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Short Communications

Tobacco Chemistry. 45. (2*E*,6*S*)-2,6-Dimethyl-2,7-octadiene-1,6-diol, a New Monoterpenoid from Greek Tobacco

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Recent investigations have demonstrated the presence in tobacco of a large number of isoprenoids. Although the majority of these belongs to the groups of nor-compounds derived from diterpenoids and carotenoids, they also include several mono-, sesqui-, di-, tri- and polyisoprenoids.[1] The present report describes the structure determination and synthesis of a new linear monoterpene diol isolated from Greek tobacco.

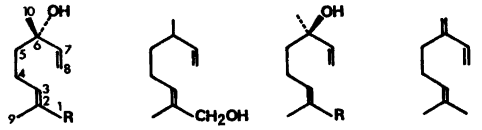
The new tobacco constituent (*1*) had the composition $C_{10}H_{18}O_2$. As shown by the IR spectrum (3600 and 3420 cm^{-1}) and the ^{13}C NMR spectrum [δ 68.3 (t) and 73.3 (s)] the two oxygen atoms were accommodated by a primary and a tertiary hydroxyl group.

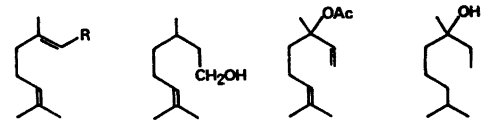
Spin-decoupling experiments demonstrated that the hydroxymethyl and a methyl group, which gave rise to a broadened two-proton singlet at δ 4.00 and a broadened three-proton singlet at δ 1.67, respectively, were attached to a fully substituted olefinic carbon and long-range coupled to an olefinic methine group (δ 5.43). The latter was adjacent to an sp^3 methylene group (δ 2.13), *i.e.* the new tobacco diol incorporates partial structure A: $-CH_2CH=C(CH_3)CH_2OH$. This result was in accordance with the ^{13}C NMR spectrum, which, besides the signal assigned to the hydroxymethyl group, included signals due to one methyl, one sp^3 methylene, one sp^2 methine and one fully substituted sp^2 carbon.

The remaining signals in the ^{13}C NMR spectrum corresponded to one methyl, one sp^3 and one sp^2 methylene, one sp^2 methine and the hydroxyl-carrying fully substituted carbon. In agreement with this the ^1H NMR spectrum included three signals in the olefinic region, which appeared as an ABX system with $J_{AB}=1.5$, $J_{AX}=10.5$ and $J_{BX}=17.5$ Hz, *i.e.* the vinyl group was attached to the fully substituted hydroxyl-bearing carbon. The latter must also be linked to the methyl group (δ 1.30) and to partial structure A *via* the remaining sp^3 methylene group. Thus, the new tobacco diol could be formulated as 2,6-dimethyl-2,7-octadiene-1,6-diol (*1*).

In harmony with this formulation a comparison showed that six signals in the ^{13}C NMR spectrum of diol *1* had chemical shift values close to those assigned to the C-4 – C-8 and C-10 signals for linalool (*2*) (*cf.* Table 1). The remaining four signals corresponded to those ascribed to the C-1 – C-3 and C-9 signals for 2,6-dimethyl-2,7-octadien-1-ol (*3*),[2] an observation which was in accordance with a 2*E*-configuration in diol *1*.

Since the oxidation of gem-dimethyl olefins with selenium dioxide has been reported to furnish the corresponding *trans*-alcohols or *trans*-aldehydes exclusively,[3] oxidation of optically pure linalool would offer a possibility to confirm the structure and to determine the configuration at C-6 in the tobacco diol (*1*). Thus, *R*-linalool (*4*) was reacted with selenium dioxide giving, after reductive work-up, a low yield (10 %) of (2*E*,6*R*)-2,6-dimethyl-2,7-octadiene-1,6-diol (*5*), whose IR, NMR and mass spectra were identical to those of the tobacco diol (*1*). Their optical rotations, however, were of opposite signs, which established that the tobacco diol (*1*) has the 6*S*-configuration.





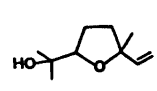


Table 1. Carbon-13 chemical shifts and assignments for compounds *1*–*3*.[a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
1	68.3	134.9	125.7	22.4	41.8	73.3	144.9	111.8	13.7	27.6
2[b]	25.3	130.3	124.6	22.6	41.2	72.7	145.0	111.3	17.5	27.2
3[b]	68.3	134.8	125.8	25.4	36.5	37.5	144.5	112.8	13.6	20.2

[a] δ-Values relative to TMS. [b] Ref. 2.

A few linear monoterpenoids have previously been found in tobacco. Besides myrcene (*6*),[4] geraniol (*7*),[5] geranic acid (*8*)[6] and citronellol (*9*),[7] these include linalool,[8,9] linalyl acetate (*10*),[8] tetrahydrolinalool (*11*)[4] and two stereoisomers of linaloyl oxide (*12*).[5] With the exception of a report that Moroccan tobacco contains *R*-linalool (*4*),[9] the absolute configurations of these compounds have not been determined. It seems likely, however, that the new diol, (2*E*,6*S*)-2,6-dimethyl-2,7-octadiene-1,6-diol (*1*), is formed in Greek tobacco by oxidation of *S*-linalool (*2*). This assumption is supported by the fact that the 6*R*-epimer of diol *1* (*5*) has been isolated from callus tissues of *Nicotiana tabacum* to which *R*-linalool (*4*) had been fed.[10]

Experimental. For instrumental details see Ref. 11.

Isolation of (2E,6S)-2,6-dimethyl-2,7-octadiene-1,6-diol (1) from tobacco. A volatile, neutral fraction (B9) of an extract obtained from 295 kg of sun-cured Greek *Nicotiana tabacum* L.[12] was chromatographed over silica gel using a hexane/ethyl acetate gradient. One of the subfractions obtained was purified further by liquid chromatography using columns packed with Bondapak C_{18}/Porasil (Waters), μ-Porasil (Waters) and μ-Bondapak CN (Waters) to afford 10 mg of (2*E*,6*S*)-2,6-dimethyl-2,7-octadiene-1,6-diol (*1*) as a colourless oil. (Found: $[M-18]^{+\cdot}$ 152.1213. Calc. for $C_{10}H_{16}O$: 152.1201); $[\alpha]_D$ +17.5° (*c* 0.79, MeOH); IR ($CHCl_3$) bands at 3600 (s) and 3420 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.30 (3 H, s), 1.67 (3 H, broad s), 4.00 (2 H, broad s), 5.08 (1 H, dd, J = 10.5 and 1.5 Hz), 5.22 (1 H, dd, J = 17.5 and 1.5 Hz), 5.43 (1 H, broad t, J = 7 Hz) and 5.95 (1 H, dd, J = 10.5 and 17.5 Hz); MS [*m/e*, (%)]: 152 (5), 137 (18), 119 (13), 110 (19), 93 (20), 82 (35), 71 (100), 67 (62), 55 (35) and 43 (84).

Data reported for (2*E*,6*R*)-2,6-dimethyl-2,7-octadiene-1,6-diol (*5*): $[\alpha]_D^{25}$ −12.8° (*c* 1.08 in MeOH); ^1H NMR: δ 3.95 (2 H, s).[10]

Preparation of (2E,6R)-2,6-dimethyl-2,7-octadiene-1,6-diol (5). A solution of *R*-linalool (*4*, 3.08 g, 2 mmol) and SeO_2 (2.22 g, 2 mmol) in EtOH (50 ml) was refluxed for 40 min. The solvent was evaporated and the residue extracted with diethyl ether. The extract was added dropwise to a cooled (0 °C) ethereal solution of $LiAlH_4$ (1.10 g) and stirred at room temperature for 0.5 h. Work up and chromatography on silica gel using ethyl acetate/hexane (1:1) as eluent afforded (2*E*,6*R*)-2,6-dimethyl-2,7-octadiene-1,6-diol (*5*, 0.35 g, 10 %), $[\alpha]_D$ −13.1° (*c* 2.96, MeOH). With the exception of the optical rotation, this diol was identical (IR, NMR and MS), to the new tobacco constituent (*1*).

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