Acta Chemica Scandinavica B 38 (1984) 21–30

Tobacco Chemistry. 59.* Six New Cembratrienetriols from Tobacco

INGER WAHLBERG, ROLF ARNDT, INGRID WALLIN, CARMEN VOGT, TOSHIAKI NISHIDA and CURT R. ENZELL

Research Department, Swedish Tobacco Company, P.O.Box 17007, S-104 62 Stockholm, Sweden

Six new cembratrienetriols have been isolated from Greek tobacco. They have been identified as the (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)- and (1*S*,2*E*,4*S*,-6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triols (*1*,*2*), the (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,-4*R*,6*R*,7*E*,10*E*,12*R*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,-10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triols (*3*–*5*) and (1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-2,6,12(20)-cembratriene-4,8,11-triol (*6*) by spectral and chemical methods. The biogeneses of these compounds are discussed in the light of results obtained from biomimetic reactions involving sensitized photooxygenation of 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 (*7*, *8*) and of (1*S*,2*E*,4*R*,6*E*,8*S*,11*E*)-cembratriene-4,8-diol (*9*). A discussion on the conformation about the 5,6-bond in various cembrane alcohols and acetates is also presented.

We have previously reported the isolation of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*10*) and (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol (*11*) from Greek tobacco and have suggested, on the basis of results obtained from biomimetic experiments, that these, as well as most other tobacco cembranoids, arise by biotransformations of the abundant (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 (*7*,*8*).[2,3] The present communication deals with the isolation of six additional cembratrienetriols from a flower extract of Greek tobacco and their syntheses *via* singlet oxygen reactions.

* For part 58 see Ref. 1.

0302-4369/84 $2.50

RESULTS

Structure determination of triols 1–5. Triols *1* and *2*, $C_{20}H_{34}O_3$, gave rise to ^1H and ^{13}C NMR spectra reminiscent of those of (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*10*) and indicative of the presence of an isopropyl group, a methyl group attached to a carbon atom carrying a tertiary hydroxyl group, a vinylic methyl group and two secondary hydroxyl groups. Of the three double bonds, one extends to an exocyclic methylene group, one is *E*-disubstituted and one is trisubstituted. Triols *1* and *2* were hence tentatively identified as 2*E*,7,12(20)-cembratriene-4,6,11-triols.

In contrast to triols *1* and *2*, triols *3*–*5* ($C_{20}H_{34}O_3$) contain one secondary and two tertiary hydroxyl groups, two *E*-disubstituted and one trisubstituted double bond. These results and a spectral comparison with (1*S*,2*E*,4*S*,6*R*,7*E*,-10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol (*11*) led to a provisional formulation of triols *3*–*5* as stereoisomers of 2*E*,7,10*E*-cembratriene-4,6,12-triol.

The tentative structural assignments of triols *1*, *3* and *5* were verified and their stereochemistries determined by simple chemical correlations. Thus, rearrangement of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*,12*S*)-11,12-epoxy-2,7-cembradiene-4,6-diol (*12*)[4] using Sharpless' method[5] afforded (1*S*,2*E*,-4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol as the major and (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol as the minor product. These proved to be identical to triols *3* and *1*, respectively. Structural evidence for triol *1* was also provided by its cyclization to (1*S*,-

Table 1. ^{13}C NMR chemical shifts and assignments for compounds *1–8, 10, 11, 15, 16, 18–23.*[a]

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
1	47.6	129.7[b]	137.1	72.1	51.8	64.7	129.6[b]	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
16	46.9	128.1	138.6	72.0	51.9	64.5	130.0	139.8	33.3[b]	33.1[b]	73.4	154.6	32.9[b]	29.1	32.5	19.0	20.6	31.4	18.3	108.7
3	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
4	48.0	129.2[b]	137.4	71.8	52.1	64.9	129.1[b]	138.8	41.6	125.9	136.9	74.0	39.8	27.5	29.3	17.6	21.4	30.3	18.0	27.3
10	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
2	47.3	128.6	140.8	74.0	47.1	69.1	126.3	136.2	34.1	33.1	73.2	154.8	32.8	29.7	33.0	19.0	20.9	33.3	17.8	107.9
11	50.8	127.3	138.3	74.3[b]	47.2	69.4	128.4	134.5	40.7	124.6	138.9	74.0[b]	40.1	26.5	30.1	17.8	21.8	31.6	18.0	30.0
5	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
6	49.5	131.1	137.5	73.0[b]	46.2	123.8	139.2	73.3[b]	29.6[c]	28.9[c]	74.2	150.8	36.8	28.6[c]	32.3	19.6	20.4	26.3	29.3	110.3
7	46.3	130.5	136.1	71.7	52.7	64.5	131.3	136.5	38.9	23.1	124.5	133.0	36.5	27.7	33.0	19.4	20.5	28.7	15.9	15.0
8	46.5	127.7	137.7	72.5	52.5	66.2	131.0	135.9	38.9	23.4	124.6	133.2	36.9	28.1	33.1	19.4	20.7	30.1	16.1	15.0
18[d]	46.8	128.6	136.9	71.1	50.4	68.3	130.6	138.5	35.9[c]	25.1	60.8	59.3	36.9[c]	28.0	33.3	19.0	20.4	28.5	16.6[b]	16.2[b]
20[e]	49.1	129.1	136.9	71.7	49.8	68.7	125.0	141.0	41.0	124.5	138.0	73.7	39.9	25.6	29.7	17.7	21.5	30.3	18.3	29.8
23[f]	46.1	130.1	136.3	70.9	50.9	68.5	127.1	139.0	38.8	23.1	124.2	133.1	36.5	27.6	33.1	19.3	20.5	28.3	16.0	14.9
19[g]	48.2	129.5	138.3	72.0	47.8	69.5	124.4	140.2	30.4	30.4	75.5	147.7	34.5	30.1	31.9	19.2	20.7	30.4	16.8	112.2
21[h]	48.3	130.0	137.8	72.1	48.1	69.5	124.4	140.9	30.9	32.0	72.9	152.1	34.9	29.9	31.9	19.2	20.7	30.7	16.6	110.5
22[i]	49.5	128.0	138.0[b]	72.0	48.6	69.8	124.1	139.7	40.9	124.3	138.5[b]	73.7	40.1	26.1	30.2	18.0	21.4	29.7[c]	18.3	29.4[c]
15[k]	46.3	127.8	137.1	72.3	50.7	68.8	126.6	139.2	38.8	23.1	124.3	133.4	36.6	27.8	32.9	19.4	20.7	29.6	16.1	14.8

[a] δ-values in $CDCl_3$ relative to TMS. [b,c] Assignment may be reversed. [d] $OCOCH_3$ 170.8: $OCOCH_3$ 21.5. [e] $OCOCH_3$ 170.6; $OCOCH_3$ 21.4. [f] $OCOCH_3$ 170.7; $OCOCH_3$ 21.4. [g] $OCOCH_3$ 170.4 and 169.8; $OCOCH_3$ 21.4 and 21.3. [h] $OCOCH_3$ 170.0; $OCOCH_3$ 21.4. [i] $OCOCH_3$ 169.9; $OCOCH_3$ 21.4. [k] $OCOCH_3$ 170.2; $OCOCH_3$ 21.4.

2*E*,4*R*,6*E*,8*R*,11*S*)-8,11-epoxy-2,6,12(20)-cembratrien-4-ol (*13*)[6] on treatment with weak acid (*vide infra*). Triol *5* was correlated *via* its monoacetate to (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-6-acetoxy-2,7,10-cembratriene-4,12-diol (*14*), a compound which has previously been obtained as a minor product by sensitized photo-oxygenation and subsequent reduction of monoacetate *15*.[2]

With the structures of triols *1*, *3* and *5* at hand, ^{13}C NMR results were utilized to determine the relative stereochemistries of triols *2* and *4*. Thus, a comparison of the shieldings of C-2 to C-7 and C-18 in triol *2* with those of the corresponding carbon atoms in the 4*R*,6*R*,11*S*- and 4*S*,6*R*,11*S*-triols *1* and *10* (*cf.* Table 1) allowed the assignment of a 1*S*,2*E*,4*S*,6*R*,7*E*-stereochemistry to triol *2*. The configuration at the remaining asymmetric centre in triol *2*, C-11, was deduced to be *R* from the chemical shift values of the C-12, C-19 and C-20 signals, which were significantly different from those of the corresponding signals for the 11*S*-triols *1* and *10*.

By analogy, the formulation of triol *4* as (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triol was based on a comparison of the shieldings of C-2 to C-7, C-18 and C-19 and of C-10, C-14 and C-20 with those of the corresponding carbon atoms in the 4*R*,6*R*,12*S*-, 4*S*,6*R*,12*R*- and 4*S*,6*R*,12*S*-triols *3*, *5* and *11*.

Confirmatory structural evidence was provided by biomimetic syntheses involving sensitized photo-oxygenation of the 4*R*,6*R*- and 4*S*,6*R*-diols *7* and *8*. Both the 7,8 and 11,12 double bonds in these diols are susceptible to attachment of singlet oxygen. The 7,8 double bond is, however, considerably less reactive than the 11,12 double bond due to the deactivating effect of the hydroxyl group at C-6. It is therefore possible to control the degree of oxidation and, after reduction, isolate the desired 4,6,11- and 4,6,12-triols.

Of the triols thus obtained from the 4*R*,6*R*-diol (*7*), (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol, the (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,-12*S*)- and (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triols were indistinguishable from triols *1*, *3* and *4*, respectively. The fourth triol, (1*S*,2*E*,4*R*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triol (*16*), as yet not found in tobacco, exhibited the signals due to C-12, C-19 and C-20 at δ 154.6, 18.3 and 108.7, chemical shift values that are diagnostic of the 11*R*-configuration (*cf.* Table 1).

By analogy, the 4*S*,6*R*-diol (*8*) gave rise to (1*S*,2*E*,4*S*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*10*), the (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*)-2,7,10-cembratriene-4,6,12-triols (*11*,*5*) as well as (1*S*,2*E*,4*S*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triol, which was identical in all respects to triol *2*.

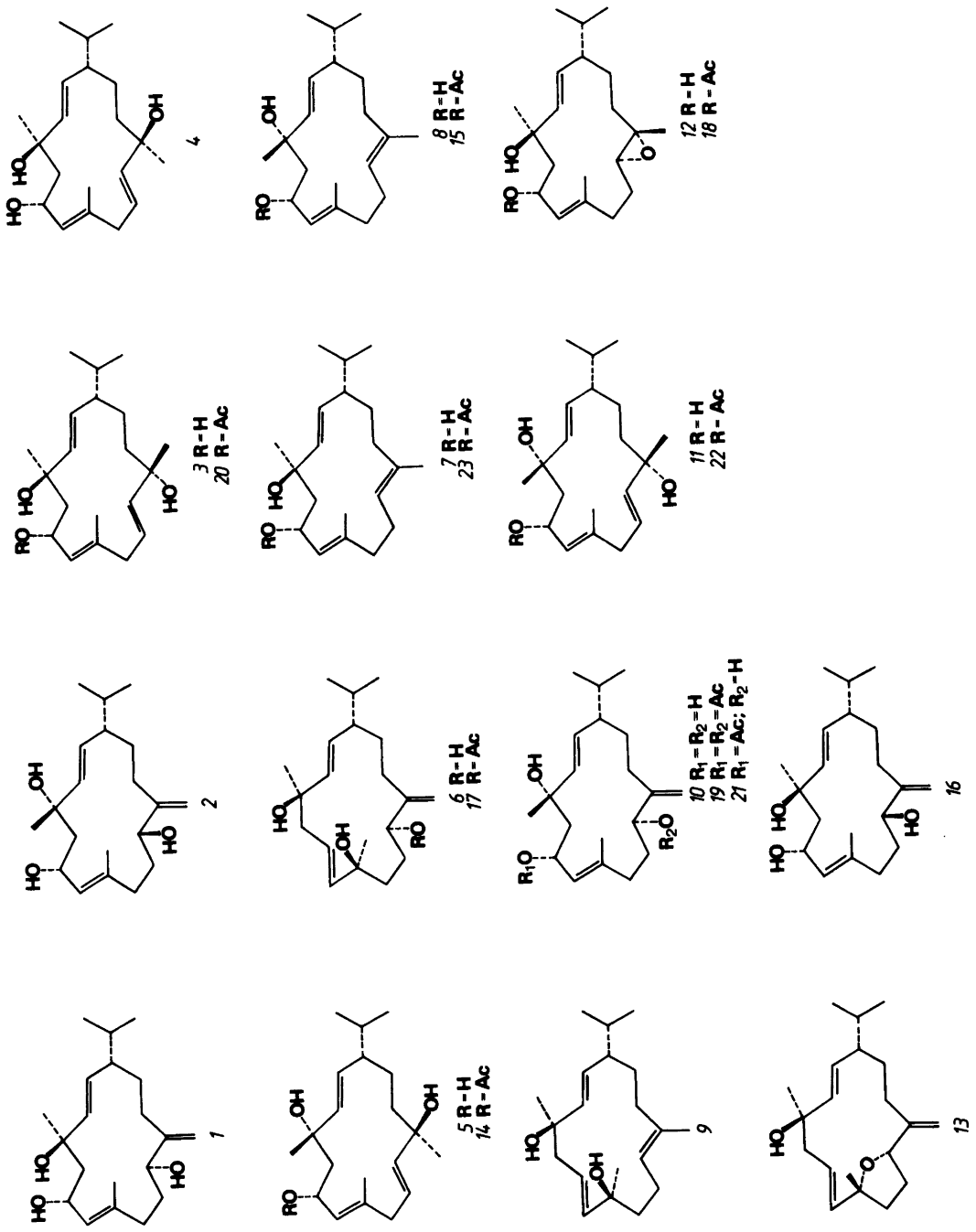
It follows from the results summarized in Table 2 that in the reactions of the 4*R*,6*R*- and 4*S*,6*R*-diols (*7*,*8*) with singlet oxygen the hydroperoxides corresponding to the 11*S*- and 12*S*-triols are formed in preference to their 11*R*- and 12*R*-counterparts. This stereoselectivity may be accounted for by conformational arguments similar to those presented previously for acetate *15*.[2]

It is also evident that the generation of all four products from each 4,6-diol (*7*,*8*) occurs with hydrogen abstraction from the 1,2-disubstituted side of the trisubstituted 11,12 double bond. This result is consistent with the recent finding that *syn* ene additions are favoured in acyclic and most cyclic systems.[7,8]

Structure determination of triol 6. The spectral data demonstrated that compound *6*, $C_{20}H_{34}O_3$, contains an isopropyl group (two methyl doublets at δ 0.85 and 0.88; IR bands at 1385 and 1375 cm^{-1}), two methyl groups attached to the same carbon atoms as the two tertiary hydroxyl groups (^1H NMR singlets at δ 1.27 and 1.39; ^{13}C NMR signals at δ 73.0 (s) and 73.3 (s); OH-absorption in the IR spectrum of the monoacetate *17*) and one secondary hydroxyl group (one-proton multiplet at δ 4.24 shifted to δ 5.38 in the ^1H NMR spectrum of *17*). Of the three double bonds, one extends to an exocyclic methylene group and two are *E*-disubstituted. These results demonstrate that triol *6* is monocyclic and incorporates a fourteen-membered ring. A 2,6,12(20)-cembra-

Table 2. Relative yields, as determined by integration of HPLC traces, of the products obtained by sensitized photo-oxygenation of *7*, *8* and *15* followed by reduction.

Starting material	Product (%) 11*S*	11*R*	12*S*	12*R*
7	58	2	31	9
8	63	1	31	5
15	54	–	43	3


4
8 R-H
15 R-Ac
12 R-H
18 R-Ac
3 R-H
20 R-Ac
7 R-H
23 R-Ac
11 R-H
22 R-Ac
2
6 R-H
17 R-Ac
10 R1=R2=H
19 R1=R2=Ac
21 R1=Ac; R2=H
16
1
5 R-H
14 R-Ac
9
13

triene-4,8,11-triol structure seemed most likely from a biogenetic point of view.

This assignment was readily verified, since triol *6* proved to be identical to the 4,8,11-triol obtained as the minor product on treatment of the 4*R*,6*R*,11*S*-triol *1* with weak acid (*vidi supra*). This conversion also determines that triol *6* has a 1*S*,2*E*,6*E*,11*S*-stereochemistry but does not allow an unambigous assignment of the chiralities of C-4 and C-8. The reason for this is that in the analogous acid-induced conversion of 4,6-diols (*7*,*8*) to 4,8-diols epimerization does occur at C-4, and in addition to the major 4*R*,8*S*- and 4*S*,8*S*-diols, a 4*S*,8*R*-diol is formed.[9]

In order to resolve these stereochemical uncertainties the 4*R*,8*S*-diol *9* was reacted with singlet oxygen. Following reduction of the reaction mixture with triethyl phosphite and separation by HPLC the major product was isolated. This compound was indistinguishable from triol *6* and was hence formulated as (1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-2,6,12(20)-cembratriene-4,8,11-triol.

Biogenesis. The results obtained by the biomimetic reactions described above support the view that the 4,6,11- and 4,6,12-triols (*1*–*5*, *10*, *11*), which are present in the cuticular wax of the leaf and flower, are formed in tobacco *via* sensitized photo-oxygenation or enzyme-assisted oxidation of the 11,12 double bond in the 4,6-diols (*7*, *8*; *cf.* Scheme 1).[3] The biogenesis of the 4*R*,8*S*,11*S*-triol *6* may take place by an initial conversion of the 4*R*,6*R*-diol (*7*) to the 4*R*,8*S*-diol (*9*) with subsequent oxidation or by an acid-induced rearrangement of a preformed 4*R*,6*R*,11*S*-triol (*1*).

Comments upon the conformation about the 5,6 bond in various cembrane alcohols and acetates. A comparison of the ^{1}H and ^{13}C NMR data as well as results from X-ray diffraction determinations have led us to focus our attention on the conformation about the 5,6 bond in various cembrane alcohols and acetates. Thus, (1*S*,2*E*,-4*R*,6*R*,7*E*,11*S*,12*S*)-11,12-epoxy-6-acetoxy-2,7-cembradien-4-ol (*18*) exists in the crystalline state as conformer A, in which the dihedral angle involving the *pro-R* hydrogen at C-5 and H-6 is 94° and that involving the *pro-S* hydrogen and H-6 is 147° (Scheme 2).[4] The 4*S*,6*R*,11*S*-triol *10*, on the other hand, has conformation B and the corresponding angles are 54 and 64°.[2]

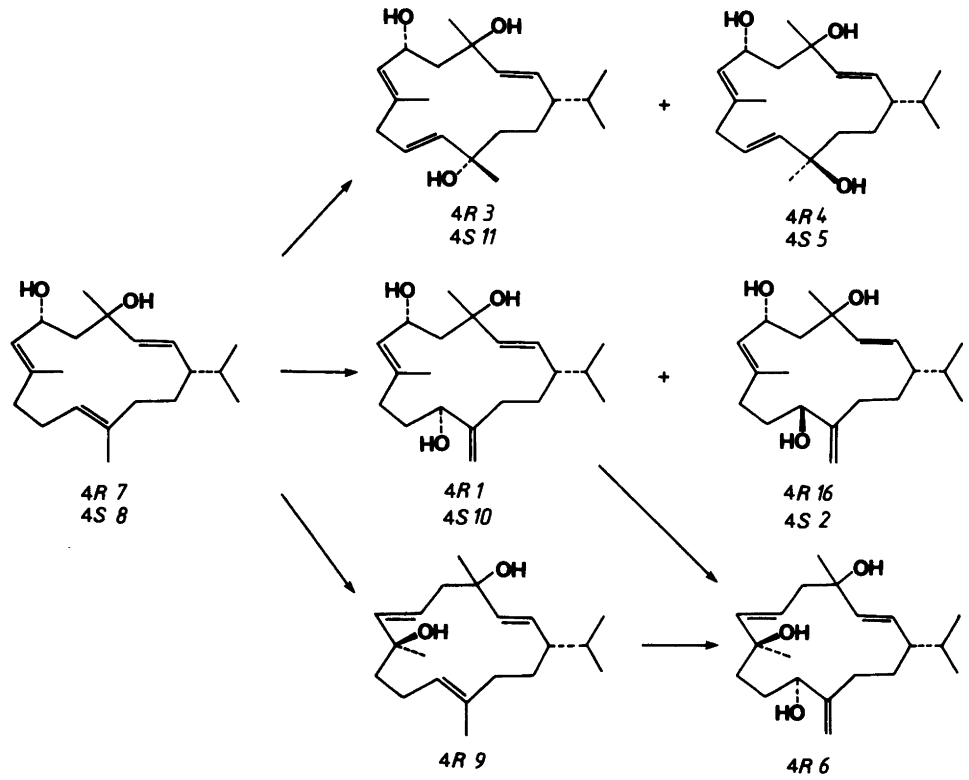
An analysis of the ^{1}H NMR spectra suggests that these conformations are retained in solution. The two hydrogens at C-5, which resonate at δ 1.90 and 2.03 in epoxide *18* and at δ 1.80 and 2.22 in triol *10*, have vicinal couplings (^3J) to H-6 of 8.7 and 1.6 Hz (*18*) and 2.7 and 5.5 Hz (*10*), respectively (*cf.* Table 3). These couplings are in conformity with the dihedral angles in conformers A and B, respectively. As a result, the downfield H-5 signal in the spectra of both compounds can be ascribed to the *pro-R* hydrogen and the upfield signal to the *pro-S* hydrogen.

The assignments made for epoxide *18* were reinforced by lanthanide induced shift (LIS) measurements using Eu(dpm)$_3$. The hydroxyl group at C-4 proved to be the preferential complexing site. H-6 (100)* and the *pro-R* hydrogen at C-5 (74) suffered the largest induced shifts, whereas a considerably smaller effect (39) was observed on the *pro-S* hydrogen. This result is in accordance with the conclusion that the *pro-R* hydrogen is *exo* to the carbocyclic ring and more favourably oriented spatially for interaction with the shift reagent than the *pro-S* hydrogen.

In order to avoid competing complex formation with all three hydroxyl groups, LIS experiments were not performed on triol *10* itself but on the diacetylated derivative 19.[2] The latter compound was judged from relevant chemical shift values and coupling constants to have a similar orientation around the 5,6 bond as triol *10*. As expected preferential LIS interaction was observed at the hydroxyl group at C-4. However, the two hydrogens at C-5 were found to undergo induced shifts (100, 99) of equal magnitudes, a result which is best accommodated by a conformer of type B.

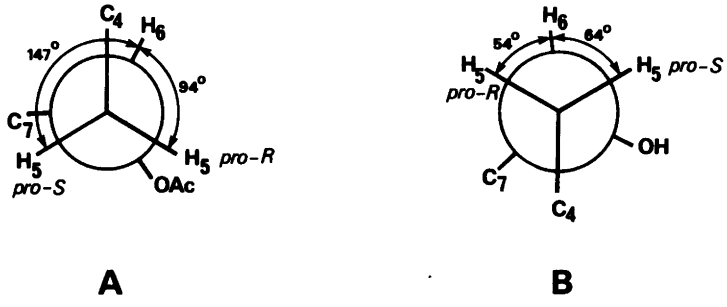
With these results at hand, the ^{1}H NMR data compiled in Table 3 indicate that triols *1*, *16*, *3* and *4* as well as acetate *20*, all of which have 4*R*-configurations, are conformationally reminiscent of epoxide *18* (conformer A), whereas the triols and acetates of the 4*S*-series (*10*, *2*, *11*, *5*, *19*,*21*,[2] *22*[2]) are likely to exist in a conformation of type B. It is particularly noteworthy that the ^{1}H NMR results for both the 4*R*,6*R*- and 4*S*,6*R*-diols (*7*, *8*) and their corresponding monoacetates (*23*, *15*) are consistent with a conformer such as B.

* The measurements were made with the linear LIS range (shift reagent/substrate *ca.* 0–0.5) and were normalized by assigning the value 100 to the proton signal exhibiting the largest shift.



Scheme 1. Probable biogenesis of triols *1–6*, *10* and *11*.

These conformational differences are also reflected, in a diagnostic manner, in the ^{13}C NMR spectra (Table 1). Thus, the C-4, C-5 and C-6 signals are present at virtually invariant positions in the spectra of the 4*R*,6*R*-diol (*7*) and the triols of the 4*R*-series (*1*, *16*, *3*, *4*). In the 4*S*-series, however, the diol (*8*) proved to differ significantly from the triols (*10*, *2*, *11*, *5*) with respect to the shieldings of these carbon atoms, *i.e.* C-4: δ 72.5 (diol *8*) as against δ 74.0–74.4 (triols), C-5: δ 52.5 as against δ 46.5–47.2 and C-6: δ 66.2 as against δ 68.5–69.4. An analogous situation is encountered for C-5 in the spectra of acetates *15*, *18–23*.



Scheme 2. Conformation about the 5,6 bond in compound *18* (A) and in compound *10* (B).

Table 3. Chemical shift values (δ) and coupling constants (J in Hz) for the H-5a, H-5b, H-6 and H-7 signals in the ^{1}H NMR spectra of compounds *1–5, 7, 8, 10, 11, 15, 16* and *18–23*.

Compound	H-5a (*pro-S*)	H-5b (*pro-R*)	H-6	H-7
4*R*-Series Triols				
1	1.93 $J_{5a,6}$=8.6	2.04 $J_{5b,6}$=3.0	4.70 $J_{6,7}$=8.9	5.24
16	1.90 $J_{5a,6}$=10.1	2.11 $J_{5b,6}$=2.8	4.82 $J_{6,7}$=8.6	5.29
3	1.80 $J_{5a,6}$=10.4	2.07 $J_{5b,6}$=3.0	4.72 $J_{6,7}$=8.9	5.27
4	1.79 $J_{5a,6}$=10.0	2.06 $J_{5b,6}$=2.8	4.73 $J_{6,7}$=8.8	5.20
Diol				
7	1.86 $J_{5a,6}$=8.5	2.05 $J_{5b,6}$=1.7	4.82 $J_{6,7}$=9.0	5.27
Acetates				
18	1.90 $J_{5a,6}$=8.7	2.03 $J_{5b,6}$=1.6	5.80 $J_{6,7}$=9.9	5.32
20	1.91 $J_{5a,6}$=8.7	2.00 $J_{5b,6}$=3.3	5.74 $J_{6,7}$=9.1	5.20
23	1.95 $J_{5a,6}$=7.9	2.05 $J_{5b,6}$=1.8	5.75 $J_{6,7}$=9.8	5.25
4*S*-Series Triols				
10	1.80 $J_{5a,6}$=2.7	2.22 $J_{5b,6}$=5.5	4.67 $J_{6,7}$=9.1	5.59
2	1.68 $J_{5a,6}$=2.6	2.24 $J_{5b,6}$=6.0	4.78 $J_{6,7}$=8.7	5.55
11	1.75 $J_{5a,6}$=2.1	2.20 $J_{5b,6}$=6.1	4.80 $J_{6,7}$=8.2	5.54
5	1.75 $J_{5a,6}$=2.1	2.19 $J_{5b,6}$=6.6	4.77 $J_{6,7}$=9.0	5.53
Diol				
8	1.96 $J_{5a,6}$=7.9	2.03 $J_{5b,6}$=2.9	4.49 $J_{6,7}$=9.2	5.34
Acetates				
19	1.96 $J_{5a,6}$=3.0	2.14 $J_{5b,6}$=7.8	5.64 $J_{6,7}$=9.2	5.34
21	1.99 $J_{5a,6}$=3.3	2.09 $J_{5b,6}$=7.5	5.65 $J_{6,7}$=9.5	5.35
22	1.91 $J_{5a,6}$=3.4	2.07 $J_{5b,6}$=7.6	5.74 $J_{6,7}$=9.7	5.29
15	1.97 $J_{5a,6}$=8.0	2.02 $J_{5b,6}$=3.2	5.54 $J_{6,7}$=10.2	5.24

EXPERIMENTAL

With the exception of accurate mass measurements, which were carried out on a Kratos MS50 Stereo DS55 SM/DS 55S mass spectrometer-computer system and the NMR spectra, which were recorded on a Varian XL-200 spectrometer, the instruments specified in Ref. 10 were used.

Isolation. 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. Part of fraction C (6.2 g) was separated further into eight fractions, C1–C8, using a PrepPak-500/C_{18} cartridge and methanol–water (65:35) as an eluent. Repeated HPLC of fraction C3 (272 mg) using columns packed with Spherisorb 5 and Spherisorb/5 CN led to the isolation of 7.5 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triol (*2*) and 17 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triol (*5*).

Flash chromatography (silica gel; hexane–ethyl acetate 30:70) was used to separate fraction D into six fractions, D1–D6. Fraction D5 (5.7 g) was subjected to repeated HPLC using columns packed with PrepPak-500/C_{18}, Spherisorb 5, Spherisorb/5 CN and Spherisorb 5 ODS, which gave 30 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*1*), 18 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol (*3*), 11 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triol (*4*) and 12 mg of (1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-2,6,12(20)-cembratriene-4,8,11-triol (*6*).

(1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-Cembratriene-4,6,11-triol (*1*) had m.p. 146–147 °C; $[\alpha]_D$ +37° (*c* 0.69, EtOH); (Found: $[M-18]^{\cdot+}$ 304.2391. Calc. for $C_{20}H_{32}O_2$: 304.2402); IR (KBr) bands at 3300, 3080, 1665, 1645, 1385 and 1365 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.82 (d, J=6.7 Hz)/ (0.85 (d, J=6.7 Hz) (H-16/H-17), 1.36 (s, H-18), 1.74 (d, J=1.2 Hz, H-19), 1.93 (dd, J=8.6 and −14.0 Hz, H-5a), 2.04 (dd, J=3.0 and −14.0 Hz, H-5b), 4.03 (dd, J=0.8 and 6.5 Hz, H-11), 4.70 (ddd, J=3.0, 8.6 and 8.9 Hz, H-6), 4.90 (q, J=1.4 Hz, H-20a), 5.06 (dd, J=0.8 and 1.4 Hz, H-20b), 5.24 (dd, J=1.2 and 8.9 Hz, H-7), 5.38 (dd, J=8.0 and 16.0 Hz, H-2) and 5.44 (d, J=16.0 Hz, H-3); MS [*m/z* (%, composition)]: 304 (2), 286 (21, $C_{20}H_{30}O$), 268 (4), 253 (3, $C_{19}H_{25}$), 243 (15), 225 (10, $C_{17}H_{21}$), 215 (7), 203 (8, $C_{11}H_{23}O_3$), 159 (19, $C_{12}H_{15}$), 147 (24, $C_{11}H_{15}$), 133 (28, $C_{10}H_{13}$), 121 (36, C_9H_{13}), 105 (38, C_8H_9), 93 (44, C_7H_9), 81 (56), 69 (39), 55 (47)

and 43 (100).

(1*S*,2*E*,4*S*,6*R*,7*E*,11*R*)-2,7,12(20)-Cembratriene-4,6,11-triol (*2*) was an oil and had $[\alpha]_D$+44° (*c* 0.61, $CHCl_3$); (Found: $[M-18]^{\cdot+}$ 304.2404. Calc. for $C_{20}H_{32}O_2$: 304.2402); IR ($CHCl_3$) bands at 3600, 3450, 3080, 1665, 1645, 1385 and 1370 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (d, *J*=6.8 Hz)/0.84 (d, *J*=6.7 Hz) (H-16/H-17), 1.26 (s, H-18), 1.67 (d, *J*=1.3 Hz, H-19), 1.68 (dd, *J*=2.6 and −14.2 Hz, H-5a), 2.24 (dd, *J*=6.0 and −14.2 Hz, H-5b), 4.09 (m, H-11), 4.78 (ddd, *J*=2.6, 6.0 and 8.7 Hz, H-6), 4.92 (broad s, H-20a), 5.16 (broad s, H-20b), 5.4−5.6 (overlapping signals, H-2 and H-3) and 5.55 (dd, *J*=1.3 and 8.7 Hz, H-7); ^1H NMR (C_6D_6): δ 5.34 (d, *J*=15.4 Hz, H-3) and 5.66 (dd, *J*=9.8 and 15.4 Hz, H-2); MS [*m/z* (%, composition)]: 304 (0.2), 286 (1, $C_{20}H_{30}O$), 271 (1), 261 (1), 243 (2), 225 (1, $C_{17}H_{21}$), 215 (1), 203 (2), 136 (15, $C_{10}H_{16}$ and $C_9H_{12}O$), 121 (12, C_9H_{13} and C_8H_9O), 109 (18, C_8H_{13} and C_7H_9O), 93 (21, C_7H_9), 81 (23, C_6H_9 and C_5H_5O), 69 (20, C_5H_9 and C_4H_5O), 55 (22, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

(1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-Cembratriene-4,6,12-triol (*3*) was an oil and had $[\alpha]_D$+86° (*c* 0.51, EtOH); (Found: $[M-18]^{\cdot+}$ 304.2442. Calc. for $C_{20}H_{32}O_2$: 304.2402); IR ($CHCl_3$) bands at 3610, 3430, 1670, 1390 and 1375 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.77 (d, *J*=6.7 Hz)/0.84 (d, *J*=6.7 Hz) (H-16/H-17), 1.29 (s, H-20), 1.36 (s, H-18), 1.80 (d, *J*=1.2 Hz, H-19), 1.80 (dd, *J*=10.4 and −13.4 Hz, H-5a), 2.07 (dd, *J*=3.0 and −13.4 Hz, H-5b), 2.62 (dd, *J*=8.7 and −16.2 Hz, H-9a), 2.82 (dd, *J*=5.3 and −16.2 Hz, H-9b), 4.72 (ddd, *J*=3.0, 8.9 and 10.4 Hz, H-6), 5.27 (d, *J*=8.9 Hz, H-7), 5.30 (dd, *J*=7.5 and 16.1 Hz, H-2), 5.45 (d, *J*=16.1 Hz, H-3), 5.45 (d, *J*=15.4 Hz, H-11) and 5.73 (ddd, *J*=5.3, 8.7 and 15.4 Hz, H-10); MS [*m/z* (%, composition)]: 304(1), 286 (7, $C_{20}H_{30}O$), 268 (3, $C_{20}H_{28}$), 243 (5, $C_{17}H_{23}O$ and $C_{18}H_{27}$), 225 (3, $C_{17}H_{21}$), 215 (2, $C_{16}H_{23}$), 203 (3, $C_{15}H_{23}$ and $C_{14}H_{19}O$), 159 (10, $C_{12}H_{15}$), 145 (13, $C_{11}H_{13}$), 136 (35, $C_{10}H_{16}$ and $C_9H_{12}O$), 121 (19, C_9H_{13} and C_8H_9O), 109 (20, C_8H_{13} and C_7H_9O), 93 (32, C_7H_9), 81 (37, C_6H_9 and C_5H_5O), 69 (23, C_5H_9 and C_4H_5O), 55 (25, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

(1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*R*)-2,7,10-Cembratriene-4,6,12-triol (*4*) had m.p. 86−87 °C; $[\alpha]_D$+93° (*c* 0.40, EtOH); (Found: $[M-18]^{\cdot+}$ 304.2408. Calc for $C_{20}H_{32}O_2$: 304.2402); IR ($CHCl_3$) bands at 3600, 3420, 1660, 1385 and 1375 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.77 (d, *J*=6.7 Hz)/0.85 (d, *J*=6.7 Hz) (H-16/H-17), 1.29 (s, H-20), 1.36 (s, H-18), 1.79 (dd, *J*=10.0 and −13.5 Hz, H-5a), 1.82 (d, *J*=1.2 Hz, H-19), 2.06 (dd, *J*=2.8 and −13.5 Hz, H-5b), 2.64 (dd, *J*=6.6 and −15.3 Hz, H-9a), 2.80 (dd, *J*=6.7 and −15.3 Hz, H-9b), 4.73 (ddd, *J*=2.8, 8.8 and 10.0 Hz, H-6), 5.20 (dd, *J*=1.2 and 8.8 Hz, H-7), 5.31 (dd, *J*=7.7 and 16.0 Hz, H-2), 5.46 (d, *J*=16.0 Hz, H-3), 5.50 (d, *J*=15.7 Hz, H-11) and 5.67 (ddd, *J*=6.6, 6.7 and 15.7 Hz, H-10); MS [*m/z* (%, composition)]: 304 (1), 286 (9, $C_{20}H_{30}O$), 268 (8, $C_{20}H_{28}$), 253 (3, $C_{19}H_{25}$), 243 (8), 225 (5, $C_{17}H_{21}$), 215 (2, $C_{12}H_{23}O_3$), 203 (5, $C_{11}H_{23}O_3$), 159 (12, $C_{12}H_{15}$), 145 (17, $C_{11}H_{13}$), 136 (39, $C_{10}H_{16}$), 121 (25, C_9H_{13} and C_8H_9O), 105 (24, C_8H_9), 93 (38, C_7H_9), 81 (46, C_6H_9 and C_5H_5O), 69 (28, C_5H_9 and C_4H_5O), 55 (30, C_4H_7 and C_3H_3O), and 43 (100, C_2H_3O and C_3H_7).

(1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-2,7,10-Cembratriene-4,6,12-triol (*5*) had m.p. 87−88 °C; $[\alpha]_D$+124° (*c* 0.14, EtOH); (Found: $[M-18]^{\cdot+}$ 304.2419. Calc. for $C_{20}H_{32}O_2$: 304.2402); IR ($CHCl_3$) bands at 3600, 3450, 1665, 1385 and 1370 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.81 (d, *J*=6.8 Hz)/0.86 (d, *J*=6.8 Hz) (H-16/H-17), 1.23 (s, H-20), 1.29 (s, H-18), 1.68 (broad s, H-19), 1.75 (dd, *J*=2.1 and −14.3 Hz, H-5a), 2.19 (dd, *J*=6.6 and −14.3 Hz, H-5b), 2.72 (m, H-9a, H-9b), 4.77 (ddd, *J*=2.1, 6.6 and 9.0 Hz, H-6), 5.53 (broad d, *J*=9.0 Hz, H-7) and 5.4−5.7 (overlapping signals, H-2, H-3, H-10 and H-11); ^1H NMR (C_6D_6): 2.49 (dd, *J*=6.7 and −17.0 Hz, H-9a), 2.55 (dd, *J*=6.7 and −17.0 Hz, H-9b), 5.36 (d, *J*=15.7 Hz, H-11), 5.38 (d, *J*=15.3 Hz, H-3), 5.50 (dt, *J*=6.7 and 15.7 Hz, H-10) and 5.72 (dd, *J*=9.7 and 15.3 Hz, H-2); MS [*m/z* (%, composition)]: 304 (1), 289 (1, $C_{19}H_{29}O_2$), 286 (2, $C_{20}H_{30}O$), 271 (1, $C_{19}H_{27}O$), 261 (2), 243 (5), 215 (2), 203 (4, $C_{15}H_{23}$ and $C_{14}H_{19}O$), 136 (25, $C_{10}H_{16}$), 121 (22, C_9H_{13}), 109 (34, C_8H_{13} and C_7H_9O), 95 (32), 81 (33), 69 (33), 55 (30) and 43 (100).

(1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-2,6,12(20)-Cembratriene-4,8,11-triol (*6*) had m.p. 164−165 °C; $[\alpha]_D$+42° (*c* 0.41, EtOH); (Found: $[M-18]^{\cdot+}$ 304.2419. Calc. for $C_{20}H_{32}O_2$: 304.2402); IR ($CHCl_3$) bands at 3590, 3420, 3080, 1645, 1385 and 1375 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.85 (d, *J*=6.6 Hz)/0.88 (d, *J*=6.4 Hz) (H-16/H-17), 1.27 (s)/1.39 (s) (H-18/H-19), 4.24 (m, H-11), 4.87 (broad s, H-20a), 4.98 (broad s, H-20b), 5.25 (dd, *J*=8.3 and 15.8 Hz, H-2), 5.39 (d, *J*=15.8 Hz, H-3) and 5.5−5.6 (overlapping signals, H-6 and H-7); ^1H NMR (C_6D_6): δ 2.24 (ddd, *J*=0.6, 9.0 and −13.6 Hz, H-5a), 2.32 (ddd, *J*=1.2, 5.7 and −13.6 Hz, H-5b), 5.25 (ddd, *J*=0.6, 1.2 and 15.4 Hz, H-7) and 5.50 (ddd, *J*=5.7, 9.0 and 15.4 Hz, H-6); MS [*m/z* (%, composition)]: 304 (0.5), 286 (2, $C_{20}H_{30}O$), 271 (1, $C_{19}H_{27}O$), 261 (2), 243 (4), 233 (2, $C_{16}H_{25}O$), 203 (3, $C_{14}H_{19}O$), 159 (8, $C_{12}H_{15}$), 147 (10), 133 (13, $C_{10}H_{13}$), 123 (16, C_9H_{15}), 109 (18, C_8H_{13} and C_7H_9O), 95 (22), 81

(26), 71 (31, C_4H_7O and C_5H_{11}), 55 (29, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

Conversion of (1S,2E,4R,6R,7E,11S,12S)-11,12-epoxy-2,7-cembradiene-4,6-diol (12) to (1S,-2E,4R,6R,7E,10E,12S)-2,7,10-cembratriene-4,6,-12-triol (3) and (1S,2E,4R,6R,7E,11S)-2,7,12(20)-cembratriene-4,6,11-triol (1). To a stirred suspension of 21 mg of diphenyl diselenide in 5 ml of isopropanol was added, under nitrogen, 5.5 mg of $NaBH_4$. After addition of 35 mg of *12* the reaction mixture was refluxed for 30 h. The reaction mixture was cooled (0 °C) and 2.5 ml of tetrahydrofuran was added, followed by dropwise addition of 0.3 ml of hydrogen peroxide (30 %). After 4 h the resulting slurry was diluted with water and extracted with ether. The organic phase was washed with aqueous sodium carbonate (10 %) and water, dried and concentrated. The residue was separated by flash chromatography over silica gel and HPLC (Spherisorb 5; hexane–ethyl acetate 20:80) to give 9.4 mg of starting material (*12*), 4.0 mg of (1*S*,-2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol, whose ^{1}H NMR and mass spectra agreed with those of triol *3*, and 0.8 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,6,12(20)-cembratriene-4,6,11-triol, whose ^{1}H NMR and mass spectra were identical with those of triol *1*.

Treatment of (1S,2E,4R,6R,7E,11S,)-2,7,-12(20)-cembratriene-4,6,11-triol (1) with acid. To a solution of 44 mg of *1* in 5 ml of chloroform was added 0.3 ml of aqueous HCl (10 %). The reaction mixture was kept at room temperature for 24 h, washed with water and aqueous sodium carbonate, dried and evaporated. The residue was separated by HPLC using a column packed with Spherisorb 5 ODS and methanol–water (80:20) to give 7.0 mg of (1*S*,2*E*,4*R*,6*E*,8*R*,11*S*)-8,11-epoxy-2,6,12(20)-cembratrien-4-ol (*13*), whose m.p., optical rotation, IR, ^{1}H NMR and MS data agreed with those of an authenic sample,[6] and 7.8 mg of (1*S*,2*E*,4*R*,6*E*,8*S*,-11*S*)-2,6,12(20)-cembratriene-4,8,11-triol, which was identical to the naturally occurring triol *6*.

Acetylation of (1S,2E,4S,6R,7E,10E,12R)-2,7,10-cembratriene-4,6,12-triol (5). Treatment of 8 mg of triol *5* with acetic anhydride in pyridine for 3.5 h at room temperature followed by work-up and purification by HPLC using a column packed with Spherisorb 5 ODS gave 2.4 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-6-acetoxy-2,7,10-cembratriene-4,12-diol (*14*), whose optical rotation, IR, ^{1}H NMR and mass spectra were identical with those of an authentic sample.[2]

Photo-oxygenation of the (1S,2E,4R,6R,7E,-11E)- and (1S,2E,4S,6R,7E,11E)-2,7,11-cembratriene-4,6-diols (7, 8). A solution of 400 mg of *7* and 30 mg of Rose Bengal in 25 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 h when TLC showed that all starting material had been consumed, 1 ml of triethyl phosphite was added, and the reaction mixture was kept at room temperature for 4 h. The solvent was removed under reduced pressure, and the residue was recrystallized from ethyl acetate to give 83 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*1*). Part of the mother liquor was separated by HPLC using columns packed with Spherisorb 5 Nitrile and Spherisorb to afford 29 mg of *1*, 3.5 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triol (*16*), 22 mg of (1*S*,2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol (*3*) and 5.2 mg of (1*S*,2*E*,-4*R*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triol (*4*).

A solution of 1.6 g of (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*)-2,7,11-cembratriene-4,6-diol (*8*) and 50 mg of Rose Bengal in 25 ml of methanol was reacted with singlet oxygen for 50 min using the apparatus described above. After addition of 1.9 ml of triethyl phosphite the reaction mixture was kept at room temperature for 3 h. Removal of the solvent and separation of the residue by flash chromatography over silica gel and HPLC using columns packed with PrePak-500/C_{18}, Spherisorb and Spherisorb 5 Nitrile yielded 113 mg of starting material (*8*), 247 mg of (1*S*,2*E*,4*S*,6*R*,-7*E*,11*S*)-2,7,12(20)-cembratriene-4,6,11-triol (*10*, m.p. 112 °C, $[\alpha]_D$+54° (*c* 0.17, EtOH)),[2] 1.2 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triol (*2*), 125 mg of (1*S*,2*E*,4*S*,-6*R*,7*E*,10*E*,12*S*)-2,7,10-cembratriene-4,6,12-triol (*11*, m.p. 143–144 °C, $[\alpha]_D$+167° (*c* 0.90 EtOH))[2] and 27.6 mg of (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,-12*R*)-2,7,10-cembratriene-4,6,12-triol (*5*).

Of these, the (1*S*,2*E*,4*R*,6*R*,7*E*,11*S*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,11*R*)-2,7,12(20)-cembratriene-4,6,11-triols were identical (optical rotation, IR, ^{1}H NMR and MS) to triols *1* and *2* and the (1*S*,-2*E*,4*R*,6*R*,7*E*,10*E*,12*S*)-, (1*S*,2*E*,4*R*,6*R*,7*E*,-10*E*,12*R*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,10*E*,12*R*)-2,7,10-cembratriene-4,6,12-triols to *3*, *4* and *5*, respectively.

(1*S*,2*E*,4*R*,6*R*,7*E*,11*R*)-2,7,12(20)-Cembratriene-4,6,11-triol (*16*) had m.p. 82–84 °C; $[\alpha]_D$+63° (*c* 0.57, EtOH); IR ($CHCl_3$): 3600, 3410, 3080, 1660, 1645, 1385 and 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.80 (d, J=6.7 Hz)/(0.84 (d, J=6.2 Hz) (H-16/H-17), 1.40 (s, H-18), 1.83 (d, J=1.2 Hz, H-19), 1.90 (dd, J=10.1 and −13.6 Hz, H-5a), 2.11 (dd, J=2.8 and −13.6 Hz, H-5b), 4.04 (t, J=6.0 Hz, H-11), 4.82 (ddd, J=2.8, 8.6 and 10.1 Hz, H-6), 4.93 (broad s, H-20a), 5.18

(broad s, H-20b), 5.24 (dd, J=8.8 and 16.2 Hz, H-2), 5.29 (broad d, J=8.6 Hz, H-7) and 5.49 (d, J=16.2 Hz, H-3); MS [*m/z*(%)]: 304 (M–18, 0.3), 286 (1), 271 (1), 261 (2), 243 (4), 233 (2), 215 (2), 203 (3), 177 (9), 159 (8), 147 (11), 135 (12), 121 (21), 109 (22), 95 (31), 81 (33), 69 (33), 55 (32) and 43 (100).

Acetylation of (1S,2E,4R,6E,8S,11S)-2,6,12-(20)-cembratriene-4,8,11-triol (6). Treatment of 6 mg of triol *6* with acetic anhydride in pyridine for 3 h at room temperature followed by work-up and chromatography over silica gel gave 1.6 mg of (1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-11-acetoxy-2,6,12(20)-cembratriene-4,8-diol (*17*), which was an oil and had IR ($CHCl_3$) bands at 3600, 3420, 3090, 1730, 1650 and 1245 cm^{-1}; ^1H NMR ($CDCl_3$); δ 0.85 (d, J=6.5 Hz)/0.88 (d, J=6.5 Hz) (H-16/H-17), 1.27 (s)/1.39 (s) (H-18/H-19), 2.07 (s, $OCOCH_3$), 2.29 (dd, J=8.0 and −13.9 Hz, H-5a), 2.41 (dd, J=5.0 and −13.9 Hz, H-5b), 4.90 (broad s, H-20a), 4.93 (broad s, H-20b), 5.25 (dd, J=8.4 and 15.9 Hz, H-2), 5.38 (m, H-11), 5.40 (d, J=15.9 Hz, H-3), 5.48 (d, J=15.4 Hz, H-7) and 5.56 (ddd, J=5.0, 8.0 and 15.4 Hz, H-6); MS [*m/z* (%)]: 346 (M–18, 0.1), 304 (0.1), 286 (1), 243 (3), 228 (2), 203 (2), 185 (8), 173 (3), 159 (10), 133 (23), 119 (11), 107 (18), 93 (24), 81 (25), 71 (32), 55 (24) and 43 (100).

Photo-oxygenation of (1S,2E,4R,6E,8S,11E)-2,6,11-cembratriene-4,8-diol (9). A solution of 37 mg of *9* and 10 mg of Rose Bengal in 25 ml of methanol was reacted with singlet oxygen for 1 h using the apparatus described above. After addition of 100 ul of triethyl phosphite the reaction mixture was kept at room temperature for 30 min. Concentration *in vacuo* and separation by HPLC using a column packed with Spherisorb 5 afforded 12 mg of (1*S*,2*E*,4*R*,6*E*,8*S*,11*S*)-2,6,12(20)-cembratriene-4,8,11-triol, which was identical to tobacco triol *6*.

LIS measurements. The relative induced shifts were for *18*: H-6 (100), H-5b (74), H-5a (39), H-3 (36), H-7 (26), H-11 (24), H-18 (19), H-2 (17), H-19 (12), $OCOCH_3$ (10), H-20 (8), H-16/H-17 (4) and for *19*: H-5b (100), H-5a (99), H-18 (84), H-6 (76), H-2 (74), H-3 (67), H-7 (46), H-11 (46), H-19 (27), $OCOCH_3$ (23), H-20b (16), H-20a (12), $OCOCH_3$ (10), H-16/H-17 (8/6).

Acetylation of (1S,2E,4R,6R,7E,10E,12S)-2,7,10-cembratriene-4,6,12-triol (3). A solution of 35 mg of *3* in 0.5 ml of acetic anhydride and 1 ml of pyridine was left at 4 °C overnight. Work-up and separation by HPLC (Spherisorb 5 ODS, methanol–water 80:20) gave 11 mg of (1*S*,2*E*,-4*R*,6*R*,7*E*,10*E*,12*S*)-6-acetoxy-2,7,10-cembratriene-4,12-diol (*20*), which had m.p. 115–116 °C; $[\alpha]_D$+28° (c 0.35, EtOH), IR ($CHCl_3$) bands at 3680, 3430, 1725, 1625 and 1247 cm^{-1}, ^1H NMR ($CDCl_3$): δ 0.77 (d, J=6.7 Hz)/0.86 (d, J=6.7 Hz) (H-16/H-17), 1.30 (s)/1.34 (s) (H-18/H-20), 1.76 (d, J=1.2 Hz, H-19), 1.91 (dd, J=8.7 and −13.6 Hz, H-5a), 2.00 (dd, J=3.3 and −13.6 Hz, H-5b), 2.02 (s, $OCOCH_3$), 2.61 (dd, J=8.5 and −15.7 Hz, H-9a), 2.81 (dd, J=5.6 and −15.7 Hz, H-9b), 5.20 (broad d, J=9.1 Hz, H-7), 5.4–5.6 (overlapping signals, H-2, H-3), 5.44 (d, J=15.3 Hz, H-11), 5.70 (ddd, J=5.6, 8.5 and 15.3 Hz, H-10) and 5.74 (ddd, J=3.3, 8.7 and 9.1 Hz, H-6); MS [*m/z* (%)]: 304 (M–60, 1), 286 (1), 271 (0.2), 243 (2), 225 (0.5), 215 (1), 203 (1), 163 (4), 151 (3), 137 (5), 123 (21), 109 (20), 95 (33), 81 (42), 71 (25), 55 (24) and 43 (100).

Acknowledgement. We are grateful to Mr. Ole Homestad and Dr. David Jones for recording the mass spectra.

REFERENCES

1. Wahlberg, I., Eklund, A.-M., Nishida, T., Enzell, C. R. and Berg, J.-E. *Tetrahedron Lett. 24* (1983) 843.
2. Wahlberg, I., Wallin, I., Narbonne, C., Nishida, T., Enzell, C. R. and Berg, J.-E. *Acta Chem. Scand. B 36* (1982) 147.
3. Enzell, C. R. and Wahlberg, I. *Recent Adv. Tob. Sci. 6* (1980) 64.
4. Behr, D., Wahlberg, I., Nishida, T., Enzell, C. R., Berg, J.-E. and Pilotti, A.-M. *Acta Chem. Scand. B 34* (1980) 195.
5. Sharpless, K. B. and Lauer, R. F. *J. Am. Chem. Soc. 95* (1973) 2697.
6. Rowland, R. L., Rodgman, A., Schumacher, J. N., Roberts, D. L., Cook, L. C. and Walker, W. E. *J. Org. Chem. 29* (1964) 16.
7. Schulte-Elte, K. H., Muller, B. L. and Rautenstrauch, V. *Helv. Chim. Acta 61* (1978) 2777.
8. Schulte-Elte, K. H. and Rautenstrauch, V. *J. Am. Chem. Soc. 102* (1980) 1738.
9. Wahlberg, I., Behr, D., Eklund, A.-M., Nishida, T., Enzell, C. R. and Berg, J.-E. *Acta Chem. Scand. B 36* (1982) 443.
10. Behr, D., Wahlberg, I., Nishida, T. and Enzell, C. R. *Acta Chem. Scand. B 31* (1977) 573.

Received February 21, 1983.