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7,8-EPOXY-4-BASMEN-6-ONE, A TOBACCO DITERPENOID HAVING A NOVEL SKELETON[1]

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Abstract: A diterpenoid, probably cembrane-derived and having a novel skeleton, has been isolated from Greek tobacco. Its structure has been determined by spectroscopic methods and X-ray analysis.

Recent phytochemical studies have revealed that, as a result of their genetic origin, tobacco varieties such as Virginia and Burley produce diterpenoids of the cembrane type, whereas Oriental tobaccos normally elaborate both cembranoids and labdanoids.[2] These diterpenoids are present in a substantial amount in the cuticular wax of the leaf and flower, the number of cembranoids identified to-date exceeding forty and the number of labdanoids approaching thirty.[3,4] The vast majority of these compounds has not as yet been obtained from other plants or from animal sources and may hence be specific to tobacco.

The cembranoids and labdanoids were the only carbocyclic diterpenoids known to occur in tobacco, when we encountered a diterpenoid having a novel cembrane-derived carbotricyclic skeleton. The present report describes the isolation and structure determination of this compound.

The new compound 1, $C_{20}H_{30}O_2$,[5] was obtained in a 3.1 mg yield from the volatile neutral portion of a diethyl ether extract of 295 kg of sun-cured leaves of Greek tobacco (Serres) by repeated chromatography over silica gel followed by HPLC using columns packed with Partisil M9 PAC and Spherisorb 5 Nitrile.[6] An analysis of its spectral data revealed the presence of an isopropyl group (methyl doublets at δ 0.81 and 0.97 in the ^{1}H NMR spectrum; IR bands at 1385 and 1375 cm^{-1}), two methyl groups attached to fully substituted carbon atoms (methyl singlets at δ 1.16 and 1.30) and one vinylic methyl group (methyl doublet at δ 1.99, J = 1.4 Hz). These results were consonant with a diterpene structure.

The occurrence of an α,β-unsaturated oxo group (IR band at 1658 cm^{-1}; ^{13}C NMR signals at δ 195.2 (s), 157.6 (s) and 129.9 (d)) and an ether oxygen linked to two fully substituted carbon atoms (two overlapping singlets at δ 74.5; no OH-absorption in the IR-spectrum) excluded a cembrane structure and demonstrated that the new compound (1) is carbotricyclic.

In order to determine the structure and relative stereochemistry , compound 1 was subjected to X-ray analysis. A least squares fitting of fifteen 2θ-values measured by a Philips PW 1100 diffractometer revealed that the unit cell has orthorhombic symmetry with the lattice constants: *a* = 16.519, *b* = 12.608 and *c* = 8.468 Å. The systematic extinctions were uniquely accommodated by space group $P2_12_12_1$ with Z = 4. All unique diffraction maxima were recorded using $2\theta \le 140^\circ$ and graphite monochromated CuKα radiation (1.54178 Å). Lorentz and polarization corrections were applied but no correction was made for absorption, μ (CuKα) = 0.543 mm^{-1}. Of the 1929 reflections measured, 1333 were considered observed $(|F_0| \ge 3\sigma(F_0))$.

The structure was solved by the MULTAN[7] direct phase determination procedure using the 238 normalized structure factors having the greatest magnitudes. The phase set having the highest reliability index revealed the positions of twenty of the twenty-two non-hydrogen atoms. The remaining non-hydrogen atoms and the hydrogen atoms were located using a difference F-map. A full-matrix least-squares refinement, in which the non-hydrogen atoms were included with anisotropic thermal parameters and the hydrogen atoms with fixed isotropic thermal parameters (equal to the final isotropic value of their parent atom) converged to a present *R*-value of 0.065.

The X-ray results, which are visualized by a computer-generated drawing in Fig. 1,[8] demonstrate that compound 1 is a diterpenoid having a novel carbotricyclic skeleton. By assigning the name basmane[9] to the skeleton and adopting the numbering system shown in 2, the new compound can be characterized as (1*S**,2*S**, 4*Z*,7*R**,8*S**,11*R**,12*R**)-7,8-epoxy-4-basmen-6-one (1).[10]

The two five-membered rings are fused to the eight-membered ring in a *cis*-manner. Ring A has an envelope conformation with C-1 representing the flap, whereas ring C is essentially planar and located roughly perpendicularly to the plane of ring B. The latter ring exists in a saddle-like conformation. Several of the carbon-carbon bond lengths deviate from the expected values, an observation that suggests that the ring system is strained.[8]

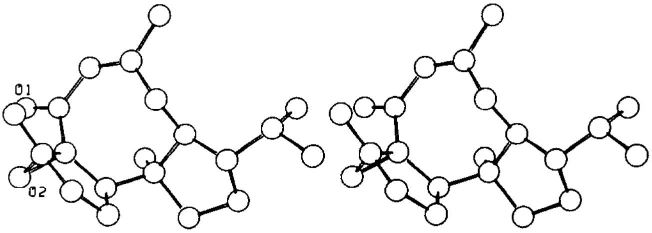
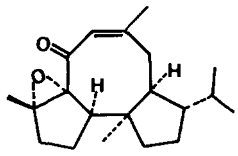
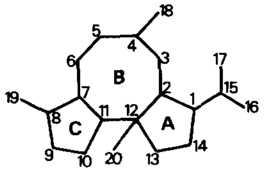


Fig. 1. A stereoscopic view of the new tobacco constituent (1).



1



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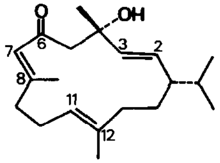

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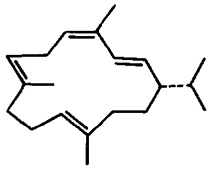

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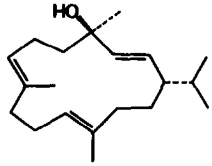

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Tobacco cembranoids, as exemplified by (1S,2E,4S,7E,11E)-4-hydroxy-2,7,11-cembratrien-6-one (3), commonly incorporate 2,3-, 7,8- and 11,12-double bonds and an oxygen-containing substituent at C-6. In view of this, it is reasonable to assume that the new basmane (1) is formed in tobacco from a parent cembranoid by intramolecular proton-induced cyclization reactions connecting C-2 with C-12 and C-7 with C-11. These reactions when compared with those giving rise to hydrophenanthrenes by treatment of cembrene (4) and isocembrol (5) with acid would then proceed by a different mechanism.[11]

The discovery of the new basmane (1) in tobacco is an addition to the growing group of cembrane-derived diterpenoids in nature. Among these are compounds of the tigliane, daphnane, ingenane and lathyrane types isolated from plants of the Euphorbiaceae family[12] and the trinervitanes, kempanes and rippertanes ejected by nasute termites.[13]

Acknowledgement. We are grateful to Professor Peder Kirkegaard for his stimulating interest in the X-ray work.

References and notes

1. Part 58 in the series Tobacco Chemistry.

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3. C.R. Enzell and I. Wahlberg Recent Adv. Tob. Sci. 6 (1980) 64.

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5. 7,8-Epoxy-4-basmen-6-one had m.p. 109-110^{0}C; $\{\alpha\}_D$ + 195^{0} (c 0.2, $CHCl_3$);
IR (CCl_4) bands at 1658, 1385 and 1375 cm^{-1};
^{1}H NMR ($CDCl_3$): δ 0.81 (d, J = 6.7 Hz)/0.97 (d, J = 6.7 Hz) (H-16/H-17), 1.16 (s, H-20), 1.30 (s, H-19), 1.99 (d, J = 1.4 Hz, H-18), 2.65 (2H, overlapping signals) and 6.10 (q, J = 1.2 Hz, H-5);
^{13}C NMR ($CDCl_3$): δ 15.0 (q), 15.8 (q), 22.3 (t), 22.6 (q), 27.2 (t), 27.5 (q), 27.5 (d), 32.5 (t), 33.7 (t), 34.3 (q), 41.6 (t), 47.3 (d), 47.6 (s), 53.3 (d), 54.7 (d), 74.5 (s), 74.5 (s), 129.9 (d),157.6 (s) and 195.2 (s).

MS { m/z (%, composition)}: 302 (M, 4, $C_{20}H_{30}O_2$), 287 (3, $C_{19}H_{27}O_2$), 259 (8), 245 (68, $C_{17}H_{25}O$), 231 (11), 217 (5, $C_{15}H_{21}O$), 201 (9), 178 (16, $C_{11}H_{14}O_2$), 163 (22), 149 (33, $C_{10}H_{13}O$), 135 (44), 123 (58, C_9H_{15}), 109 (30), 95 (28), 81 (43, C_6H_9 and C_5H_5O), 69 (41, C_5H_9 and C_4H_5O), 55 (40, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

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8. A full report will be published by J.-E. Berg elsewhere.
9. From the leaf class basma, of which the Serres tobacco is a member.
10. Since all known tobacco cembranoids have a 1S-configuration, this configuration is also assigned to the new basmane.
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