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Tobacco Chemistry. 40. Syntheses of (12*R*,13*R*)- and (12*S*,13*S*)-8,12-Epoxy-14-labden-13-ol and (13*R*)- and (13*S*)-8,13-Epoxy-14-labden-12-one, Four Tobacco Diterpenoids

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Two of the title compounds, (12*R*,13*R*)- and (12*S*, 13*S*)-8,12-epoxy-14-labden-13-ol (*9*, *10*) were obtained as major products on peracid oxidation of (12*Z*)-abienol (*8*), a reaction also furnishing small amounts of (12*R*,13*R*)- and (12*S*,13*S*)-8,13-epoxy-14-labden-12-ol (*12*, *11*), which were converted to the other two title compounds (13*R*)- and (13*S*)-8,13-epoxy-14-labden-12-one (*6*, *5*) by oxidation using Jones' reagent. The stereostructures of *9* and *10* were determined by an X-ray analysis of (12*R*)-14,15-bisnor-8,12-epoxylabdane-13-one (*16*), prepared by oxidative degradation of the 8,12-epoxyalchohol (*9*), and by consideration of the reaction mechanism involved in the peracid oxidation.

^{13}C NMR data for the synthetic and some related compounds are given and the effects of steric factors on their ^{13}C shieldings are discussed.

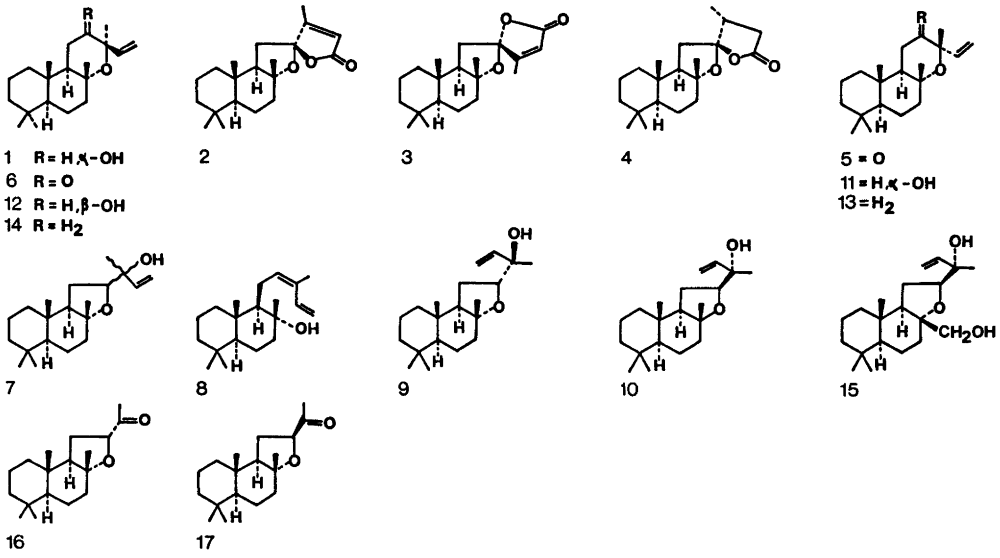
Recent phytochemical studies have disclosed that cultivars of *N. tabacum* L. generally produce diterpenoids of either the thunbergane or the labdane types.[1,2] The majority of the tobacco labdanoids known to date have been encountered in commercial Turkish and Greek tobaccos. They comprise (12*S*, 13*R*)-8,13-epoxy-14-labden-12-ol (*1*),[3] α- and β-levantenolide (*2*, *3*) [4,5] and α_2-levantanolide (*4*) [6] of Turkish tobacco, and (13*S*)- and (13*R*)-8,13-epoxy-14-labden-12-one (*5*, *6*) [7] and four stereoisomers of 8,12-epoxy-14-labden-13-ol (*7*) [8] of Greek tobacco. Since these compounds differ only with respect to their side-chain oxygenation and stereochemistry, it is reasonable to assume that they may be formed in tobacco by the non-stereospecific oxidation of an appropriate labdane precursor. (12*Z*)-abienol (*8*), which is present in the gummy exudate of green leaves of labdane producing tobacco cultivars, is an attractive possibility, particularly since studies have shown that it is lost during leaf processing.[2] The present communication describes the synthesis of four of the above tobacco labdanoids from (12*Z*)-abienol (*8*).

RESULTS

Treatment of (12*Z*)-abienol (*8*) with *m*-chloroperbenzoic acid in chloroform afforded two major products *9* (71 %) and *10* (25 %). These proved to be identical to two of the stereoisomers of (12ξ,13ξ)-8,12-epoxy-14-labden-13-ol (*7*), previously encountered in Greek tobacco and then designated "Ib" and "Id" respectively.[8]

Two alcohols, *11* and *12*, each comprising some 2 % of the reaction mixture, were also obtained. Both compounds gave mass spectra displaying diagnostically important peaks at *m/e* 306 (M), 291 (M − 15), 273 (M − 33), 236 (A), 235, 206 (B), 192 (C) and 177 (192 − 15), which are indicative of 8,13-epoxy-labdenes having a hydroxyl substituent at C-12 (Fig. 1).[7]

In agreement with this the ^1H NMR spectra of these compounds (*11*, *12*) displayed signal patterns typical of a vinyl group attached



to a non-protonated carbon, *i.e.* one-proton doublets of doublets at δ 5.20 ($J_{AB}=2.5$ and $J_{AX}=10$ Hz), 5.42 ($J_{AB}=2.5$ and $J_{BX}=17.5$ Hz) and 5.84 ($J_{AX}=10$ and $J_{BX}=17.5$ Hz) and at δ 5.23 ($J_{AB}=1.5$ and $J_{AX}=11$ Hz), 5.42 ($J_{AB}=1.5$ and $J_{BX}=18$ Hz) and 6.32 ($J_{AX}=11$ and $J_{BX}=18$ Hz), respectively. The presence of the hydroxyl group in *11* and *12* was confirmed by the IR spectra (*11*: 3580 cm^{-1} and *12*: 3630 and 3460 cm^{-1}) and by the ^1H NMR spectra, which contained a one-proton triplet at δ 3.69 ($J=3.5$ Hz) and a one-proton doublet of doublets at δ 3.50 ($J=5$ and 10 Hz), respectively. Furthermore, it was concluded from the magnitudes of these coupling constants that the secondary hydroxyl group at C-12 in *11* is axial (α-oriented), while that in *12* is equatorial (β-oriented). The ^{13}C NMR spectra of the two alcohols (*11* and *12*) containing signals due to one sp^2 methine, one sp^2 methylene, one sp^3 oxygen-carrying methine and two sp^3 oxygenated and non-protonated carbon atoms were in harmony with these assignments. (*cf.* Table 1). Oxidation using Jones' reagent converted the axial alcohol (*11*) to the ketone *5*, which was identical with (13*S*)-8,13-epoxy-14-labden-12-one previously found in Greek tobacco.[7] Since oxidation of the equatorial alcohol (*12*) afforded (13*R*)-8,13-epoxy-14-labden-12-one (*6*),[7] the alcohols obtained as minor products of the peracid oxidation of (12*Z*)-abienol (*8*) can be formulated as (12*S*, 13*S*)- and (12*R*,13*R*)-8,13-epoxy-14-labden-12-ol (*11* and *12*).

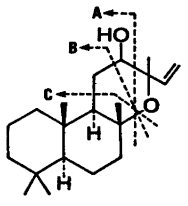


Fig. 1. Characteristic cleavage reactions in the mass spectra of 8,13-epoxy-14-labden-12-ols.

Configuration of the (12ξ,13ξ)-8,12-epoxy-14-labden-13-ols 9 *and* 10. Since the ^{13}C NMR spectrum of the 8,12-epoxy alcohol *9* exhibited C-12 and C-17 signals at 81.6 and 21.3 ppm, while the corresponding signals for the isomer *10* were located at 85.3 and 25.4 ppm, it was concluded that these compounds differ with respect to the orientation of the C-12 substituent. In the absence of information on the steric dependence of the effects of substituents on the shieldings of the carbon atoms of tetrahydrofuran rings, these data did not, however, allow configurational assignments. Nor was conclusive evidence obtained when lanthanide-induced shift (LIS) measurements were employed, although these were useful for the assignments of the ^{13}C NMR spectra of *9* and *10*.

Table 1. Carbon-13 chemical shifts and assignments for *5*, *6*, *8*–*14*, *16* and *17*.

Compound	Carbon 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
13	39.0	18.6	42.1	33.2	56.4	19.9	43.2	74.8	55.7	36.9	15.4	35.8	73.0	147.8	110.1	28.5	25.5	33.4	21.3	15.3
11	38.7	18.5	42.1	33.2	56.4	19.9	42.6	75.4	49.1	36.4	23.0	70.4	76.8	143.1	116.1	27.5	25.4	33.3	21.2	15.6
5	38.6	18.3	41.8	33.2	55.9	19.7	41.8	75.2	52.6	36.8	33.1	211.8	82.7	141.5	114.9	26.6	22.5	33.3	21.5	14.4
14	39.4	18.7	42.2	33.4	56.5	19.9	43.1	76.1	58.5	39.6	15.9	34.9	73.3	147.8	109.5	32.7	24.0	33.3	21.3	15.9
12	39.3	18.6	42.3[a]	33.3	56.3	19.9	42.1[a]	76.0[b]	57.8	36.8	25.2	77.6	76.2[b]	140.5	116.9	28.0	25.5	33.3	21.2	16.0
6	38.7	18.3	41.9[a]	33.2	56.0	19.7	42.1[a]	75.6	54.6	37.0	33.8	211.8	81.8	142.4	113.1	28.6	22.2	33.4	21.5	14.6
9	39.8[a]	18.4	42.4	33.1	57.3	20.6	39.6[a]	81.4	60.2	36.3	24.0	81.6	74.5	143.1	112.9	23.5	21.3	33.5	21.1	14.8
16	39.9[a]	18.3	42.4	33.1	57.2	20.7	39.8[a]	82.8	59.5	36.4	27.1	81.0	211.1			26.7	21.5	33.5	21.1	14.9
10	40.8	18.4	42.5	33.1	57.1	21.4	40.2	81.3	60.8	36.4	24.0	85.3	73.2	144.3	112.5	23.2	25.4	33.5	21.0	15.9
17	40.0	18.4	42.5	33.1	57.1	20.8	40.0	82.4	60.7	36.4	26.1	82.7	211.3			26.8	23.0	33.5	21.1	15.4
8	40.2	18.6	41.9	33.3	56.2	20.3	44.0	74.3	62.2	39.0	23.2	133.9	130.8	133.7	113.7	19.9	24.4	33.5	21.6	15.5

[a,b] Assignment may be reversed.

In order to clarify this question the two allylic alcohols *9* and *10* were converted by careful osmium tetroxide–sodium periodate oxidation to the corresponding nor-ketones *16* and *17*, respectively. Both these nor-compounds gave mass spectra containing diagnostic peaks at *m/e* 263 (M−15), 235 (M−43), 217 and 191, IR spectra having carbonyl bands at 1720 cm^{-1} and ^1H NMR spectra showing characteristic methyl singlets at δ 2.21 (*16*) and 2.25 (*17*).

Saturation of the 17-methyl singlet at δ 1.17 produced a 13 % nuclear Overhauser enhancement of the H-12 signal for the nor-ketone *16*, whereas the intensity of the H-12 signal for the other nor-ketone *17* was not enhanced when its C-17 signal at δ 1.07 was irradiated. This result is in accordance with 12*R*-configurations in the tetrahydrofurans *9* and *16* and 12*S*-configurations in the tetrahydrofurans *10* and *17*. The ^1H NMR spectra of *9* and *10* supported this view. Thus, while *9* gave rise to a one-proton triplet at δ 3.94 ($J = 5.5$ Hz), the spectrum of *10* contained a multiplet at δ 3.86 ($W_{1/2} =$ 16 Hz) reminiscent of the H-12 signal for (12*S*)-8,12-epoxylabdane-13,17-diol (*15*).[9]

Conclusive evidence for the absolute configurations at C-12 was obtained from an X-ray analysis of the nor-ketone *16*, which crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 19.811$ Å, $b = 10.904$ Å, $c = 7.574$ Å, $Z = 4$. The crystals were unstable in X-rays and in air at room temperature. The structure was solved by direct methods using data collected on two crystals with the computer-controlled Philips PW1100 diffractometer. Data from only one of the crystals ($30° \leq \theta \leq 70°$) were, however, used in the structure refinement ($R = 0.072$). Non-hydrogen atoms were refined with anisotropic thermal parameters but hydrogen atoms have so far not been included in the least-squares procedure. A stereoscopic view of the nor-ketone *16*, summarising the *X*-ray result to be discussed in detail elsewhere, is given in Fig. 2.

Thus, the 8,12-epoxy alcohols *9* and *10* have 12*R*- and 12*S*-configurations, respectively; the chiralities of the remaining unknown asymmetric centre, C-13, in these compounds followed from a consideration of the reaction mechanism involved in the peracid oxidation of (12*Z*)-abienol (*8*).

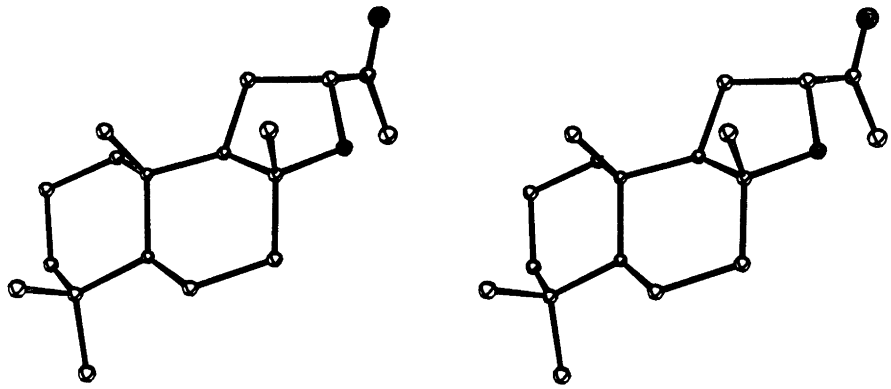
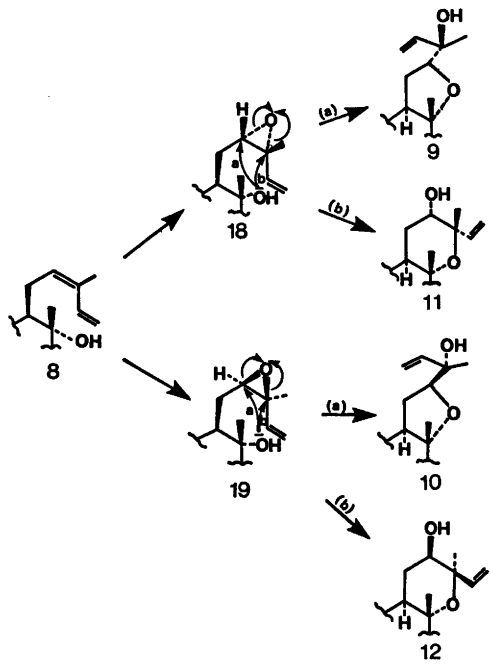


Fig. 2. A stereoscopic view of (12*R*)-14,15-bisnor-8,12-epoxylabdan-13-one (*16*).

Peracid oxidation of linalool is known to proceed *via* the initial generation of two diastereomeric 1,2-epoxides, which are easily converted by acid or heat to two pairs of diastereomeric 1,4- and 1,5-epoxides, the former of which is the main product.[10] It is evident from the structures and proportions of the products obtained that (12*Z*)-abienol (*8*) and peracid react in an analogous manner (*cf.* Scheme 1). Thus, the formation of the two minor oxidation products *11* and *12*, whose structures have been established as (12*S*,13*S*)- and (12*R*,13*R*)-8,13-epoxy-14-labden-12-ol, may be explained as being due to an attack of the 8α-hydroxyl group at the fully substituted C-13 in the intermediate epoxides (12*S*,13*R*)- and (12*R*,13*S*)-12,13-epoxy-14-labden-8-ol (*18*, *19*), respectively, or their equivalents. Similarly, an S_N2 type of oxide opening at the secondary epoxide carbon, C-12, by attack of the 8α-hydroxyl group in the epoxides *18* and *19* would give the diastereomeric (12*R*,13*R*)- and (12*S*,13*S*)-8,12-epoxy-14-labden-13-ols. Since it has been established from the results presented above that, of the 8,12-epoxy alcohols, *9* has the 12*R*- and *10* the 12*S*-configuration, it can be concluded that their chiralities at C-13 are *R* and *S*, respectively.



Scheme 1. Reaction mechanism for the peracid oxidation of (12*Z*)-abienol (*8*).

In conformity with previous findings,[10,11] the use of an acidic medium increased the proportions of the 1,5-epoxides (*11*, *12*). Thus, treatment of (12*Z*)-abienol (*8*) with *m*-chloroperbenzoic acid in acetic acid afforded a mixture of *9*, *10*, *11*, *12* in the ratio 53:15:19:13.

^{13}C NMR spectra. ^{13}C NMR spectroscopy was used in the present study to facilitate the structure determination of the various synthetic products. Since these comprise pairs of diastereoisomers, it was also of interest to evaluate the effects of steric factors on their ^{13}C shieldings.

Table 1 lists the ^{13}C shieldings of (12*Z*)-abienol (*8*) and its oxidation products (*5*, *6*, *9*–*12*, *16*, *17*), as well as those of manoyloxide

(*13*) and epimanoyloxide (*14*), which have been included for comparison. The assignments of the resonances due to C-1 to C-7, C-9, C-10, and C-18 to C-20 for these compounds rest primarily on a comparison with published data for other labdanoids.[12,13] The C-5 and C-9 signals appeared as broad and well-resolved doublets, respectively, in the single-frequency off-resonance decoupled spectra, an observation which corroborated their previous assignment. The identification of the remaining signals for the 8,13-ether bridged compounds (*5*, *6*, *11*, *12*) was guided by the substituent parameters previously obtained for podocarpanes having a 12-oxo or 12-hydroxyl group.[14] The use of shift reagents, $Yb(fod)_3$ and Yb (dpm_3), solved the assignments of the spectra of (12*Z*)-abienol (*8*) and the 8,12-ether bridged compounds *9* and *10*, while the shift analysis for the nor-compounds *16* and *17* was completed by spectral comparison with *9* and *10*.

Reversal of the configuration at C-13 in manoyloxide (*13*→*14*) causes deshielding of C-9 (2.8 ppm) and of C-16 (4.2 ppm), the latter then occupying an equatorial orientation. In contrast, C-17 undergoes shielding (−1.5 ppm), which indicates that the syndiaxial effect of the vinyl group is smaller than that of the methyl group.

Introduction of an axial hydroxyl group in manoyloxide (*13*→*11*) produces a shielding effect at C-9 (−6.6 ppm). As expected, the γ-effect on C-9 caused by the equatorial hydroxyl group in (12*R*,13*R*)-8,13-epoxy-14-labden-12-ol (*12*) is considerably smaller (−0.7 ppm), thus confirming the configurations at C-12 in *11* and *12*.

The methyl group at C-13 being γ-gauche to the equatorial hydroxyl group at C-12 in (12*R*,13*R*)-8,13-epoxy-14-labden-12-ol (*12*) suffers an expected upfield shift of 4.7 ppm. This result is of diagnostic importance since, having established the orientation of the hydroxyl group, the chemical shift value of the C-16 signal in this compound (*12*; 28.0 ppm), when compared with the corresponding values for manoyloxide (*13*; 28.5 ppm) and epimanoyloxide (*14*; 32.7 ppm) is compatible only with an α-orientation of the C-16 methyl group. The small shielding effect (−1.0 ppm) observed at C-16 on introduction of an axial hydroxyl group in manoyloxide (*13*→*11*) can be explained in terms of an γ-*anti* heteroatom effect.[15]

It is noteworthy that the shielding at C-14 and the deshielding at C-15 caused by the introduction of the hydroxyl group is larger in (12*R*,13*R*)- than in (12*S*,13*S*)-8,13-epoxy-14-labden-12-ol (*12*, *11*), an effect which in the case of the different C-14 shieldings may possibly be related to the fact that C-14 experiences γ-gauche interactions with two larger atoms at C-12 in *12* (OH and C-11), but with only one larger atom (OH) in *11*.

The introduction of a 12-oxo group in manoyloxide (*13*→*5*) and in epimanoyloxide (*14*→*6*) causes shielding at C-16. As previously observed in related cases,[12] the effect is larger at the equatorial than at the axial methyl group, −4.1 as against −1.9 ppm.

With the stereochemistry of the 8,12-epoxy alcohols *9* and *10* at hand, it can be concluded that the interaction between C-17 and the β-oriented substituent at C-12 in *10* gives rise to a deshielding of C-17 (25.4 ppm in *10* as against 21.3 ppm in *9*), which may be analogous to the syn-diaxial δ-effect previously observed for substituents attached to six-membered rings.[16–19] A similar effect, although less marked, is found in the spectra of the nor-compounds *16* and *17*, *i.e.* the C-17 signal occurs at 23.0 ppm in the spectrum of the compound having the acetyl-group β-oriented (*17*), while it appears at 21.5 ppm in the spectrum of the C-12 epimer (*16*).

EXPERIMENTAL

Melting points, rotations, infrared and mass spectra were recorded on Leitz Wetzlar, Perkin-Elmer 141, Perkin-Elmer 257 and LKB 2091 instruments respectively. ^1H NMR (100 MHz) and Fourier transform ^{13}C NMR (25.16 MHz) spectra were obtained in $CDCl_3$ solutions using TMS as internal standard on a Varian XL-100 spectrometer equipped with S-124 FT and disc accessories and controlled by a Varian 620/L (16K) computer. Gas chromatography (GC) was performed on a Varian 1700 instrument using a glass capillary column (0.35 mm × 25 m) coated with Emulphor for analytical work and a steel column (10 mm × 2 m) packed with Apiezon L (2.5 %) on Chromosorb for preparative work. GC integrations were carried out on an Autolab System 1 integrator.

Isolation of (12Z)-abienol (8). Commercial Canada balsam, Chroma-Gesellschaft, Stutt-

gart-Untertürkheim, was chromatographed over silica gel using a light petrol/acetone gradient to give (12*Z*)-abienol, indistinguishable from an authentic sample,[20] in approximately 10 % yield. The homogeneity of the isolated material was checked by ^1H and ^{13}C NMR spectroscopy. Relative shifts of the ^{13}C NMR signals for *8* on addition of Yb(fod)$_3$ were: C-1 12; C-2 7; C-3 6; C-4 8; C-5 17; C-6 21; C-7 54; C-8 100; C-9 47; C-10 22; C-11 32; C-12 18; C-13 10; C-14 6; C-15 2; C-16 0; C-17 51; C-18 4; C-19 6; C-20 16. The measurements were made within the linear LIS range (shift reagent substrate ratio 0 – 0.5) and were normalized by arbitrarily assigning the value 100 to the carbon signal exhibiting the largest shift.

Treatment of (12Z)-abienol (8) with m-chloroperbenzoic acid. A: A solution of 516 mg of (12*Z*)-abienol (*8*) in 20 ml of acetic acid was stirred with 360 mg of *m*-chloroperbenzoic acid. After 45 min at room temperature the reaction mixture was diluted with water and extracted with ether. The ether solution was washed with aqueous $NaHCO_3$, dried and evaporated. Chromatography over silica gel furnished 65 mg of (12*S*,13*S*)-8,13-epoxy-14-labden-12-ol (*11*) and 273 mg of a mixture consisting of three components. This was separated by preparative GC into 110 mg of (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (*9*), 31 mg of (12*S*,13*S*)-8,12-epoxy-14-labden-13-ol (*10*) and 69 mg of (12*R*,13*R*)-8,13-epoxy-14-labden-12-ol (*12*).

(12S,13S)-8,13-epoxy-14-labden-12-ol, (*11*) gum, $[\alpha]_D + 30°$ (*c* 1.2 in $CHCl_3$), (Found: M^+ 306. Calc. for $C_{20}H_{34}O_2$: mol. wt 306) IR band at 3580 cm^{-1}, ^1H NMR peaks at δ 0.80 (6 H, s), 0.86 (3 H, s) 1.29 (3 H, s), 1.33 (3 H, s), 3.69 (1 H, t, $J = 3.5$ Hz), 5.20 (1 H, dd, $J = 2.5$ and 10 Hz), 5.42 (1 H, dd, $J = 2.5$ and 17.5 Hz) and 5.84 (1 H, dd, $J = 10$ and 17.5 Hz) and MS peaks at *m/e* (%): 306 (M, 0.1), 291 (1), 288 (0.4), 273 (2), 236 (2), 235 (2), 221 (2), 217 (2), 206 (1), 192 (100), 191 (17), 177 (98), 149 (6), 137 (13), 136 (15), 123 (33), 95 (22), 81 (25), 69 (31), 55 (23), and 41 (24).

(12R,13R)-8,12-epoxy-14-labden-13-ol, (*9*) was identical in all respects ($[\alpha]_D$, IR, ^1H NMR, MS and GC retention time on a capillary column) with isomer "Ib" of Greek tobacco.[8] Relative shifts of the ^{13}C NMR signals on addition of Yb(dpm)$_3$ were: C-1 0; C-2 0; C-3 0; C-4 0; C-5 2; C-6 4; C-7 10; C-8 22; C-9 21; C-10 5; C-11 33; C-12 57; C-13 100; C-14 47; C-15 27; C-16 58; C-17 12; C-18 0; C-19 0; C-20 3.

(12S,13S)-8,12-epoxy-14-labden-13-ol, (*10*) gum, $[\alpha]_D$ −15° (*c.* 2.3 in $CHCl_3$) had IR bands at 3580, 3480 and 1645 cm^{-1}, ^1H NMR peaks at δ 0.83 (3 H, s), 0.87 (6 H, s), 1.19 (6 H, s), 3.86 (1 H, m, $W_{1/2} = 16$ Hz), 5.11 (1 H, dd, $J = 1.5$ and 10.5 Hz), 5.30 (1 H, dd, $J = 1.5$ and 17 Hz), and 5.98 (1 H, dd, $J = 10.5$ and 17 Hz). Relative shifts of the ^{13}C NMR signals on addition of Yb(dpm)$_3$ were: C-1 3; C-2 1; C-3 1; C-4 1; C-5 3; C-6 3; C-7 7; C-8 21; C-9 15; C-10 5; C-11 28; C-12 44; C-13 100; C-14 46; C-15 28; C-16 53; C-17 12; C-18 0; C-19 0; C-20 1. The mass spectrum and the GC retention time were indistinguishable from those of isomer "Id" of Greek tobacco.[8]

(12R,13R)-8,13-epoxy-14-labden-12-ol, (*12*) had m.p. 100 – 102 °C, $[\alpha]_D + 37°$ (*c.* 0.78, $CHCl_3$) (Found: M^+ 306. Calc. for $C_{20}H_{34}O_2$: mol. wt 306). IR bands at 3630 and 3460 cm^{-1}, ^1H NMR peaks at δ 0.77 (3 H, s), 0.79 (3 H, s), 0.86 (3 H, s), 1.34 (3 H, s), 1.45 (3 H, s), 3.50 (1 H, dd, $J = 5$ and 10 Hz), 5.23 (1 H, dd, $J =$ 1.5 and 11 Hz), 5.42 (1 H, dd, $J = 1.5$ and 18 Hz), and 6.32 (1 H, dd, $J = 11$ and 18 Hz) and MS peaks at *m/e* (%): 306 (M, 1), 291 (1), 288 (1), 273 (1), 236 (2), 235 (3), 221 (3), 217 (2), 206 (1), 192 (100), 191 (23), 177 (99), 149 (18), 137 (15), 136 (16), 123 (33), 95 (20), 81 (23), 69 (30), 55 (19) and 41 (21).

B: Treatment of 500 mg of (12*Z*)-abienol (*8*) with 400 mg of *m*-chloroperbenzoic acid in 20 ml $CHCl_3$ for 1 h at ambient temperature afforded a mixture from which 131 mg of (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (*9*) and 50 mg of (12*S*,13*S*)-8,12-epoxy-14-labden-13-ol (*10*) were isolated by preparative GC.

Preparation of (13S)-8,13-epoxy-14-labden-12-one (5). To a solution of 38 mg of *11* in 5 ml of acetone, 0.7 ml of Jones' reagent [14 mg CrO_3 in 0.7 ml of aqueous H_2SO_4 (20 %)] was added with stirring. After 10 min at room temperature the reaction mixture was worked up in the usual manner. Chromatography over silica gel gave 19 mg of (13*S*)-8,13-epoxy-14- labden-12-one (*5*), which was identical in all respects with an authenthic sample.[7]

Preparation of (13R)-8,13-epoxy-14-labden-12-one (6). Treatment of 20 mg of *12* with 0.4 ml of Jones' reagent in 5 ml of acetone afforded 15 mg of (13*R*)-8,13-epoxy-14-labden-12-one (*6*), indistinguishable from an authentic sample.[7]

Preparation of (12R)-14,15-bisnor-8,12-epoxylabdan-13-one (16). A solution of 70 mg of *9* in 20 ml of dioxane/H_2O (3:1) was stirred with 15 mg of osmium tetroxide at 0 °C for 10 min. After addition of 300 mg of sodium periodate the mixture was stirred at 0 °C for 60 h. Dilution with water, extraction with ether and chromatography over silica gel using a hexane/ether gradient afforded 39 mg of (12*R*)-14,15-bisnor-8,12-epoxylabdan-13-one (*16*), which had m.p.'s 77 – 79, 108 – 109 °C, IR band at 1720 cm^{-1}, ^1H NMR peaks at δ 0.84 (6 H, s), 0.88 (3 H, s), 1.17 (3 H, s), 2.21 (3 H, s) and 4.38 (1 H, dd, $J = 3.5$ and 9.5 Hz) and MS peaks at *m/e* (%): 263 (M – 15, 1), 235 (35), 217 (18), 191(100), 137 (38) 109 (28), 95 (21), 81 (21), 69 (33), 55 (14), 43 (24) and 41 (21).

Preparation of (12S)-14,15-bisnor-8,12-epoxylabdan-13-one (17). Treatment of 30 mg of *10* with 5 mg of osmium tetroxide and 100 mg of sodium periodate in 5 ml of dioxane/H_2O (3:1) at 0 °C for 6 h gave 13 mg of (12*S*)-14.15-bisnor-8,12-epoxylabdan-13-one (*17*), which had m.p.'s

82–84, 105–107 °C, IR band at 1720 cm^{-1}, ^1H NMR peaks at δ 0.83 (6 H, s) 0.88 (3 H, s), 1.07 (3 H, s), 2.25 (3 H, s) and 4.32 (1 H, t, $J = 8$ Hz), MS peaks at m/e (%): 278 (M, 1), 263 (3) 235 (42), 217 (20), 191 (100), 137 (45), 109 (26), 95 (18), 81 (20), 69 (43), 55 (15), 43 (18) and 41 (21).

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