Tobacco Chemistry. 53.* Two New Nor-Drimanes from Greek Tobacco

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Compounds belonging to the labdane/nor-labdane and drimane/nor-drimane groups have been identified in certain tobacco varieties, *e.g.* oriental tobaccos.[1] Their presence has aroused interest, since they are partly responsible for the characteristic flavour notes of these tobaccos. We now report the isolation of two new nor-drimanes (*1*, *2*) from Greek tobacco.

Results. The first compound (*1*), $C_{14}H_{26}O_2$, is a diol (OH-absorption in the IR spectrum) having a secondary and a tertiary hydroxyl group (^{13}C NMR signals at δ 86.9 (d) and 74.0 (s); *cf.* Table 1). It contains four methyl groups, of which one, resonating at δ 1.22, is attached to the carbon atom carrying the tertiary hydroxyl group, and the remaining three, also giving rise to singlets in the ^1H NMR spectrum, are linked to other fully substituted carbon atoms. Since the ^1H and ^{13}C NMR spectra were devoid of signals due to double bonds, it followed that diol *1* was carbobicyclic and an 11-nor-8,ξ-drimanediol structure seemed most plausible from a biogenetic point of view.[1]

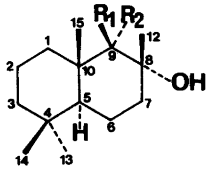
A comparison, which showed that nine signals in the ^{13}C NMR spectrum of diol *1* were of appropriate multiplicities and had chemical shift values close to those recorded for the C-1 to C-4, C-6, C-8, C-10, C-18 and C-19 signals for sclareol (*3*),[2] was in harmony with this view and indicated that the secondary hydroxyl group in diol *1* was present in ring B. Its allocation to C-9 followed from the NMR results, *i.e.* the proton under the secondary hydroxyl group resonated as a singlet and the chemical shift value of the signal ascribed to C-10, δ 39.4 (s), is only compatible with the presence of a substituent at C-9 (β-effect,[3] *cf.* Table 1, which also includes data for compounds *4*–*6* for comparison purposes). Since the spectral data of diol *1* were similar but not identical to those of 11-nor-8,9*S*-drimanediol (*4*),[4] diol *1* was provisionally identified as the corresponding 9*R*-epimer.

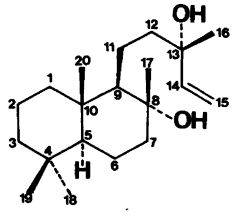
This assignment was readily verified by chemical means. Thus, treatment of 11-nor-8-hydroxy-9-drimanone (*7*)[4] with $LiAlH_4$ yielded, as expected, two diols (*1*, *4*, ratio 10:1), of which the major, 11-nor-8,9*R*-drimanediol, proved to be indistinguishable from the new tobacco diol (*1*).

The second tobacco isolate (*2*), $C_{14}H_{26}O$, gave IR, mass, ^1H and ^{13}C NMR spectra identical to those of synthetic (±)-11-nor-8-drimanol.[5] Its absolute configuration was determined by chemical means. Thus, treatment of 8-hydroxy-11-drimanal (*8*)[6] with tris(triphenylphosphine)rhodium chloride[7] yielded 11-nor-8-drimanol, which exhibited essentially the same optical activity as the naturally occurring compound (*2*).

As has been proposed previously for structurally related C_{14}-compounds,[4,8] the two new alcohols (*1*, *2*), formally classified as nor-drimanes, may in fact arise in tobacco by biodegradation of labdanic (C_{20}) precursors. A plausible pathway, which involves an initial and experimentally verified conversion of 12*Z*-abienol (*9*) to the C_{18}-enone *11 via* the intermediate hydroperoxide *10*,[9] is shown in Scheme 1. The enone (*11*) undergoes degradation to give 11-nor-8-hydroxy-9-drimanone (*7*), which is reduced to diol *1*, or to yield 8-hydroxy-11-drimanal (*8*), which may give rise to mono-ol *2* either directly by decarbonylation or *via* the acid (*12*) and decarboxylation. Support for this pathway is

* For part 52 see Ref. 16.





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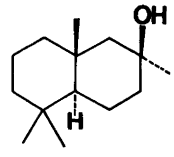

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1 R_1 = OH; R_2 = H
2 R_1 = R_2 = H
4 R_1 = H; R_2 = OH
6 R_1 = CH_3; R_2 = H
7 R_1, R_2 = O
8 R_1 = CHO; R_2 = H

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Table 1. Carbon-13 chemical shifts and assignments for compounds *1* – *6*.[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	38.7	18.3	41.9	33.0	53.3	19.9	40.0	74.0	86.9	39.4		22.2	33.2	21.6	13.7					
2	42.4	18.6	42.7	33.0	54.4	20.7	43.0	71.1	59.8	35.0		29.1	33.2	21.2	20.9					
3[2]	39.5	18.8	41.9	33.1	55.9	20.4	43.9	74.3	61.4	39.0	18.4	44.8	73.0	146.2	110.3	26.2	24.0	33.3	21.4	15.3
4[4]	36.9	18.2	42.0	33.0	45.2	20.0	35.5	72.6	84.1	39.0		27.0	33.0	21.7	20.4					
5[5]	42.6	18.6	42.6	33.1	54.4	18.4	41.3	71.0	57.1	34.7		33.1	33.3	21.4	20.9					
6[12]	39.9	18.7	42.0	33.3	56.2	20.5	44.5	73.1	55.6	37.8	7.4	23.1	33.5	21.6	14.4					

[a] δ-Values in $CDCl_3$ relative to TMS.

provided by the fact that, besides 12*Z*-abienol (*9*), which is the major labdanoid of the cuticular wax of the green leaf,[10] compounds *7*[4] and *11*,[6] as well as the 13*R*- and 13*S*-alcohols corresponding to hydroperoxide *10*[11] have been found present in tobacco. It cannot presently be excluded, however, that 8-hydroxy-11-drimanal (*8*) may be a genuine sesquiterpenoid derived from 8,11-drimanediol (*13*), which is a tobacco constituent.[12]

Mass spectra. The mass spectral fragmentation of compounds *1* and *2* include reactions that are worth commenting upon. Thus, diol *1* decomposes to form a characteristic ion of mass 196. The reaction involves loss of a CH_2O fragment and may proceed as indicated in Scheme 2 with breakages of the 9,10 and 8,9 bonds. An analogous reaction leading to elimination of carbon monoxide is observed in the spectrum of 11-nor-8-hydroxy-9-drimanone (*7*).

The influence of stereochemistry on the fragmentation pattern[13] is demonstrated by a comparison of the spectra of 11-nor-8-drimanol (*2*) and the corresponding 8-epimer (*5*). Thus, as shown in Table 2 the 8*R*-alcohol *2* gives rise to a more intense $[M-18]^{\cdot+}$ peak than the 8*S*-alcohol *5*, whereas the reverse is true for the $[M-15]^+$ peaks. This result is rationalized by the fact that a transannular 1,4 dehydration reaction involving the tertiary hydrogen at C-5 is only possible in the 8*R*-epimer *2*.

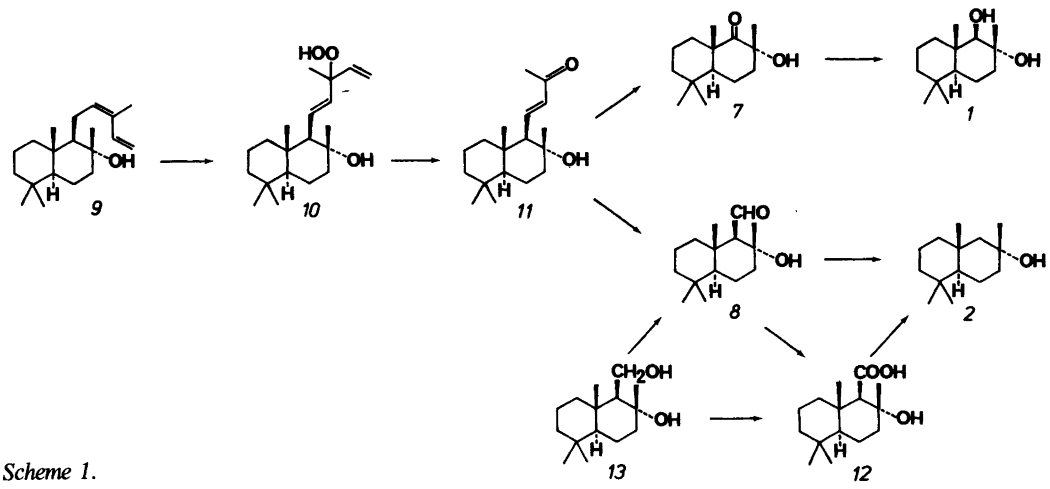
Experimental. With the exception of accurate mass measurements, which were carried out on a Kratos' MS50-Stereo DS50 SM/DS50 S mass spectrometer/computer system, the instruments specified in Ref. 14 were used.

Isolation. 11-Nor-8,9*R*-drimanediol (*1*, 1.5 mg) was isolated from fraction B9 and 11-nor-8-drimanol (*2*, 2 mg) from fraction B7 of an extract obtained from 295 kg of sun-cured Greek tobacco[15] by column chromatography over silica gel followed by HPLC using columns packed with μ-Bondapak/CN and μ-Porasil.

11-Nor-8,9*R*-drimanediol (*1*) had m.p. 153 – 154 °C, $[\alpha]_D$ –15° (*c* 0.06, $CHCl_3$); (Found: $M^{\cdot+}$ 226.1902. Calc. for $C_{14}H_{26}O_2$: 226.1932); IR (CCl_4)

Table 2. Intensities, $I/\sum_{40}^{M} I$, of the M, $[M-15]^+$ and $[M-18]^{\cdot+}$ peaks in the mass spectra of compounds *2* and *5* (70 eV).

Compound	I_M	I_{M-15}	I_{M-18}
2	0.05	0.2	2.9
5[5]	0.08	2.1	1.8

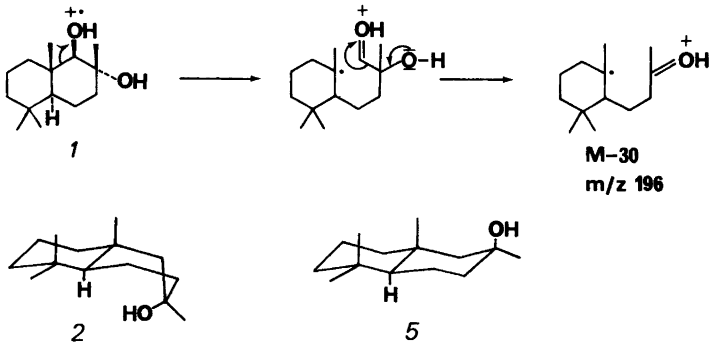


Scheme 1.

bands at 3590, 3450, 1390 and 1370 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (3H, s), 0.89 (6H, s), 1.22 (3H, s) and 3.12 (1H, s); MS [*m/z* (%, composition)]: 226 (M, 24), 211 (3, $C_{13}H_{23}O_2$), 208 (10, $C_{14}H_{24}O$), 196 (30, $C_{13}H_{24}O$), 193 (13, $C_{13}H_{21}O$), 177 (23, $C_{13}H_{21}$), 138 (66, $C_{10}H_{18}$), 123 (51, C_9H_{15}), 109 (43), 95 (70, C_7H_{11}), 82 (55, C_6H_{10} and C_5H_6O), 69 (54, C_5H_9), 55 (39, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

11-Nor-8-drimanol (*2*) was obtained as an oil, which had $[\alpha]_D$ −10° (*c* 0.03; $CHCl_3$) (Found: $M^{\cdot+}$ 210.2016. Calc. for $C_{14}H_{26}O$: 210.1983); ^1H NMR ($CDCl_3$): δ 0.78 (3H, s), 0.87 (3H, s), 0.97 (3H, s) and 1.32 (3H, s); the IR and mass spectral data agreed with those published for (±)-11-nor-8-drimanol.[5]

Preparation of the 9R- and 9S-11-nor-8,9-drimanediols (1 and 4). A solution of 5.6 mg of 11-nor-8-hydroxy-9-drimanone (*7*)[4] in 5 ml of ether was reacted with an excess of LAH at room temperature for 15 min. Work up and separation by HPLC using a column packed with μ-Porasil and hexane–ethyl acetate (60:40) as an eluent furnished the two diastereomeric 8,9-diols. The most polar of these, 11-nor-8,9*R*-drimanediol (*1*, 4.9 mg) had m.p. 153 −155 °C, $[\alpha]_D$ −7.9°; (*c* 0.44, $CHCl_3$) and gave IR, mass, ^1H and ^{13}C NMR spectra identical to those of tobacco diol *1*. The least polar diol, 11-nor-8,9*S*-drimanediol (*4*, 0.5 mg), was identified by comparison of its ^1H NMR and mass spectra with those of an authentic sample.[4]



Scheme 2.

Preparation of 11-nor-8-drimanol (2). A solution of 9.6 mg of 8-hydroxy-11-drimanal (*8*)[6] in 3.5 ml of xylene was refluxed with 38.6 mg of tris(triphenylphosphine)rhodium chloride for 5 h.[7] The reaction mixture was diluted with water, extracted with ether and evaporated to afford a residue. This was purified by chromatography over silica gel followed by HPLC using a column packed with μ-Porasil and hexane – ethyl acetate (80:20) as an eluent to give 4.2 mg of 11-nor-8-drimanol, which had $[\alpha]_D$ $-4°$ (*c* 0.4, $CHCl_3$). Its IR, ^1H NMR and mass spectra were identical to those of the naturally occurring *2*.

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