 Nitrile afforded 80 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cebratriene-4,6-diol (2) and 40 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cebratriene-4,6-diol (5).

Of these, the (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-

cebratriene-4,6-diols were identical (optical rotation, IR,  $^1\text{H NMR}$  and MS) to compounds 1 and 2 and the (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cebratriene-4,6-diols to compounds 3, 4 and 5, respectively.

*Conversion of hydroperoxides 1-5 to corresponding triols (8-12).* A solution of 6.9 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cebratriene-4,6-diol (1) and 10  $\mu\text{l}$  of triethyl phosphite in 1 ml of methanol was kept at room temperature for 5 min. Removal of the solvent and separation by HPLC using a column packed with Spherisorb and hexane-ethyl acetate (20:80) as an eluent afforded 6.0 mg of a product, whose IR,  $^1\text{H NMR}$  and mass spectra were identical to those of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-2,7,12(20)-cebratriene-4,6,11-triol (8).<sup>3</sup>

Using the same method, (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-11-hydroperoxy-2,7,12(20)-cebratriene-4,6-diol (2), (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-12-hydroperoxy-2,7,10-cebratriene-4,6-diol (3-5) were converted to compounds, which were indistinguishable from (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cebratriene-4,6,11-triol (9),<sup>1</sup> (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cebratriene-4,6,12-triol (10-12),<sup>1,3</sup> respectively.

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