

Tobacco Chemistry. 75.¹ Two New Cembratrienetriols from Tobacco

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Two new diterpenoids of the cembrane class have been isolated from flowers of Greek tobacco. They have been identified as (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*R*)-2,7,11-cembratriene-4,6,13-triol (**1**) and (1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-2,7,11-cembratriene-4,6,20-triol (**2**) by spectral methods and syntheses. The biogenesis of the new compounds is discussed. The crystal structure of the 6-acetate (**6**) of triol **1** has been determined and a full account of the X-ray work is given.

More than seventy cembranoids have been reported as constituents of tobacco to date. They are present as complex mixtures in the cuticular wax of the leaf and flower, where they co-occur with aliphatic hydrocarbons, fatty alcohols, wax esters and sucrose esters. The first cembranoids to be isolated were the (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*)-2,7,11-cembratriene-4,6-diols (**3**, **4**).² Later studies have shown that they are the major cembranoids and also the principal precursors of most of the other tobacco cembranoids.³

We now report the isolation and structural elucidation of two new cembratrienetriols (**1**, **2**), which are plausible metabolites of the diols **3** and **4**, from a chloroform extract of flowers from Greek tobacco. They were obtained by repetitive liquid chromatography.

Results

Structure elucidation. The first new compound (**1**), C₂₀H₃₄O₃, has two secondary and one tertiary hydroxy group [OH-absorption in the IR spectrum; ¹H NMR signals at δ 3.88 and 4.80; ¹³C NMR signals at δ 64.3 (d), 77.3 (s) and 77.4 (d), Table 1]. Triol **1** also possesses three double bonds, of one which is *E*-1,2-disubstituted (*J*_{1,2} 15.6 Hz) and the other two are trisubstituted [¹³C NMR signals at δ 128.2 (d), 130.2 (d), 131.9 (d), 135.0 (s), 135.8 (s) and 135.9 (d)]. Hence it was concluded that triol **1** is carbomonocyclic.

The presence of two vinylic methyl groups (¹H NMR: δ 1.53 and 1.68), one methyl group attached to the carbon atom carrying the tertiary hydroxy group [¹H NMR: δ 1.39 (s)] and an isopropyl group (two three-proton doublets at δ 0.82 and 0.84 in the ¹H NMR spectrum) indicated that the triol **1** is a diterpenoid of the cembrane class. Support for this view was provided by ¹H-¹H and

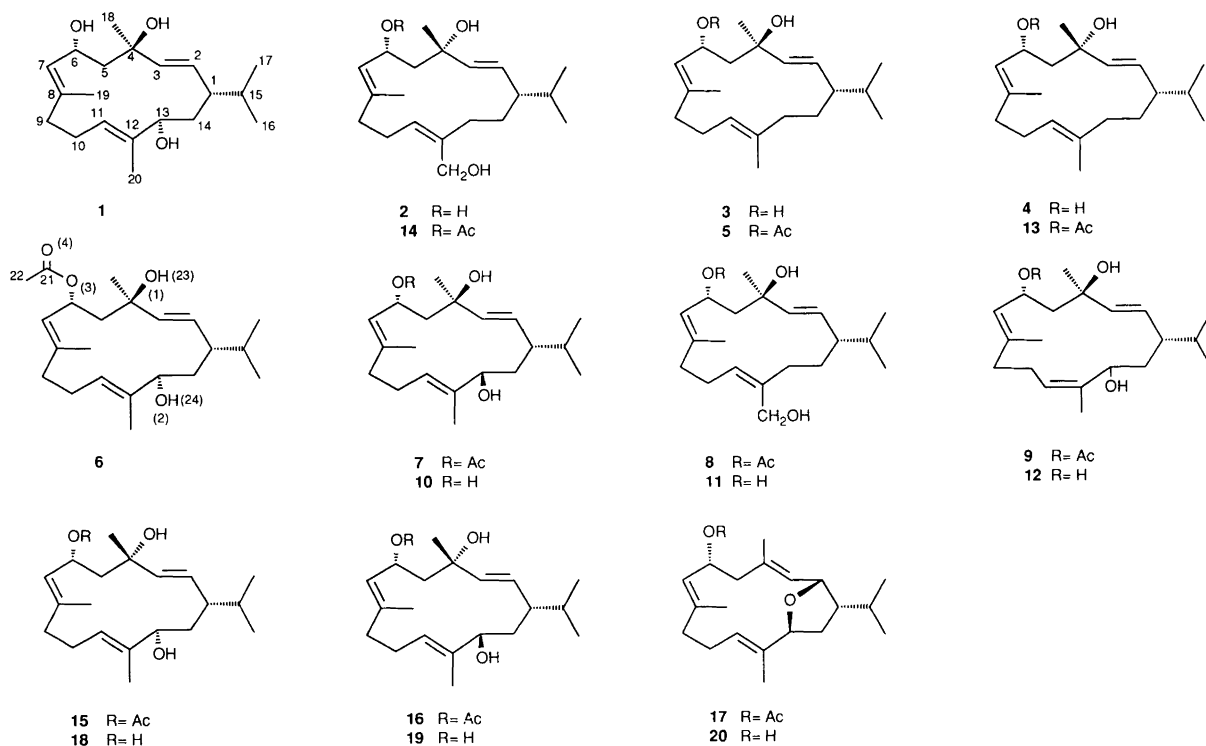
¹H-¹³C shift correlation spectroscopy, which allowed a tentative formulation of **1** as a 2,7,11-cembratriene-4,6,13-triol.

This assignment was verified by chemical methods and by X-ray analysis. Thus, treatment of the acetate **5** of the (4*R*,6*R*)-diol **3** with *tert*-butyl hydroperoxide and a catalytic amount of SeO₂ gave rise to a mixture from which four major oxidation products (**6**–**9**) were isolated. Each of these was subjected to hydrolysis under alkaline conditions to give the triols **1** and **10**–**12**, respectively. The triol derived from the oxidation product **6** proved to be identical with triol **1**, hence demonstrating that the absolute configuration is 1*S*, 4*R*, 6*R*. The chirality of C-13, the remaining asymmetric carbon atom in triol **1**, was resolved as *R* by X-ray analysis of the corresponding 6-acetate (**6**) (see below).

Of the remaining triols, **10** was identified as the 13*S*-epimer of triol **1**, **11** as (1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*)-2,7,11-cembratriene-4,6,20-triol and **12** as a (1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*,13*ξ*)-2,7,11-cembratriene-4,6,13-triol. Triol **10** displayed the signal due to H-13 as an apparent multiplet at δ 4.03, but owing to overlap of signals prerequisite coupling information was not available from the COSY spectrum. The HMBC spectrum of the 6-acetate (**7**) of triol **10** was more informative and included, *inter alia*, a three-bond correlation between C-13 and H-20. Additional structural evidence was obtained by a comparison of the ¹³C NMR spectra of the triols **10** and **1**. Thus, the signals due to C-1, C-11 and C-20 are present at δ 44.7, 124.7 and 13.5 in the ¹³C NMR spectrum of **10** as against at δ 46.2, 128.2 and 9.5 in the spectrum of **1**, all other signals being present at virtually invariant positions for the two triols.

The 4*R*,6*R*,20-triol **11** displayed the signals due to H-20a and H-20b as doublets at δ 4.00 and 4.23 in the ¹H NMR spectrum, while C-20 resonated at δ 60.0. No NOE was observed between the protons attached to C-20

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and H-11 in the 6-acetate (**8**) of triol **11**, hence showing that the 11,12 double bond has *Z*-geometry. The ^1H NMR spectrum of the triol **12** exhibited H-13 as a doublet of doublets at δ 4.47. Correlations are found in the COSY spectrum between, *inter alia*, H-13 and the two protons at C-14 and between the latter and H-1, thus allocating the newly introduced hydroxy group to C-13. C-10, C-13 and C-20 resonate at δ 26.2, 69.2 and 17.9 in the ^{13}C NMR spectrum, shifts which are consistent with an 11,12 double bond of *Z*-geometry.

The spectroscopic data of the second new compound (**2**) are very similar to those of the 4*R*,6*R*,20-triol **11**, which would suggest that **2** is the corresponding 4*S*-isomer. In order to verify this structural assignment, the acetate (**13**) of the 4*S*,6*R*-diol **4** was treated with SeO_2 . As in the case of acetate **5**, a mixture of products (**14–17**) was formed. After separation by HPLC and alkaline hydrolysis, four major products (**2, 18–20**) were obtained. One of these gave rise to the same spectroscopic data and had the same optical rotation as the new tobacco isolate

Table 1. ^{13}C NMR chemical shift values and assignments for compounds **1, 2, 6–12** and **14–20**.^a

Compound	Carbon																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	46.2	130.2	135.9	71.3	52.4	64.3	131.9	135.8 ^b	38.7	22.8	128.2	135.0 ^b	77.4	35.3	33.2	19.6	20.1	28.5	15.7	9.5
2	46.6	127.8	138.0	72.7	51.2	66.6	130.8	136.4	38.8	23.2	127.9	136.7	28.3	32.5	33.1	19.2	20.7	30.4	16.3	60.0
6	46.1	130.2	135.8	70.8	50.9	68.4	127.3	138.7	38.6	22.8	127.9	135.2	77.4	35.2	33.3	19.6	20.0	28.0	15.8	9.6
7	44.6	131.3	135.7	70.9	50.3	68.4	126.0	140.0	38.5	23.4	123.7	135.9	76.2	35.7	33.2	19.1	20.1	28.5	16.6	13.9
8	46.4	130.2	136.2	71.0	50.8	68.4	127.4	139.0	38.8	22.4	127.6	136.4	27.8	32.1	32.9	19.1	20.6	28.4	16.1	59.9
9	45.3	129.5	136.5	71.5	48.6	68.8	125.4	140.4	39.8	25.6	128.3	137.4	69.6	36.7	33.5	18.9	20.0	30.1	17.1	18.0
10	44.7	131.2	135.7	71.3	51.9	64.3	130.2	137.2	38.4	23.3	124.7	135.6	76.6	35.9	33.2	19.1	20.2	29.0	16.7	13.5
11	46.5	131.8	136.3	71.4	52.4	64.4	130.2	136.2	38.9	22.5	128.0	136.2	27.9	32.1	32.8	19.2	20.7	28.9	16.1	60.0
12	45.2	129.7	137.0	72.1	49.9	65.2	129.5	138.6	40.0	26.2	128.0	137.6	69.2	37.1	33.3	19.0	20.2	31.1	16.9	17.9
14	46.6	127.8	137.3	72.2	50.7	68.6	127.0	138.8	38.9	22.6	128.0	136.6	28.2	32.3	32.9	19.3	20.8	29.7	16.4	59.7
15	46.3	127.6	137.0	72.2	50.9	68.5	127.2	138.6	38.6	22.9	127.9	135.3	77.4	35.7	33.1	19.5	20.4	29.7	16.0	9.6
16	44.8	129.1	136.9	71.8	50.0	68.7	125.7	139.7	38.7	23.4	124.0	136.1	76.7	36.2	33.2	19.1	20.3	29.1	16.7	13.2
17	51.9	79.1	130.3	133.4	42.3	69.9	126.3	141.1	38.6	23.2	121.4	136.2	81.6	35.3	31.4	21.2	21.7	18.2	15.4	13.7
18	46.2	127.5	137.4	72.4	52.7	66.1	131.3	136.1	38.7	22.9	128.1	135.2	77.4	35.7	33.2	19.5	20.4	30.0	15.9	9.6
19	44.9	129.0	137.5	72.4	50.6	66.8	128.9	137.2	38.4	23.8	125.5	136.0	77.7	36.7	33.6	19.0	20.2	30.3	16.8	12.5
20	52.0	79.3	130.7	133.8	45.0	66.6	129.4	139.3	38.6	23.2	121.6	136.1	81.5	35.4	31.4	21.3	21.6	18.3	15.0	13.7

^a δ -values in CDCl_3 relative to TMS. ^bAssignment may be reversed.

6	OCOCH_3	171.2	OCOCH_3	21.6	14	OCOCH_3	170.0	OCOCH_3	21.4
7	OCOCH_3	171.1	OCOCH_3	21.5	15	OCOCH_3	170.0	OCOCH_3	21.4
8	OCOCH_3	171.0	OCOCH_3	21.5	16	OCOCH_3	170.0	OCOCH_3	21.4
9	OCOCH_3	171.1	OCOCH_3	21.5	17	OCOCH_3	170.3	OCOCH_3	21.5

(2) hence confirming that this is (1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-2,7,11-cembratriene-4,6,20-triol.

Compound **18** was identified as the 4*S*-isomer of the 4*R*,6*R*,13*R*-triol **1**. This conclusion was based on the fact that all signals, except for those due to C-2 to C-4, C-6 and C-18, are present at virtually invariant positions in the ¹³C NMR spectra of these two triols. Analogous results were obtained by a comparison of the ¹³C NMR spectra of the 6-acetates **6** and **15** of triols **1** and **18**, respectively. Similarly, the good agreement of the chemical shift values of the C-1, C-8 to C-17, C-19 and C-20 in the ¹³C NMR spectra of the 4*R*,6*R*,13*S*-triol **10** and triol **19** formed the basis for the assignment of an 11*E*-geometry and a 13*S*-configuration to the latter.

On exposure to a trace of acid, triol **19** was converted into compound **20**. The latter has the composition C₂₀H₃₂O₂ and is less polar than triols **2**, **18** and **19**. It was identified as (1*S*,2*R*,3*E*,6*R*,7*E*,11*E*,13*S*)-2,13-epoxy-3,7,11-cembratrien-6-ol with extensive use of 2D-NMR methods and is evidently formed from triol **19** by dehydration involving the hydroxy group at C-4, double-bond migration and attack of the hydroxy group at C-13 on C-2 (Scheme 1). In the ¹H NMR spectrum of **20**, H-2 appears as a doublet of doublets at δ 4.52 and H-13 as a broad signal at δ 4.40. A correlation was found between H-2 and C-13 in the HMBC spectrum of acetate **17** hence confirming the presence of the epoxy bridge between C-2 and C-13. H-3 gives rise to a doublet of sextets at δ 4.94 which is coupled to H-2 and H-18. The newly formed 3,4 double bond has *E*-geometry as concluded from the chemical shift value, δ 18.3, of the C-18 signal and the absence of an NOE enhancement between H-3 and H-18 for the acetate **17**.

The NOESY spectrum of acetate **17** included correlations between H-2 and H-18, H-3 and H-6, H-3 and H-11, H-3 and H-19, H-6 and H-19, H-7 and H-11 and H-13 and H-20. These results were used to establish the 2*R*-configuration in **20**, a conclusion also consistent with the mechanism expected to be involved in its formation from **19** (Scheme 1).

Biogenesis. The insight into the biotransformations of the 4,6-diols (**3**, **4**) is rather extensive owing to the isolation and structural elucidation of a number of tobacco

cembranoids during the past fifteen years and to the biomimetic studies by which many of these compounds have been interrelated. The results obtained accord with the view that the 4,6-diols **3** and **4** are key metabolites in the biogenesis of most of the other tobacco cembranoids and that reactions such as oxidations, reductions, acid- and base-induced rearrangements, eliminations and dehydrations are involved.³ The two new tobacco triols **1** and **2** are no exception; they are likely to arise by allylic oxidation of the 4*R*,6*R*-diol (**3**) and 4*S*,6*R*-diol (**4**), respectively. Consonant with this is the patent describing the preparation of (a) 4,6,20-triol(s) from (a) 4,6-diol(s) with the aid of bacteria.⁴

Crystallography. Final fractional coordinates with estimated standard deviations and equivalent isotropic temperature factors for the non-hydrogen atoms of acetate **6** are listed in Table 2. Intramolecular bond lengths and bond angles, both with estimated standard deviations, are found in Tables 3 and 4, while selected non-bonded distances less than 3.5 Å and possible hydrogen bonds are given in Table 5. A stereoscopic drawing of the molecule is shown in Fig. 1, and crystal and experimental data are detailed in Table 6.

There are two molecules in the asymmetric unit. These are bonded with a hydrogen bond O(2B)–O(1A) of 2.988 Å. All bond lengths are within the expected

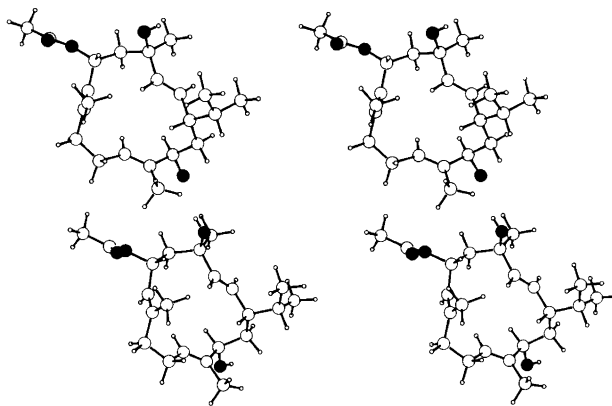
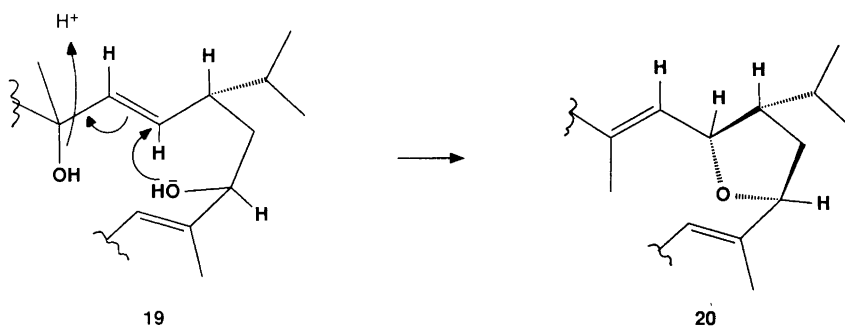


Fig. 1. Stereoscopic view of the two molecules in the asymmetric unit of the acetate **6**.



Scheme 1. Proposed mechanism for the formation of the 2*R*,13*S*-epoxide **20** from the 4*S*,6*R*,13*S*-triol **19**.

Table 2. Atom coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{\AA}^2 \times 10^2$) for the non-hydrogen atoms in the acetate **6**.

	x	y	z	U_{eq}^a
Molecule 1				
C(1A)	-220(4)	-2179(5)	5710(3)	4.62
C(2A)	186(4)	-1922(5)	4945(3)	4.49
C(3A)	1021(4)	-2486(5)	4626(2)	4.41
C(4A)	1384(4)	-2302(5)	3836(2)	4.47
C(5A)	2685(4)	-1856(6)	3840(3)	4.89
C(6A)	3687(4)	-2652(6)	4203(2)	4.67
C(7A)	4103(4)	-2414(6)	5019(3)	5.28
C(8A)	4236(5)	-3125(7)	5592(3)	6.62
C(9A)	4744(6)	-2693(8)	6386(3)	7.86
C(10A)	3802(6)	-2534(7)	6913(3)	7.63
C(11A)	2880(5)	-1637(6)	6610(3)	5.64
C(12A)	1871(4)	-1394(5)	6897(3)	4.90
C(13A)	995(4)	-575(6)	6457(3)	5.05
C(14A)	-230(4)	-1111(6)	6210(3)	5.48
C(15A)	-1476(5)	-2776(6)	5633(4)	6.89
C(16A)	-2474(7)	-2032(11)	5378(7)	14.12
C(17A)	-1524(8)	-3832(7)	5162(5)	9.39
C(18A)	524(5)	-1504(6)	3345(3)	5.93
C(19A)	3821(8)	-4361(8)	5518(5)	9.61
C(20A)	1479(7)	-1918(8)	7609(4)	8.66
C(21A)	5535(6)	-3213(8)	3728(3)	7.06
C(22A)	6510(7)	-2801(11)	3284(5)	10.74
O(1A)	1314(3)	-3422	3487(2)	5.12
O(2A)	849(4)	403(5)	6933(2)	6.76
O(3A)	4706(3)	-2380(5)	3776(2)	6.47
O(4A)	5460(5)	-4130(6)	4011(4)	9.74
Molecule 2				
C(1B)	1626(4)	-6012(5)	719(2)	4.51
C(2B)	1694(4)	-5628(5)	-87(3)	4.49
C(3B)	2622(4)	-5828(5)	-469(3)	4.21
C(4B)	2676(4)	-5601(5)	-1302(3)	4.72
C(5B)	3715(4)	-4799(6)	-1457(3)	5.31
C(6B)	4999(5)	-5204(5)	-1166(3)	5.32
C(7B)	5472(4)	-4786(5)	-402(3)	5.07
C(8B)	5921(4)	-5358(6)	206(3)	5.32
C(9B)	6394(4)	-4747(7)	922(4)	6.95
C(10B)	5601(5)	-4861(8)	1569(3)	7.81
C(11B)	4340(4)	-4393(6)	1337(3)	5.58
C(12B)	3383(4)	-4543(5)	1714(3)	4.88
C(13B)	2166(4)	-4092(5)	1362(3)	4.55
C(14B)	1227(4)	-5030(6)	1226(3)	5.03
C(15B)	769(5)	-7067(6)	741(3)	5.50
C(16B)	-515(5)	-6882(7)	368(4)	7.92
C(17B)	1318(6)	-8128(6)	404(4)	7.34
C(18B)	1499(5)	-5135(7)	-1701(3)	6.55
C(19B)	5963(6)	-6653(7)	249(4)	7.45
C(20B)	3390(6)	-5218(7)	2441(3)	7.76
C(21B)	6777(5)	-5217(7)	-1823(4)	6.53
C(22B)	7510(6)	-4488(8)	-2288(4)	8.54
O(1B)	2968(4)	-6672(5)	-1645(2)	6.70
O(2B)	1686(3)	-3241(4)	1848(2)	5.44
O(3B)	5771(4)	-4688(4)	-1690(2)	6.64
O(4B)	7052(5)	-6155(6)	-1591(3)	9.48
O(W)	8955(4)	-3242(5)	1751(2)	6.55

$$^a U_{\text{eq}} = \frac{1}{3} \sum_i \sum_j U_{ij} \cdot \mathbf{a}_i^* \cdot \mathbf{a}_j^* \cdot \mathbf{a}_i \cdot \mathbf{a}_j$$

Table 3. Bond lengths (\AA) in the acetate **6**.

Molecule 1		Molecule 2	
C(2A)-C(1A)	1.508(9)	C(2B)-C(1B)	1.506(9)
C(14A)-C(1A)	1.531(9)	C(14B)-C(1B)	1.554(8)
C(15A)-C(1A)	1.553(9)	C(15B)-C(1B)	1.562(9)
C(3A)-C(2A)	1.319(8)	C(3B)-C(2B)	1.321(8)
C(4A)-C(3A)	1.517(8)	C(4B)-C(3B)	1.506(8)
C(5A)-C(4A)	1.538(8)	C(5B)-C(4B)	1.538(9)
C(18A)-C(4A)	1.531(9)	C(18B)-C(4B)	1.514(9)
O(1A)-C(4A)	1.446(7)	O(1B)-C(4B)	1.445(7)
C(6A)-C(5A)	1.533(9)	C(6B)-C(5B)	1.535(9)
C(7A)-C(6A)	1.490(7)	C(7B)-C(6B)	1.476(8)
O(3A)-C(6A)	1.471(7)	O(3B)-C(6B)	1.467(7)
C(8A)-C(7A)	1.307(9)	C(8B)-C(7B)	1.314(9)
C(9A)-C(8A)	1.538(11)	C(9B)-C(8B)	1.496(9)
C(19A)-C(8A)	1.517(14)	C(19B)-C(8B)	1.515(11)
C(10A)-C(9A)	1.495(10)	C(10B)-C(9B)	1.531(11)
C(11A)-C(10A)	1.519(10)	C(11B)-C(10B)	1.517(10)
C(12A)-C(11A)	1.317(8)	C(12B)-C(11B)	1.333(8)
C(13A)-C(12A)	1.515(9)	C(13B)-C(12B)	1.517(9)
C(20A)-C(12A)	1.512(10)	C(20B)-C(12B)	1.510(10)
C(14A)-C(13A)	1.517(9)	C(14B)-C(13B)	1.513(9)
O(2A)-C(13A)	1.441(7)	O(2B)-C(13B)	1.456(7)
C(16A)-C(15A)	1.440(13)	C(16B)-C(15B)	1.517(10)
C(17A)-C(15A)	1.487(11)	C(17B)-C(15B)	1.533(10)
C(22A)-C(21A)	1.493(11)	C(22B)-C(21B)	1.493(11)
O(3A)-C(21A)	1.349(9)	O(3B)-C(21B)	1.322(8)
O(4A)-C(21A)	1.190(10)	O(4B)-C(21B)	1.197(10)

range except for C(16A)-C(15A) of 1.440(13) \AA and C(17A)-C(15A) of 1.487(11) \AA in molecule 1. These are shorter than C(16B)-C(15B) of 1.517(10) \AA and C(17B)-C(15B) of 1.533(10) \AA in molecule 2. This discrepancy is obviously due to the large thermal factors of the C(16A) and C(17A) atoms. There are six possible intramolecular hydrogen bonds and three intermolecular hydrogen bonds.

Experimental

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter, IR spectra on a Perkin-Elmer FT-IR 1725X spectrometer and part of the HPLC work was carried out using a Delta Prep 3000 solvent delivery system. For other instrumental details see Ref. 5.

Isolation. A chloroform extract of flowers of *Nicotiana tabacum* (Basma) was separated into five fractions, A (12.7 g), B (4.7 g), C (8.0 g), D (30 g), E (3.6 g), by flash chromatography (SiO_2 ; hexane-EtOAc-methanol). Fraction D was separated into eight fractions by flash chromatography over silica gel. Repeated HPLC of part of fraction D6 (7.5 g) using columns packed with Spherisorb 5 CN, Lichrosorb Diol and Spherisorb 5 gave 1.2 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*R*)-2,7,11-cembratriene-4,6,13-triol (**1**) and 4.9 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-2,7,11-cembratriene-4,6,20-triol (**2**).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*R*)-2,7,11-Cembratriene-4,6,13-triol (**1**) had m.p. 127–129°C; $[\alpha]_{\text{D}} + 136^\circ$ (*c* 0.20, CHCl_3) (Found: $[M-18]^+ \cdot 304.2399$. Calc. for $\text{C}_{20}\text{H}_{32}\text{O}_2$: 304.2431); IR (CHCl_3): 3695, 3602, 3439,

Table 4. Bond angles (deg) in the acetate 6.

Molecule 1		Molecule 2	
C(14A)–C(1A)–C(2A)	112.4(5)	C(14B)–C(1B)–C(2B)	112.2(5)
C(15A)–C(1A)–C(2A)	111.9(5)	C(15B)–C(1B)–C(2B)	111.0(5)
C(15A)–C(1A)–C(14A)	110.4(5)	C(15B)–C(1B)–C(14B)	110.6(5)
C(3A)–C(2A)–C(1A)	125.9(5)	C(3B)–C(2B)–C(1B)	124.3(5)
C(4A)–C(3A)–C(2A)	127.0(5)	C(4B)–C(3B)–C(2B)	126.5(5)
C(5A)–C(4A)–C(3A)	113.4(4)	C(5B)–C(4B)–C(3B)	113.6(5)
C(18A)–C(4A)–C(3A)	113.2(5)	C(18B)–C(4B)–C(3B)	112.9(5)
C(18A)–C(4A)–C(5A)	108.7(5)	C(18B)–C(4B)–C(5B)	108.9(5)
O(1A)–C(4A)–C(3A)	105.1(5)	O(1B)–C(4B)–C(3B)	107.3(5)
O(1A)–C(4A)–C(5A)	108.2(5)	O(1B)–C(4B)–C(5B)	104.0(5)
O(1A)–C(4A)–C(18A)	108.0(5)	O(1B)–C(4B)–C(18B)	109.9(5)
C(6A)–C(5A)–C(4A)	115.7(5)	C(6B)–C(5B)–C(4B)	116.2(5)
C(7A)–C(6A)–C(5A)	114.9(5)	C(7B)–C(6B)–C(5B)	115.0(5)
O(3A)–C(6A)–C(5A)	102.7(5)	O(3B)–C(6B)–C(5B)	104.6(5)
O(3A)–C(6A)–C(7A)	106.8(5)	O(3B)–C(6B)–C(7B)	105.9(5)
C(8A)–C(7A)–C(6A)	128.9(7)	C(8B)–C(7B)–C(6B)	130.0(6)
C(9A)–C(8A)–C(7A)	119.9(7)	C(9B)–C(8B)–C(7B)	120.9(6)
C(19A)–C(8A)–C(7A)	122.2(7)	C(19B)–C(8B)–C(7B)	123.7(6)
C(19A)–C(8A)–C(9A)	117.8(7)	C(19B)–C(8B)–C(9B)	115.3(6)
C(10A)–C(9A)–C(8A)	113.7(6)	C(10B)–C(9B)–C(8B)	114.6(6)
C(11A)–C(10A)–C(9A)	111.0(6)	C(11B)–C(10B)–C(9B)	111.2(6)
C(12A)–C(11A)–C(10A)	125.6(6)	C(12B)–C(11B)–C(10B)	125.8(6)
C(13A)–C(12A)–C(11A)	117.5(5)	C(13B)–C(12B)–C(11B)	118.4(6)
C(20A)–C(12A)–C(11A)	125.3(6)	C(20B)–C(12B)–C(11B)	124.9(6)
C(20A)–C(12A)–C(13A)	117.0(6)	C(20B)–C(12B)–C(13B)	116.5(6)
C(14A)–C(13A)–C(12A)	112.9(6)	C(14B)–C(13B)–C(12B)	112.3(5)
O(2A)–C(13A)–C(12A)	108.0(5)	O(2B)–C(13B)–C(12B)	111.5(5)
O(2A)–C(13A)–C(14A)	109.7(5)	O(2B)–C(13B)–C(14B)	107.1(5)
C(13A)–C(14A)–C(1A)	115.8(5)	C(13B)–C(14B)–C(1B)	112.8(5)
C(16A)–C(15A)–C(1A)	114.1(7)	C(16B)–C(15B)–C(1B)	115.0(6)
C(17A)–C(15A)–C(1A)	113.2(6)	C(17B)–C(15B)–C(1B)	110.8(5)
C(17A)–C(15A)–C(16A)	110.4(8)	C(17B)–C(15B)–C(16B)	110.1(6)
O(3A)–C(21A)–C(22A)	110.2(9)	O(3B)–C(21B)–C(22B)	111.1(7)
O(4A)–C(21A)–C(22A)	127.1(8)	O(4B)–C(21B)–C(22B)	125.2(7)
O(4A)–C(21A)–O(3A)	122.8(7)	O(4B)–C(21B)–O(3B)	123.7(7)
C(21A)–O(3A)–C(6A)	116.7(6)	C(21B)–O(3B)–C(6B)	119.4(6)

1378 and 1368 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3): δ 0.82 (d, J 6.5 Hz)/0.84 (d, J 6.3 Hz) (H-16/H-17), 1.39 (s, H-18), 1.53 (q, J 1.2 Hz, H-20), 1.68 (d, J 1.3 Hz, H-19), 1.83 (dd, J 8.7 and -14.3 Hz, H-5a), 2.03 (dd, J 1.4 and -14.3 Hz, H-5b), 3.88 (dd, J 5.0 and 11.2 Hz, H-13), 4.80 (ddd, J 1.4,

Table 5. Selected non-bonded distances (\AA) and possible hydrogen bonds in the acetate 6.

Intramolecular				
Molecule 1:	O(4A)–O(3A)	2.230		
Molecule 2:	O(4B)–O(3B)	2.222		
	C(3B)–C(1B)	2.501		
Intermolecular, molecule 1–molecule 2:				
	O(2B)–O(1A)	2.988		
Intermolecular: ^a				
	O(4B)–O(2B ⁱ)	2.875	O(2A)–O(1A ⁱⁱ)	2.793
	O(W)–O(2A ⁱⁱⁱ)	2.805	O(W)–O(2B ⁱⁱⁱⁱ)	3.022
	O(W)–O(1B ⁱⁱⁱⁱ)	2.807		

^a Key to symmetry operations relating designated atoms to reference atoms at (x, y, z): (i) $1.0 - x, -0.5 + y, -z$; (ii) $-x, 0.5 + y, 1.0 - z$; (iii) $1.0 - x, -0.5 + y, 1.0 - z$; (iiii) $1.0 + x, y, z$; (iiiiii) $1.0 - x, 0.5 + y, -z$.

8.7 and 9.9 Hz, H-6), 5.24 (m, H-11), 5.26 (dd, J 7.6 and 15.6 Hz, H-2), 5.27 (d, J 9.9 Hz, H-7) and 5.31 (d, J 15.6 Hz, H-3); MS [m/z (%): 304 (0.6, $M - 18$), 286 (1), 271 (0.7), 261 (1), 243 (3), 233 (1), 223 (1), 203 (3), 189 (3), 177 (3), 163 (8), 149 (7), 137 (12), 123 (20), 109 (21), 95 (29), 81 (50), 69 (31), 55 (53) and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-2,7,11-Cembratriene-4,6,20-triol (**2**) was obtained as an oil and had $[\alpha]_{\text{D}} + 105^\circ$ (c 0.92, CHCl_3); IR (CHCl_3): 3603, 3446, 1666, 1385 and 1369 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3): δ 0.80 (d, J 6.8 Hz)/0.83 (d, J 6.7 Hz) (H-16/H-17), 1.34 (s, H-18), 1.68 (d, J 1.3 Hz, H-19), 3.97 (d, $J - 11.9$ Hz, H-20a), 4.24 (d, $J - 11.9$ Hz, H-20b), 4.52 (ddd, J 4.4, 6.0 and 9.0 Hz, H-6), 5.26 (t, J 6.4 Hz, H-11), 5.34 (d, J 15.2 Hz, H-3), 5.37 (dq, J 1.3 and 9.0 Hz, H-7) and 5.40 (dd, J 8.0 and 15.2 Hz, H-2); MS [m/z (%): 304 (0.1, $M - 18$), 289 (0.3), 286 (0.8), 271 (0.6), 261 (0.8), 255 (0.7), 243 (3), 225 (1), 215 (2), 203 (2), 185 (3), 175 (3), 159 (8), 147 (8), 133 (10), 121 (15), 107 (17), 95 (24), 93 (24), 81 (39), 69 (30), 55 (41) and 43 (100).

Oxidation of (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*)-6-acetoxy-2,7,11-cembratrien-4-ol (**5**). A solution of 50 mg of SeO_2 and

Table 6. Experimental conditions for the crystal structure determination of the acetate **6**.

Formula	2(C ₂₂ H ₃₆ O ₄) · H ₂ O
Formula weight	746.06
Space group	P2 ₁
Unit cell dimensions	<i>a</i> = 11.1233(20) Å <i>b</i> = 11.6830(19) Å <i>c</i> = 17.7141(30) Å β = 96.79(1)°
Unit cell volume	2285.8(6) Å ³
Formula units per unit cell, Z	2
Calculated density, D _x	2.17 g cm ⁻³
Radiation	Cu K
Wavelength, λ	1.54184 Å
Linear absorption coefficient	11.18 cm ⁻¹
Temperature, T	293(1) K
Crystal shape	Prismatic
Crystal size	0.09 × 0.06 × 0.27 mm
Diffractometer	Simens/Stoe AED 2
Determination of unit cell	
Number of reflections used	25
θ-range	15.0–30.0°
Intensity data collection	
Maximum [sin(θ)/λ]	0.56 Å ⁻¹
Range of <i>h</i> , <i>k</i> and <i>l</i>	–12 to 12, 0 to 13 and 0 to 19
Standard reflections	3
Intensity instability	<1%
Number of collected reflections	4166
Number of observed reflections	3726
Number of unique reflections	3650
Internal R value	0.024
Criterion for significance	<i>F</i> > 3 · σ(<i>F</i>)
Structure refinement	
Minimization of	∑ <i>w</i> · Δ <i>F</i> ²
Anisotropic thermal parameters	All non-hydrogen atoms
Isotropic thermal parameters	Hydrogen atoms
Number of refined parameters	770
Weighting scheme	[σ ² (<i>F</i>) + 0.0020 <i>F</i> ²] ⁻¹
Final <i>R</i> for observed refls.	0.063
Final <i>w_R</i> for observed refls.	0.070
Final <i>w_R</i> for all 3650 refls.	0.072
Final (Δ/σ) _{max}	0.025
Final Δρ _{min} and Δρ _{max}	–0.27 and 0.51 e Å ⁻³

250 μl of *tert*-butyl hydroperoxide in 30 ml of CH₂Cl₂ was stirred at room temperature for 30 min. To the solution were added 340 mg of **3**. The reaction mixture was stirred at room temperature for 90 min, diluted with Et₂O, washed with aqueous KOH (10%), saturated aqueous FeSO₄, and water and dried. After removal of the solvent the residue was separated by flash chromatography (SiO₂; hexane–EtOAc 85 : 15) into five fractions, 1 (148 mg), 2 (12.1 mg), 3 (60.0 mg), 4 (53.2 mg) and 5 (4.8 mg). Fraction 1 consisted of starting material. Fractions 3 and 4 were separated further by HPLC (Lichrosorb 5 Diol; hexane–EtOAc 70 : 30), while fractions 2 and 5 were complex mixtures not examined further. Fraction 3 gave 40 mg of **7** and 9.8 mg of **8**, and fraction 4 gave 22 mg of **6** and 16 mg of **9**.

(1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*R*)-6-Acetoxy-2,7,11-cembra-triene-4,13-diol (**6**) had m.p. 70–72°C; [α]_D + 74° (*c* 1.4, CHCl₃); IR (CHCl₃): 3602, 3465, 1715, 1670, 1375, 1369 and 1256 cm⁻¹; ¹H NMR (CDCl₃): δ 0.83 (d, *J* 6.8

Hz)/0.85 (d, *J* 6.8 Hz) (H-16/H-17), 1.37 (s, H-18), 1.53 (br s, H-20), 1.72 (d, *J* 1.3 Hz, H-19), 1.91 (dd, *J* 8.2 and –14.7 Hz, H-5a), 2.04 (s, –OCOCH₃), 2.05 (dd, *J* 1.3 and –14.7 Hz, H-5b), 3.87 (dd, *J* 4.9 and 11.2 Hz, H-13), 5.20 (m, H-11), 5.26 (br d, *J* 10.1 Hz, H-7) 5.26 (dd, *J* 8.1 and 15.6 Hz, H-2), 5.32 (d, *J* 15.6 Hz, H-3) and 5.71 (ddd, *J* 1.3, 8.2, and 10.1 Hz, H-6); MS [*m/z* (%): 364 (0.1, *M*), 304 (2), 287 (16), 269 (9), 261 (2), 243 (11), 229 (4), 215 (4), 203 (5), 189 (12), 161 (24), 145 (12), 135 (10), 123 (13), 107 (17), 97 (20), 81 (40), 69 (23), 55 (40) and 43 (100).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*S*)-6-Acetoxy-2,7,11-cembra-triene-4,13-diol (**7**) has m.p. 90–92°C; [α]_D + 88° (*c* 0.85, CHCl₃); IR (CHCl₃): 3673, 3600, 3550, 1714, 1668, 1604, 1373 and 1254 cm⁻¹; ¹H NMR (CDCl₃): δ 0.82 (d, *J* 6.7 Hz)/0.84 (d, *J* 6.7 Hz) (H-16/H-17), 1.37 (s, H-18), 1.58 (br d, H-20), 1.75 (d, *J* 1.4 Hz, H-19), 1.91 (dd, *J* 8.6 and –14.5 Hz, H-5a), 2.03 (dd, *J* 1.5 and –14.5 Hz, H-5b), 2.04 (s, –OCOCH₃), 4.08 (m, H-13), 5.25 (br d, *J* 9.8 Hz, H-7), 5.26 (m, H-11), 5.40 (d, *J* 15.8 Hz, H-3), 5.46 (dd, *J* 7.5 and 15.8 Hz, H-2) and 5.75 (ddd, *J* 1.5, 8.6 and 9.8 Hz, H-6); MS [*m/z* (%): 304 (0.2, *M* – 60), 287 (0.7), 286 (0.9), 269 (0.4), 261 (0.3), 243 (2), 225 (0.7), 215 (1), 203 (1), 189 (2), 173 (1), 161 (8), 147 (5), 139 (7), 123 (10), 107 (12), 97 (21), 81 (43), 69 (18), 55 (46) and 43 (100).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*)-6-Acetoxy-2,7,11-cembra-triene-4,20-diol (**8**) had m.p. 123–125°C; [α]_D + 136° (*c* 0.45, CHCl₃); IR (CHCl₃): 3602, 3478, 1716, 1667, 1372 and 1256 cm⁻¹; ¹H NMR (CDCl₃): δ 0.80 (d, *J* 6.8 Hz)/0.84 (d, *J* 6.7 Hz) (H-16/H-17), 1.39 (s, H-18), 1.75 (d, *J* 1.1 Hz, H-19), 1.95 (dd, *J* 8.4 and –14.4 Hz, H-5a), 2.04 (s, –OCOCH₃), 2.06 (dd, *J* 1.5 and –14.4 Hz, H-5b), 3.99 (d, *J* –11.9 Hz, H-20a), 4.23 (d, *J* –11.9 Hz, H-20b), 5.20 (t, *J* 5.7 Hz, H-11), 5.23 (dd, *J* 8.8 and 15.6 Hz, H-2), 5.27 (dd, *J* 1.1 and 9.9 Hz, H-7), 5.39 (d, *J* 15.6 Hz, H-3), 5.76 (ddd, *J* 1.5, 8.4, and 9.9 Hz, H-6); MS [*m/z* (%): 304 (0.1, *M* – 60), 286 (1), 271 (0.5), 255 (0.9), 243 (2), 225 (1), 215 (1), 201 (1), 185 (3), 173 (2), 159 (5), 147 (8), 133 (9), 121 (8), 107 (13), 93 (17), 81 (29), 71 (21), 55 (24) and 43 (100).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*,13ξ)-6-Acetoxy-2,7,11-cembra-triene-4,13-diol (**9**) had m.p. 127–129°C; [α]_D + 52° (*c* 0.48, CHCl₃); IR (CHCl₃): 3599, 3467, 1716, 1665, 1372 and 1256 cm⁻¹; ¹H NMR (CDCl₃): δ 0.85 (d, *J* 6.8 Hz)/0.86 (d, *J* 6.8 Hz) (H-16/H-17), 1.32 (s, H-18), 1.65 (d, *J* 1.5 Hz, H-20), 1.74 (d, *J* 1.4 Hz, H-19), 1.98 (dd, *J* 6.9 and –14.6 Hz, H-5a), 2.02 (dd, *J* 3.3 and –14.6 Hz, H-5b), 2.03 (s, –OCOCH₃), 4.43 (t, *J* 7.0 Hz, H-13), 5.19 (m, H-11), 5.22 (br d, *J* 9.8 Hz, H-7), 5.38 (dd, *J* 7.3 and 15.9 Hz, H-2), 5.45 (d, *J* 15.9 Hz, H-3) and 5.58 (ddd, *J* 3.3, 6.9 and 9.8 Hz, H-6); MS [*m/z* (%): 304 (0.8, *M* – 60), 287 (8), 269 (3), 258 (2), 243 (4), 225 (1), 215 (2), 203 (2), 189 (3), 161 (12), 147 (6), 139 (7), 123 (8), 107 (10), 97 (14), 81 (29), 69 (14), 55 (25) and 43 (100).

Hydrolysis of (1S,2E,4R,6R,7E,11E,13R)-6-acetoxy-2,7,11-cembra-triene-4,13-diol (6). To a solution of 6.8 mg

of **6** in 2 ml of methanol were added 5 drops of aqueous KOH (10%). After 4 h at room temperature, the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 4.2 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*R*)-2,7,11-cembratriene-4,6,13-triol, whose m.p., optical rotation, IR, ¹H NMR and mass spectra were identical with those of the naturally occurring triol **1**.

Hydrolysis of (1S,2E,4R,6R,7E,11E,13S)-6-acetoxy-2,7,11-cebratriene-4,13-diol (7). To a solution of 4.5 mg of **7** in 1 ml of methanol were added 3 drops of aqueous KOH (10%). After 4 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 2.1 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*,13*S*)-2,7,11-cebratriene-4,6,13-triol (**10**), which had m.p. 49–51°C; $[\alpha]_D + 86.5^\circ$ (*c* 1.00, CHCl₃); IR (CHCl₃): 3674, 3602, 3548, 3437, 1379 and 1360 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* 6.7 Hz)/0.83 (d, *J* 6.3 Hz) (H-16/H-17), 1.39 (s, H-18), 1.59 (d, *J* 0.8 Hz, H-20), 1.74 (d, *J* 1.3 Hz, H-19), 1.81 (dd, *J* 9.6 and -14.0 Hz, H-5a), 2.05 (dd, *J* 1.7 and -14.0 Hz, H-5b), 4.03 (m, H-13), 4.81 (ddd, *J* 1.7, 9.3 and 9.6 Hz, H-6), 5.25 (d, *J* 9.3 Hz, H-7), 5.29 (m, H-11), 5.40 (d, *J* 15.8 Hz, H-3) and 5.43 (dd, *J* 8.5 and 15.8 Hz, H-2); MS [*m/z* (%)]: 304 (0.3, *M* - 18), 286 (0.8), 271 (0.4), 261 (1), 243 (2), 233 (0.9), 215 (1), 203 (2), 189 (2), 177 (2), 163 (6), 149 (5), 137 (9), 123 (17), 109 (17), 97 (23), 81 (52), 69 (28), 55 (57) and 43 (100).

Hydrolysis of (1S,2E,4R,6R,7E,11Z)-6-acetoxy-2,7,11-cebratriene-4,20-diol (8). To a solution of 6.1 mg of **8** in 1 ml of methanol were added 3 drops of aqueous KOH (10%). After 3 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 3.8 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*)-2,7,11-cebratriene-4,6,20-triol (**11**), which had m.p. 57–58°C; $[\alpha]_D + 153^\circ$ (*c* 0.16, CHCl₃); IR (CHCl₃): 3676, 3604, 3437, 1667, 1385 and 1369 cm⁻¹; ¹H NMR (CDCl₃): δ 0.80 (d, *J* 6.8 Hz)/0.83 (d, *J* 6.8 Hz) (H-16)/(H-17), 1.41 (s, H-18), 1.72 (d, *J* 1.3 Hz, H-19), 1.86 (dd, *J* 9.1 and -14.1 Hz, H-5a), 2.06 (dd, *J* 1.6 and -14.6 Hz, H-5b), 4.00 (d, *J* -11.8 Hz, H-20a), 4.23 (d, *J* -11.8 Hz, H-20b), 4.82 (ddd, *J* 1.6, 9.1 and 9.4 Hz, H-6), 5.24 (dd, *J* 8.8 and 15.6 Hz, H-2), 5.24 (br t, *J* 6.0 Hz, H-11), 5.27 (d quintets, *J* 9.4 Hz, H-7) and 5.39 (d, *J* 15.6 Hz, H-3); MS [*m/z* (%)]: 304 (0.3, *M* - 18), 289 (0.3), 286 (3), 268 (1), 255 (2), 243 (4), 225 (3), 215 (3), 203 (3), 185 (4), 173 (5), 159 (15), 145 (15), 133 (17), 121 (20), 105 (32), 91 (40), 81 (45), 69 (38), 55 (51) and 43 (100).

Hydrolysis of (1S,2E,4R,6R,7E,11Z,13ξ)-6-acetoxy-2,7,11-cebratriene-4,13-diol (9). To a solution of 7.0 mg of **9** in 2 ml of methanol were added 5 drops of aqueous KOH (10%). After 4 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 5.4 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*Z*,13ξ)-2,7,11-cebratriene-4,6,13-triol (**12**), which had m.p. 122–124°C; $[\alpha]_D + 62^\circ$ (*c* 0.33,

CHCl₃); IR (CHCl₃): 3673, 3600, 3446, 1665, 1383 and 1370 cm⁻¹; ¹H NMR (CDCl₃): δ 0.85 (d, *J* 6.8 Hz)/0.86 (d, *J* 6.8 Hz) (H-16/H-17), 1.34 (s, H-18), 1.66 (t, *J* 1.1 Hz, H-20), 1.72 (d, *J* 1.4 Hz, H-19), 1.96 (dd, *J* 8.0 and -14.2 Hz, H-5a), 2.04 (dd, *J* 3.2 and -14.2 Hz, H-5b), 4.47 (dd, *J* 5.9 and 7.6 Hz, H-13), 4.66 (ddd, *J* 3.2, 8.0 and 9.5 Hz, H-6), 5.23 (m, H-11), 5.26 (br d, *J* 9.5 Hz, H-7), 5.37 (dd, *J* 8.0 and 16.0 Hz, H-2) and 5.48 (d, *J* 16.0 Hz, H-3); MS [*m/z* (%)]: 304 (0.1, *M* - 18), 286 (0.8), 271 (0.4), 261 (0.6), 243 (2), 225 (1), 215 (1), 203 (1), 189 (3), 177 (2), 161 (10), 145 (8), 135 (8), 123 (18), 107 (20), 93 (25), 81 (55), 69 (26), 55 (61) and 43 (100).

Oxidation of (1S,2E,4S,6R,7E,11E)-6-acetoxy-2,7,11-cebratriene-4-ol (13). A solution of 150 mg of SeO₂ and 700 μl of *tert*-butyl hydroperoxide in 60 ml of CH₂Cl₂ was stirred at room temperature for 30 min. To the solution were added 1.05 g of **13**. The reaction mixture was stirred at room temperature for 35 min, diluted with Et₂O, washed with aqueous KOH (10%), saturated aqueous FeSO₄ and water, and dried. After removal of the solvent the residue was separated by flash chromatography (SiO₂; hexane-EtOAc gradient) into six fractions, 1 (71 mg), 2 (84 mg), 3 (38 mg), 4 (85 mg), 5 (27 mg) and 6 (77 mg). Fraction 2 consisted of starting material, fraction 1 of **17** and fraction 5 of **15**. Fraction 4 was separated further by HPLC (Spherisorb 5; hexane-EtOAc 60 : 40) to give 51 mg of **14** and 45 mg of **16**. Fractions 3 and 6 were complex mixtures not examined further.

(1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-6-Acetoxy-2,7,11-cebratriene-4,20-diol (**14**) had m.p. 41–43°C; $[\alpha]_D + 113^\circ$ (*c* 1.44, CHCl₃); IR (CHCl₃): 3600, 3454, 1725, 1670, 1385, 1371 and 1251 cm⁻¹; ¹H NMR (CDCl₃): δ 0.80 (d, *J* 6.8 Hz)/0.83 (d, *J* 6.8 Hz) (H-16/H-17), 1.39 (s, H-18), 1.73 (d, *J* 1.2 Hz, H-19), 2.03 (s, -OCOCH₃), 4.00 (d, *J* -11.8 Hz, H-20a), 4.24 (d, *J* -11.8 Hz, H-20b), 5.23 (d, *J* 8.4 Hz, H-7), 5.24 (t, *J* 6.3 Hz, H-11), 5.31 (d, *J* 15.4 Hz, H-3), 5.35 (d, *J* 8.1 and 15.4 Hz, H-2) and 5.54 (ddd, *J* 3.1, 8.4 and 9.8 Hz, H-6); MS [*m/z* (%)]: 346 (0.1, *M* - 18), 304 (0.2), 286 (2), 271 (0.6), 255 (1), 243 (3), 225 (1), 215 (1), 201 (1), 185 (3), 173 (3), 159 (6), 147 (7), 133 (9), 119 (9), 107 (13), 93 (17), 81 (28), 71 (20), 55 (23) and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,11*E*,13*R*)-6-Acetoxy-2,7,11-cebratriene-4,13-diol (**15**) had m.p. 60–62°C; $[\alpha]_D + 117^\circ$ (*c* 0.945, CHCl₃); IR (CHCl₃): 3666, 3602, 3451, 1726, 1669, 1384, 1372 and 1251 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* 6.8 Hz)/0.84 (d, *J* 6.7 Hz) (H-16/H-17), 1.38 (s, H-18), 1.54 (quintet, *J* 1.3, H-20), 1.71 (d, *J* 1.3 Hz, H-19), 1.95 (dd, *J* 8.6 and -13.4 Hz, H-5a), 2.01 (dd, *J* 2.2 and -13.4 Hz, H-5b), 2.03 (s, -OCOCH₃), 3.95 (dd, *J* 5.1 and 11.0 Hz, H-13), 5.22 (d, *J* 15.3 Hz, H-3), 5.23 (dq, *J* 1.3 and 9.8 Hz, H-7), 5.26 (m, H-11), 5.36 (dd, *J* 9.3 and 15.3 Hz, H-2) and 5.49 (ddd, *J* 2.2, 8.6 and 9.8 Hz, H-6); MS [*m/z* (%)]: 304 (0.1, *M* - 60), 287 (0.6), 286 (1), 268 (0.6), 261 (0.3), 243 (2), 225 (1), 215 (1), 203 (1), 189 (3), 173 (1), 161 (6), 145 (5), 139 (5), 123 (8), 107 (9), 97 (19), 81 (35), 69 (15), 55 (34) and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,11*E*,13*S*)-6-Acetoxy-2,7,11-cembratriene-4,13-diol (**16**) had m.p. 135–137°C; $[\alpha]_D + 79^\circ$ (*c* 0.54, CHCl₃); IR (CHCl₃): 3598, 3540, 1725, 1670, 1384, 1371 and 1250 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* 6.8 Hz)/0.83 (d, *J* 6.7 Hz) (H-16/H-17), 1.35 (s, H-18), 1.60 (d, *J* 1.0 Hz, H-20), 1.75 (d, *J* 1.2 Hz, H-19), 1.95 (dd, *J* 8.9 and -13.2 Hz, H-5a), 2.00 (dd, *J* 3.3 and -13.2 Hz, H-5b), 2.03 (s, -OCOCH₃), 4.05 (br q, *J* 5.2 Hz, H-13), 5.21 (dq, *J* 1.2 and 9.7 Hz, H-7), 5.29 (t, *J* 6.5 Hz, H-11), 5.34 (d, *J* 15.4 Hz, H-3), 5.57 (ddd, *J* 3.3, 8.9 and 9.7 Hz, H-6) and 5.59 (dd, *J* 8.5 and 15.4 Hz, H-2); MS [*m/z* (%)]: 304 (0.2, *M* - 60), 287 (0.6) 286 (2), 271 (0.5), 261 (0.3), 243 (2), 225 (0.7), 215 (1), 203 (2), 187 (2), 175 (1), 161 (5), 147 (5), 135 (5), 123 (8), 107 (10), 97 (19), 81 (37), 69 (14), 55 (36) and 43 (100).

(1*S*,2*R*,3*E*,6*R*,7*E*,11*E*,13*S*)-6-Acetoxy-2,13-epoxy-3,7,11-cembratriene (**17**) had m.p. 73–75°C; $[\alpha]_D + 104^\circ$ (*c* 0.70, CHCl₃); IR (CHCl₃): 1723, 1667, 1370 and 1252 cm⁻¹; ¹H NMR (CDCl₃): δ 0.86 (d, *J* 6.2 Hz)/0.90 (d, *J* 6.2 Hz) (H-16/H-17), 1.50 (quintet, *J* 1.0 Hz, H-20), 1.66 (d, *J* 1.3 Hz, H-19), 1.76 (dt, *J* 0.6 and 1.3 Hz, H-18), 1.84 (m, H-14a), 1.94 (m, H-14b), 2.05 (s, -OCOCH₃), 2.26 (dd, *J* 9.1 and -16.3 Hz, H-5a), 2.39 (dd, *J* 4.1 and -16.3 Hz, H-5b), 4.41 (br d, *J* 6.3 Hz, H-13), 4.52 (dd, *J* 5.2 and 8.9 Hz, H-2), 4.99 (dq, *J* 1.5 and 8.9 Hz, H-3), 5.23 (d quintets, *J* 1.3 and 9.1 Hz, H-7), 5.52 (m, H-11) and 5.71 (dt, *J* 4.1 and 9.1 Hz, H-6); MS [*m/z* (%)]: 286 (5, *M* - 60), 271 (2), 253 (1), 243 (4), 225 (2), 215 (4), 203 (4), 187 (7), 175 (7), 159 (15), 145 (16), 133 (15), 121 (22), 105 (32), 93 (41), 81 (100), 69 (26), 55 (71) and 43 (99).

Hydrolysis of (1S,2E,4S,6R,7E,11Z)-6-acetoxy-2,7,11-cembratriene-4,20-diol (14). To a solution of 16 mg of **14** in 2 ml of ethanol were added 4 drops of aqueous KOH (10%). After 4 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 9.2 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*Z*)-2,7,11-cembratriene-4,6,20-triol, whose optical rotation, IR, ¹H NMR and mass spectra were identical with those of the naturally occurring triol **2**.

Hydrolysis of (1S,2E,4S,6R,7E,11E,13R)-6-acetoxy-2,7,11-cembratriene-4,13-diol (15). To a solution of 9.2 mg of **15** in 2 ml of methanol were added 5 drops of aqueous KOH (10%). After 2 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 6.1 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*,13*R*)-2,7,11-cembratriene-4,6,13-triol (**18**), which had m.p. 155–157°C; $[\alpha]_D + 116^\circ$ (*c* 0.68, CHCl₃); IR (CHCl₃): 3602, 3439, 1667, 1384 and 1368 cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (d, *J* 6.8 Hz)/0.84 (d, *J* 6.7 Hz) (H-16/H-17), 1.36 (s, H-18), 1.54 (dt, *J* 1.2 and 1.3 Hz, H-20), 1.66 (d, *J* 1.4 Hz, H-19), 1.93 (dd, *J* 8.6 and -13.3 Hz, H-5a), 2.03 (dd, 1.9 and -13.3 Hz, H-5b), 3.97 (ddd, *J* 2.9, 5.3 and 10.8 Hz, H-13), 4.44 (dddd, *J* 1.9, 2.8, 8.6 and 9.3 Hz, H-6), 5.21 (d, *J* 15.3 Hz, H-3), 5.29 (br t, *J* 4.8 Hz, H-11), 5.33 (br d, *J* 9.3 Hz, H-7)

and 5.37 (dd, *J* 9.3 and 15.3 Hz, H-2); MS [*m/z* (%)]: 289 (0.1, *M* - 33), 286 (0.4), 271 (0.3), 261 (0.7), 243 (1), 220 (1), 203 (1), 189 (2), 177 (2), 161 (4), 147 (5), 137 (9), 124 (24), 109 (17), 97 (23), 81 (49), 69 (44), 55 (55) and 43 (100).

Hydrolysis of (1S,2E,4S,6R,7E,11E,13S)-6-acetoxy-2,7,11-cembratriene-4,13-diol (16). To a solution of 5.0 mg of **16** in 2 ml of methanol were added 4 drops of aqueous KOH (10%). After 3 h at room temperature the reaction mixture was worked up and purified by HPLC (Spherisorb 5; hexane-EtOAc 30 : 70) to give 2.7 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*,13*S*)-2,7,11-cembratriene-4,6,13-triol (**19**), which had m.p. 47–49°C; $[\alpha]_D + 38^\circ$ (*c* 0.08, CHCl₃); IR (CHCl₃): 3601, 3465, 1669, 1384 and 1370 cm⁻¹; ¹H NMR (CDCl₃): δ 0.82 (d, *J* 6.8 Hz)/0.83 (d, *J* 6.8 Hz) (H-16/H-17), 1.30 (s, H-18), 1.62 (d, *J* 0.7 Hz, H-20), 1.70 (d, *J* 1.3 Hz, H-19), 2.17 (s, -OH), 4.01 (br s, H-13), 4.54 (dt, *J* 5.6 and 9.0 Hz, H-6), 5.30 (overlapping signals, *J* 8.9 Hz, H-7 and H-11), 5.37 (d, *J* 15.4 Hz, H-3) and 5.57 (dd, *J* 8.2 and 15.4 Hz, H-2); MS [*m/z* (%)]: 304 (0.4, *M* - 18), 289 (0.4), 286 (3), 268 (1), 243 (4), 222 (3), 215 (3), 187 (4), 175 (4), 161 (13), 145 (15), 137 (13), 124 (32), 109 (25), 95 (34), 81 (84), 69 (32), 55 (71) and 43 (100).

Hydrolysis of (1S,2R,3E,6R,7E,11E,13S)-6-acetoxy-2,13-epoxy-3,7,11-cembratriene (17). A solution of 12 mg of **17** in 2 ml of methanol and 5 drops of aqueous KOH (10%) was kept at room temperature for 2 h. Work-up and purification by HPLC (Spherisorb 5; hexane-EtOAc 1 : 1) gave 6.6 mg of (1*S*,2*R*,3*E*,6*R*,7*E*,11*E*,13*S*)-2,13-epoxy-3,7,11-cembratrien-6-ol (**20**), which had m.p. 79–81°C; $[\alpha]_D + 86^\circ$ (*c* 0.28, CHCl₃); IR (CHCl₃): 3674, 3604, 1665, 1386 and 1369 cm⁻¹; ¹H NMR (CDCl₃): δ 0.85 (d, *J* 6.4 Hz)/0.90 (d, *J* 6.4 Hz) (H-16/H-17), 1.32 (d, *J* 3.2 Hz, -OH), 1.50 (quintet, *J* 1.1 Hz, H-20), 1.64 (dd, *J* 0.5 and 1.2 Hz, H-19), 1.76 (dt, *J* 0.7 and 1.4 Hz, H-18), 1.84 (ddd, *J* 7.9, 7.9 and -12.4 Hz, H-14a), 1.94 (ddd, *J* 3.4, 6.9 and -12.4 Hz, H-14b), 2.44 (ddd, *J* 0.7, 3.2 and -16.6 Hz, H-5b), 4.40 (broad signal, H-13), 4.52 (dd, *J* 5.6 and 9.1 Hz, H-2), 4.57 (tt, *J* 3.2 and 8.9 Hz, H-6), 4.94 (d sextets, *J* 1.4 and 9.1 Hz, H-3), 5.29 (d quintets, *J* 1.2 and 8.9 Hz, H-7) and 5.51 (broad signal, H-11); MS [*m/z* (%)]: 304 (0.5, *M*), 289 (0.2), 286 (1), 261 (1), 243 (2), 220 (5), 203 (3), 187 (3), 177 (4), 159 (10), 149 (7), 137 (10), 124 (66), 109 (31), 95 (45), 81 (92), 69 (33), 55 (98), 43 (75) and 41 (100).

Treatment of (1S,2E,4S,6R,7E,11E,13S)-2,7,11-cembratriene-4,6,13-triol (19) with acid. A solution of 4.4 mg of **19** in 5 ml of CHCl₃ and 0.2 ml of HCl (10%) was kept at room temperature for 24 h. Work up and separation by HPLC (Spherisorb 5; hexane-EtOAc 1 : 1) gave 2.1 mg of a product which was identical with (1*S*,2*R*,3*E*,6*R*,7*E*,11*E*,13*S*)-2,13-epoxy-3,7,11-cembratrien-6-ol (**20**).

X-Ray crystallography study. Single crystals of **6** were obtained by recrystallization from a mixture of hexane and EtOAc. The space group symmetry was determined as $P2_1$ or $P2_1/m$ from systematic extinctions and from the unit cell parameters found by the least-squares method from 25 centred X-ray reflections. The intensities for three standard reflections (1 2 0, 0 4 0 and 1 3 4) were monitored every 60 min; the total deterioration of intensity was < 1%. Lorentz and polarization corrections were applied but no correction was made for absorption.

In all, 41 of the 53 non-hydrogen atoms were found by direct methods using the SHELXS86 program.⁶ The remaining non-hydrogen atoms and all but one of the hydroxy hydrogen atoms were located from difference electron density maps. All non-hydroxy hydrogen atoms were geometrically placed with a distance of 1.08 Å to the adjacent atom before each cycle and then refined. The structure was refined by the full-matrix least-squares technique using the SHELX76 program.⁷ Anisotropic temperature factors were introduced for all non-hydrogen atoms, while all hydrogen atoms were refined with all isotropic thermal factors constrained to a common value of 0.05 Å². The atomic scattering factors⁸ used for the non-hydrogen and hydrogen atoms were those included in the SHELX76 program. The final agreement factor

became $R=0.063$, $w_R=0.070$ and $w_R=0.072$ for all 3650 reflections using the weighting scheme $w = [\sigma^2(F) + gF^2]^{-1}$ with $g = 0.0020$.

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