of *10* showed, *inter alia*, signals for the anomeric carbon atoms of the xylose and galactose residues at 100.6 ppm and 102.5 ppm, respectively. The corresponding signals for *N*-benzyloxycarbonyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl)-L-serine benzyl ester [4] and methyl tetra-*O*-benzoyl-β-D-galactopyranoside appear at 99.9 and 102.4 ppm, respectively. In the spectrum of *10*, no other signals in the region of anomeric carbons were observed.

O-β-D-Galactopyranosyl-(1→4)-O-β-D-xylopyranosyl-L-serine (*4*). Compound *10* (4.91 g) was dissolved in ethyl acetate – ethanol – acetic acid – water (5:20:5:1, 150 ml) and hydrogenated at 0.5 MPa using 10 % palladium on charcoal (2.0 g) as catalyst. The reaction was complete in 24 h. Filtration and concentration gave a syrup which was dissolved in methanol (250 ml). The solution was saturated with ammonia gas and left at +4 °C for 4 days. Concentration gave a syrup, which was partitioned between water and chloroform. The water phase was washed several times with chloroform, concentrated to half the volume and lyophilized. The resulting syrup (2.6 g) showed two main silver nitrate-positive spots on paper chromatography (ethyl acetate – acetic acid – water, 3:1:1), one having the same R_F value as compound *2*, the other corresponding to compound *4*. The syrup was fractionated in 200 mg portions on a Sephadex LH-20 column (50 × 2 cm) using ethanol – water (1:1) as eluent. The ninhydrin-positive fractions were collected and minor impurities removed by gel filtration on a Bio-Gel P-2 column (5 × 100 cm) to give a total of 320 mg partially racemized *4*, having $[\alpha]_D^{25} - 27°$ (*c* 0.5, H_2O).

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Tobacco Chemistry. 46. Syntheses of (12*R*,13*S*)- and (12*S*,13*R*)-8,12-Epoxy-14-labden-13-ol and (12*S*,13*R*)-8,13-Epoxy-14-labden-12-ol, Three Tobacco Diterpenoids

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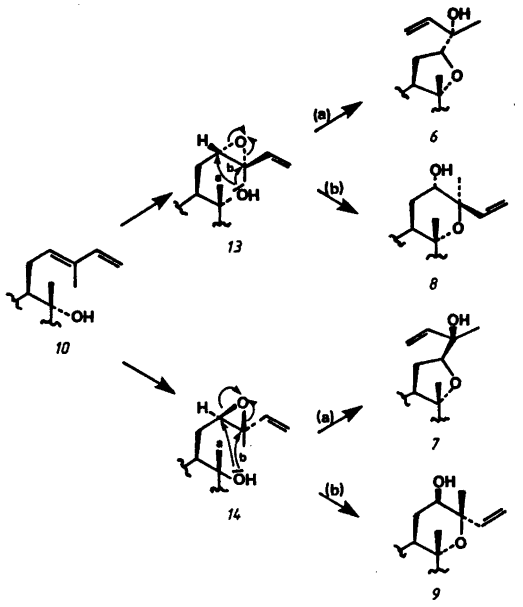
In a previous communication we described the synthesis of four tobacco diterpenoids, the (12*R*,13*R*)- and (12*S*,13*S*)-8,12-epoxy-14-labden-13-ols (*1*, *2*) and the (13*R*)- and (13*S*)-8,13-epoxy-14-labden-12-ones (*3*, *4*) from (12*Z*)-abienol (*5*),[1] a compound which has been proposed as an appropriate precursor of the tobacco labdanoids.[2] We now report the preparation of three additional tobacco labdanoids by peracid oxidation of (12*E*)-abienol (*10*), the double bond isomer of starting material *5*.

Treatment of (12*E*)-abienol (*10*) with *m*-chloroperbenzoic acid in chloroform afforded four products of low polarity (*6* – *9*), which according to GC-integration were present in the ratio 49:6:29:16, as well as two compounds of higher polarity, the (12*S*,13*S*,14ξ)- and (12*R*,13*R*,14ξ)-8,12-13,14-diepoxy-15-labdanols constituting some 20 % of the total reaction mixture. The latter two compounds are formed by a novel type of mechanism, which will be discussed elsewhere.[3]

Of the less polar products, *6* and *7* proved to be identical to two of the stereoisomers of (12ξ,13ξ)-8,12-epoxy-14-labden-13-ol, which have previously been encountered in Greek tobacco and then designated "Ia" and "Ic", respectively.[4] The configuration at C-12 in the tetrahydrofurans *6* and *7* was deduced from the ^{13}C NMR spectra (*cf.* Table 1). The C-12 and C-17 signals for compound *6* appeared at δ 81.7 and 21.4, respectively, which is close to the corresponding values, 81.6 and 21.3 ppm, for (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (*1*) and is consistent with a 12*R*-configuration in compound *6*.[1] Since the C-12 and C-17 signals were present at δ 85.5 and 25.5 for compound *7* and at δ 85.3 and 25.4 for (12*S*,13*S*)-8,12-epoxy-14-labden-13-ol (*2*), it was concluded that compound *7* has the 12*S*-configuration. With these results at hand the chiralities at C-13 followed from a consideration of the reaction mechanism involved in the peracid oxidation of (12*E*)-abienol (*10*) (*cf.* Scheme 1). Thus, an S_N2 type of oxide opening at the secondary C-12 in the intermediate epoxides *13* and *14*, or their equivalents, by attack of the 8α-hydroxyl group affords the (12*R*,13*S*)- and (12*S*,13*R*)-8,12-epoxy-14-labden-13-ols (*6*, *7*), respectively.



Scheme 1.

Of the remaining two less polar products, *8* was identical to (12*S*,13*R*)-8,13-epoxy-14-labden-12-ol, previously isolated from Turkish tobacco.[5] The second compound (*9*) gave a mass spectrum, which contained diagnostically important peaks at *m/e* 291 (M-15), 236, 235, 206, 192 and 177 [1] and was virtually identical to that of the tetrahydropyran *8*. This suggested that compound *9* was the remaining oxidation product to be expected, *i.e.* (12*R*,13*S*)-8,13-epoxy-14-labden-12-ol (Scheme 1). In agreement with this the ^{1}H NMR spectrum displayed the H-14, H-15a and H-15b signals as a typical ABX system with $J_{AB}=1.5$, $J_{AX}=10$ and $J_{BX}=17$ Hz. The H-12 signal appeared as a doublet of doublets at δ 3.53, whose coupling constants ($J=5$ and 10 Hz) confirmed the equatorial orientation of the secondary hydroxyl group at C-12.

Since three of the products obtained by peracid oxidation of (12*E*)-abienol (*10*), *i.e.* compounds *6*–*8*, are tobacco constituents,[4,5] and since none of these are formed by peracid oxidation [1] or photo-oxygenation [6] of (12*Z*)-abienol (*5*), it is reasonable to assume that both isomers of abienol (*5*, *10*) may serve as precursors of the labdanes and nor-labdanes found in processed tobacco.

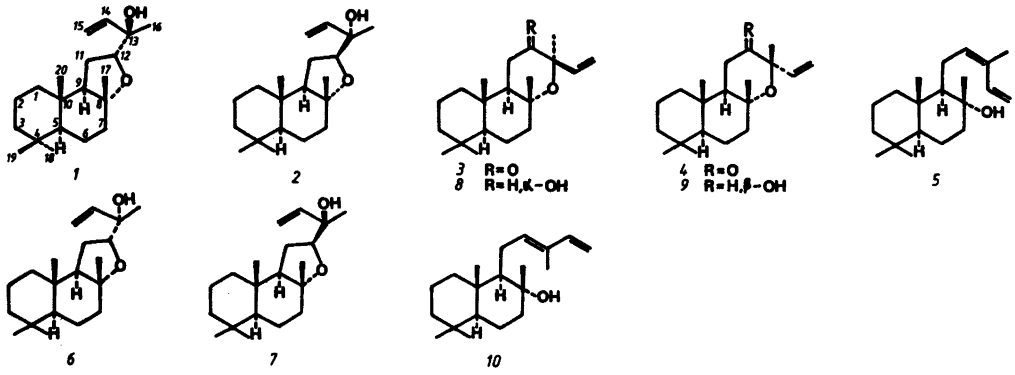
Experimental. For instrumental details, see Ref. 1.

Conversion of (12Z)-abienol (5) to (12E)-abienol (10). (12*Z*)-Abienol (*5*, 2 g), obtained from commercial Canada balsam,[1] was stirred with 2.25 g of mercuric acetate in 50 ml of acetic acid at room temperature for 20 min.

Table 1. Carbon-13 chemical shifts and assignments for compounds 6–10.[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
6	39.8[b]	18.4	42.4	33.1	57.3	20.6	39.7[b]	81.4	60.1	36.3	24.3	81.7	74.5	141.3	113.5	24.8	21.4	33.5	21.1	14.8
7	40.9	18.5	42.5	33.2	57.2	21.4	40.2	81.2	61.1	36.5	24.4	86.5	73.4	141.2	113.4	26.9	25.5	33.5	21.0	15.9
8	39.0	18.5	42.1	33.3	56.6	20.0	42.8	76.0	49.8	36.4	23.7	69.0	76.2	147.3	110.5	26.9	24.4	33.3	21.2	15.8
9	39.2	18.6	42.2	33.3	56.3	19.9	42.4	75.4	57.8	36.9	24.3	76.3	77.3	145.7	112.8	19.9	24.7	33.3	21.2	16.0
10	40.1	18.6	41.9	33.2	56.1	20.4	44.1	73.7	62.2	38.9	24.0	136.4	132.1	141.7	110.0	11.8	24.1	33.5	21.6	16.4

[a] δ-Values relative to TMS. [b] Assignment may be reversed.



Zinc dust (6 g) was added and stirring was continued for 1 h.[7] After filtration, the reaction mixture was diluted with water, extracted with ether, washed with aqueous $NaHCO_3$, dried and evaporated. The residue obtained, which according to GC analysis consisted of *5* and *10* in the ratio 1:10, was carefully chromatographed over silica gel to afford 1.3 g of (12*E*)-abienol (*10*). This sample which contained only trace amounts of the (12*Z*)-isomer (*5*), had m.p., $[\alpha]_D$, IR and ^1H NMR identical to those reported for an authentic sample.[7]

Treatment of (12E)-abienol (10) with m-chloroperbenzoic acid. A solution of 1.0 g of (12*E*)-abienol (*10*) in 40 ml of $CHCl_3$ was left with 800 mg of *m*-chloroperbenzoic acid at room temperature for 1 h. The solution was washed with aqueous $NaHCO_3$, dried, evaporated and separated by chromatography over silica gel using a hexane/acetone gradient into fractions 1–7 weighing 30, 221, 70, 145, 120, 28 and 145 mg, respectively. Fractions 1–4 were separated further by high performance liquid chromatography using a column packed with μ-Porasil (Waters) and hexane/acetone as eluent to give compounds *6–9*, while fraction 7 afforded the polar oxidation products.

(12R,13S)-8,12-Epoxy-14-labden-13-ol (6) was identical in all respects ($[\alpha]_D$, IR, ^1H NMR, MS and GC retention time on a capillary column) with isomer "Ia" of Greek tobacco.[4]

(12S,13R)-8,12-Epoxy-14-labden-13-ol (7) had m.p. 85–86°, $[\alpha]_D$ −18° (*c* 0.5 in $CHCl_3$); IR (CCl_4) bands at 3590 and 1645 cm^{-1}; ^1H NMR: δ 0.82 (3 H, s), 0.83 (3 H, s), 0.87 (3 H, s), 1.16 (3 H, s), 1.31 (3 H, s), 3.80 (1 H, m), 5.12 (1 H, dd, $J=2$ and 10.5 Hz), 5.31 (1 H, dd, $J=2$ and 17 Hz) and 5.89 (1 H, dd, $J=10.5$ and 17 Hz). The mass spectrum and the GC retention time were indistinguishable from those of isomer "Ic" of Greek tobacco.[4]

(12S,13R)-8,13-Epoxy-14-labden-12-ol (8) had m.p. 130–132° (reported 141–142°); $[\alpha]_D$, IR and ^1H NMR spectra were identical with those reported for an authentic sample.[5] *8* had MS peaks at *m/e* (%): 306 (M, 0.1), 273 (1), 262 (1), 236 (0.5), 235 (0.5), 221 (2), 206 (2), 192 (100), 177 (91), 163 (2), 149 (13), 137 (10), 136 (12), 123 (28), 95 (15), 81 (18), 69 (23), 55 (20) and 41 (18).

(12R,13S)-8,13-Epoxy-14-labden-12-ol (9) had m.p. 119–120°, $[\alpha]_D$ +24° (*c* 0.27 in $CHCl_3$); IR (CCl_4) bands at 3620, 3460 and 1640 cm^{-1}; ^1H NMR: δ 0.81 (6 H, s), 0.87 (3 H, s), 1.33 (3 H, s), 1.35 (3 H, s), 3.53 (1 H, dd, $J=5$ and 10 Hz), 5.10 (1 H, dd, $J=1.5$ and 10 Hz), 5.25 (1 H, dd, $J=1.5$ and 17 Hz) and 5.93 (1 H, dd, $J=10$ and 17 Hz); MS peaks at *m/e* (%): 291 (M−15, 1), 273 (2), 262 (2), 236 (1), 235 (1), 221 (2), 206 (2), 192 (100), 177 (83), 163 (3), 149 (13), 137 (10), 136 (11), 123 (26), 95 (12), 81 (18), 69 (22), 55 (18) and 41 (18).

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