Structure of a Benzoyl Derivative of an Epidioxy-Containing Tobacco Cembranoid

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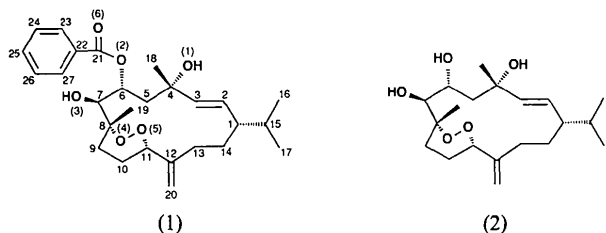
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Abstract. (1S,2E,4S,6R,7S,8R,11S)-6-Benzoyloxy-8,11-epidioxy-2,12(20)-cembradiene-4,7-diol (1), $C_{27}H_{36}O_6$, M_r = 456.58, orthorhombic, $P2_12_12_1$, a = 9.131 (2), b = 11.629 (9), c = 25.203 (7) Å, V = 2676.1 (2) Å^3, Z = 4, D_x = 1.133 (2) g cm^{-3}, λ(Cu $K\alpha$) = 1.5418 Å, μ = 6.06 cm^{-1}, $F(000)$ = 984, T = 293 K, final R = 0.066 for 1666 unique reflections. The structure has a disordered isopropyl group. The torsion angle C(14)—C(1)—C(15A)—C(16A) for group A (occupancy 0.327) is −58.7 (1.9)° whereas the corresponding angle for group B (occupancy 0.673) is −69.1 (1.1)°. The six-membered epidioxide-containing ring has a chair conformation. There are two possible intramolecular hydrogen bonds O(1)···O(3) = 2.701 (6) Å and O(2)···O(3) = 2.981 (6) Å, and one possible intermolecular hydrogen bond O(1)···O(6^i) = 2.828 (6) Å [symmetry code: (i) −x, $\frac{1}{2}$ + y, −$\frac{1}{2}$ − z].

(1)   (2)

Experimental. The isolation of 18 mg of the cembranic epidioxide (2) from a chloroform extract of flowers of Greek tobacco and the conversion of part of this material into 3.5 mg of the corresponding 6-O-benzoyl derivative (1) have been described previously (Arndt, Wahlberg, Enzell & Berg, 1988). Single crystals of (1) were obtained by recrystallization from a mixture of hexane and ethyl acetate. A colourless prismatic crystal of size 0.18 × 0.42 × 0.42 mm was studied on a Siemens/Stoe AED2 diffractometer using graphite-monochromatized Cu $K\alpha$

radiation. The unit-cell parameters were refined from the θ values of 10 reflections in the range 12.5–25.0°. The symmetry and systematic extinctions of the X-ray reflections were consistent with the space group $P2_12_12_1$. A total of 2142 reflections were collected with ω–2θ scans (3 < 2θ < 120°), of which 1666 unique reflections were considered observed [F > 4.0σ(F), 0 < h < 10, 0 < k < 13, 0 < l < 28]. The intensities were corrected for Lorentz and polarization effects, but no correction was made for absorption. The intensities of three standard reflections (210, 20$\bar{2}$ and 121) were monitored every hour; the total deterioration of intensity was < 3%.

The positions of 21 of the 33 non-H atoms were obtained by direct methods using *SHELXS*86 (Sheldrick, 1990) while the remaining non-H atoms and one of the two hydroxy H atoms were located from $\Delta\rho$ maps. The isopropyl group was found to be disordered. A disorder model involving two differently oriented isopropyl groups constrained to give C—C distances of 1.54 Å was applied. The occupation factors for each orientation were refined with the sum of occupation factors being fixed to unity. When the disordered model was applied the agreement factor dropped from R = 0.11 to R = 0.07. Except for the H atoms bonded to the isopropyl group, which were omitted, all the non-hydroxy H atoms were geometrically placed with a distance of 1.08 Å to the adjacent C atom. The structure was refined by full-matrix least-squares techniques using the program *SHELX*76 (Sheldrick, 1976) for minimizing $\Sigma w(|F_o| - |F_c|)^2$. Anisotropic displacement parameters were used for all non-hydrogen atoms with the exception of the atoms of the disordered isopropyl which were set to a common isotropic temperature factor. All H atoms were refined with all isotropic displacement factors constrained to 0.05 Å^2. The number of refined parameters was 308. Final agreement factors: R = 0.066, wR = 0.071 (wR = 0.086 for all significant reflections) using the weighting scheme $w = [\sigma^2(F) + g|F|^2]^{-1}$ with g =

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic displacement coefficients* ($\text{Å}^2 \times 10^2$)

Equivalent isotropic U is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	−2933 (8)	−6277 (6)	−3479 (2)	6.9 (2)
C(2)	−1863 (6)	−5429 (6)	−3237 (3)	5.73 (17)
C(3)	−546 (7)	−5648 (5)	−3067 (2)	5.37 (17)
C(4)	528 (6)	−4782 (5)	−2852 (3)	5.77 (19)
C(5)	1104 (7)	−5105 (6)	−2287 (3)	5.9 (2)
C(6)	−6 (6)	−5434 (5)	−1852 (2)	5.27 (17)
C(7)	−1271 (7)	−4602 (5)	−1773 (2)	5.07 (17)
C(8)	−2257 (8)	−4824 (5)	−1280 (3)	6.0 (2)
C(9)	−3819 (8)	−4402 (6)	−1375 (3)	6.6 (2)
C(10)	−4613 (7)	−5140 (5)	−1782 (3)	6.5 (2)
C(11)	−4395 (7)	−6430 (5)	−1689 (3)	6.00 (19)
C(12)	−4831 (7)	−7129 (5)	−2150 (3)	6.2 (2)
C(13)	−3802 (8)	−7195 (6)	−2621 (3)	7.0 (3)
C(14)	−4224 (7)	−6418 (7)	−3098 (3)	7.0 (2)
C(15A)	−3493 (25)	−5716 (23)	−4006 (7)	105 (2)
C(16A)	−4696 (34)	−6437 (28)	−4277 (13)	105 (2)
C(17A)	−2020 (29)	−5831 (25)	−4305 (13)	105 (2)
C(15B)	−3334 (16)	−5943 (11)	−4057 (4)	105 (2)
C(16B)	−4114 (17)	−6881 (13)	−4374 (6)	105 (2)
C(17B)	−4332 (15)	−4882 (11)	−4090 (6)	105 (2)
C(18)	1836 (7)	−4685 (7)	−3221 (3)	7.4 (3)
C(19)	−1611 (11)	−4251 (8)	−770 (3)	9.6 (3)
C(20)	−6127 (8)	−7655 (7)	−2164 (4)	8.3 (3)
C(21)	1211 (6)	−6431 (6)	−1127 (2)	5.20 (19)
C(22)	2101 (7)	−6255 (6)	−646 (2)	5.77 (1)
C(23)	2395 (11)	−7170 (8)	−320 (4)	9.9 (3)
C(24)	3252 (14)	−7065 (13)	130 (4)	14.3 (7)
C(25)	3793 (13)	−5953 (11)	262 (3)	10.9 (4)
C(26)	3488 (12)	−5067 (11)	−55 (4)	12.0 (5)
C(27)	2640 (9)	−5198 (7)	−514 (3)	8.2 (3)
O(1)	−130 (5)	−3665 (4)	−2792 (2)	6.13 (16)
O(2)	898 (5)	−5443 (4)	−1362 (2)	6.23 (14)
O(3)	−821 (6)	−3437 (3)	−1755 (2)	7.86 (18)
O(4)	−2304 (5)	−6019 (4)	−1150 (2)	6.60 (16)
O(5)	−2831 (5)	−6656 (3)	−1615 (2)	6.20 (14)
O(6)	853 (5)	−7370 (3)	−1295 (2)	6.03 (14)

$0.0090.$ $(\Delta/\sigma)_{\max} = 0.01$, $\Delta\rho_{\min} = -0.24$ and $\Delta\rho_{\max} = 0.53 \text{ e Å}^{-3}$, $S = 0.953$. Atomic scattering factors for neutral atoms and real and imaginary dispersion terms were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV).

The atom-numbering scheme of the epidioxide (1) is given in the scheme above and a *PLUTO* (Motherwell & Clegg, 1978) stereo drawing of the molecule is shown in Fig. 1. The final fractional atomic coordinates with standard deviations and equivalent isotropic temperature factors for the non-H atoms are listed in Table 1.* Bond lengths and bond angles are given in Table 2. A ring-puckering analysis (Cremer & Pople, 1975) of the epidioxide-containing six-membered ring gave $Q(2) = 0.138$ (6), $Q(3) = 0.576$ (6) and $\varphi(2) = -78.2$ (26)°, with total puckering amplitude $Q = 0.5922$ (5). All calculations were carried out on a C220 Convex computer.

It can be concluded from the X-ray study that compound (1) is the 6-*O*-benzoyl derivate of

* Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54633 (16 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AB0226]

Table 2. *Bond lengths* (Å) *and bond angles* (°) *for the non-*H *atoms*

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C(2)—C(1)	1.516 (11)	C(14)—C(1)	1.529 (11)
C(15A)—C(1)	1.566 (12)	C(15B)—C(1)	1.552 (11)
C(3)—C(2)	1.302 (9)	C(4)—C(3)	1.505 (11)
C(5)—C(4)	1.563 (11)	C(18)—C(4)	1.520 (11)
O(1)—C(4)	1.439 (9)	C(6)—C(5)	1.541 (11)
C(7)—C(6)	1.520 (10)	O(2)—C(6)	1.487 (8)
C(8)—C(7)	1.556 (11)	O(3)—C(7)	1.416 (8)
C(9)—C(8)	1.527 (12)	C(19)—C(8)	1.564 (12)
O(4)—C(8)	1.429 (8)	C(10)—C(9)	1.521 (11)
C(11)—C(10)	1.530 (11)	C(12)—C(11)	1.473 (10)
O(5)—C(11)	1.465 (8)	C(13)—C(12)	1.516 (12)
C(20)—C(12)	1.333 (11)	C(14)—C(13)	1.553 (12)
C(22)—C(21)	1.474 (10)	O(2)—C(21)	1.323 (8)
O(6)—C(21)	1.216 (8)	C(23)—C(22)	1.371 (11)
C(27)—C(22)	1.366 (11)	C(24)—C(23)	1.383 (15)
C(25)—C(24)	1.423 (16)	C(26)—C(25)	1.333 (15)
C(27)—C(26)	1.399 (13)	O(5)—O(4)	1.468 (7)
C(16A)—C(15A)	1.542 (12)	C(17A)—C(15A)	1.547 (12)
C(16B)—C(15B)	1.528 (11)	C(17B)—C(15B)	1.536 (11)
C(14)—C(1)—C(2)	108.3 (6)	C(15A)—C(1)—C(2)	106.3 (11)
C(15A)—C(1)—C(14)	109.0 (11)	C(15B)—C(1)—C(2)	111.5 (8)
C(15B)—C(1)—C(14)	115.7 (8)	C(15B)—C(1)—C(15A)	12.0 (13)
C(3)—C(2)—C(1)	126.9 (7)	C(4)—C(3)—C(2)	126.1 (7)
C(5)—C(4)—C(3)	112.7 (6)	C(18)—C(4)—C(3)	109.9 (7)
C(18)—C(4)—C(5)	108.1 (6)	O(1)—C(4)—C(3)	111.7 (6)
O(1)—C(4)—C(5)	105.2 (6)	O(1)—C(4)—C(18)	109.0 (6)
C(6)—C(5)—C(4)	119.1 (6)	C(7)—C(6)—C(5)	115.8 (6)
O(2)—C(6)—C(5)	103.2 (5)	O(2)—C(6)—C(7)	108.5 (6)
C(8)—C(7)—C(6)	116.1 (6)	O(3)—C(7)—C(6)	113.1 (6)
O(3)—C(7)—C(8)	107.6 (6)	C(9)—C(8)—C(7)	111.2 (6)
C(19)—C(8)—C(7)	111.6 (7)	C(19)—C(8)—C(9)	110.1 (7)
O(4)—C(8)—C(7)	111.2 (6)	O(4)—C(8)—C(9)	108.7 (6)
O(4)—C(8)—C(19)	103.7 (7)	C(10)—C(9)—C(8)	111.7 (6)
C(11)—C(10)—C(9)	112.9 (7)	C(12)—C(11)—C(10)	112.7 (7)
O(5)—C(11)—C(10)	108.8 (6)	O(5)—C(11)—C(12)	105.4 (6)
C(13)—C(12)—C(11)	118.6 (6)	C(20)—C(12)—C(11)	120.9 (8)
C(20)—C(12)—C(13)	120.4 (8)	C(14)—C(13)—C(12)	115.0 (7)
C(3)—C(14)—C(1)	110.9 (7)	O(2)—C(21)—C(22)	111.5 (7)
O(6)—C(21)—C(22)	124.0 (6)	O(6)—C(21)—O(2)	124.4 (6)
C(23)—C(22)—C(21)	119.6 (7)	C(27)—C(22)—C(21)	121.6 (7)
C(27)—C(22)—C(23)	118.8 (7)	C(24)—C(23)—C(22)	122.2 (11)
C(25)—C(24)—C(23)	117.9 (11)	C(26)—C(25)—C(24)	119.3 (10)
C(27)—C(26)—C(25)	121.8 (11)	C(26)—C(27)—C(22)	119.9 (9)
C(21)—O(2)—C(6)	119.9 (6)	O(5)—O(4)—C(8)	108.5 (5)
O(4)—O(5)—C(11)	109.3 (5)	C(16A)—C(15A)—C(1)	112.5 (20)
C(17A)—C(15A)—C(1)	95.4 (17)	C(17A)—C(15A)—C(16A)	110.9 (25)
C(16B)—C(15B)—C(1)	114.9 (11)	C(17B)—C(15B)—C(1)	113.0 (11)
C(17B)—C(15B)—C(16B)	105.6 (11)	C(15B)—C(17B)—C(16A)	49.6 (13)
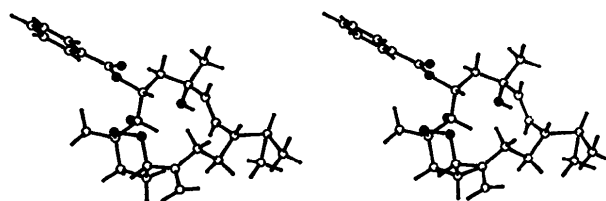
Fig. 1. A stereoscopic view of (1*S*,2*E*,4*S*,6*R*,7*S*,8*R*,11*S*)-6-benzoyloxy-8,11-epidioxy-2,12(20)-cembradiene-4,7-diol (1). The O atoms are represented as filled circles.

(1*S*,2*E*,4*S*,6*R*,7*S*,8*R*,11*S*)-8,11-epidioxy-2,12(20)-cembradiene-4,6,7-triol (2) (relative stereochemistry). As has been described elsewhere, biomimetic synthesis was then used to settle the absolute configuration (Arndt, Wahlberg, Enzell & Berg, 1988).

Related literature. The cuticular wax of the tobacco leaf and flower is a rich source of diterpenoids of the

cembrane class. Their presence is of interest, since these carbomonocyclic diterpenoids are prone to undergo biodegradation thereby giving rise to odoriferous carboacyclic products (Wahlberg & Enzell, 1987). It is also noteworthy that some tobacco cembranoids have biological functions, e.g. as growth inhibitors (Springer, Clardy, Cox, Cutler & Cole, 1975) and insect repellents (Johnson & Severson, 1984) and that several exhibit antitumour–promoter effects (Saito, Tsujino, Kaneko, Yoshida & Mizusaki, 1987).

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Structure of a 7,8-Epoxycembranoid Isolated from Tobacco

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Abstract. (1S,2E,4S,6R,7S,8S,11E)-7,8-Epoxy-2,11-cembradiene-4,6-diol monohydrate (1), $C_{20}H_{34}O_3$.-H$_2$O, M_r = 340.5, monoclinic, $P2_1$, a = 9.808 (2), b = 8.019 (4), c = 13.755 (3) Å, β = 105.73 (2)°, V = 1041.3 (6) Å^3, Z = 2, D_x = 1.086 (6) g cm^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, μ = 0.687 cm^{-1}, $F(000)$ = 376, T = 293 K, final R = 0.063 for 2388 unique reflections. The structure consists of a 14-membered cembrane ring, which is *trans*-fused to an epoxide function, the torsion angle C(6)—C(7)—C(8)—C(9) being −156.0 (4)°. There are two double bonds, one between C(2) and C(3) and one between C(11) and C(12). Both are of E geometry and have torsion angles C(1)—C(2)—C(3)—C(4) = 173.0 (4)° and C(10)—C(11)—C(12)—C(13) = −174.7 (6)°. There is one possible intramolecular hydrogen bond O(2)···O(3) = 2.921 (4) Å, O(2)—H(22)···O(3) = 109.5° and three possible intermolecular hydrogen bonds: O(1^i)···O(4) = 2.839 (8), O(2^{ii})···O(4) = 2.989 (4) and O(4)···O(3^{ii}) = 2.824 (5) Å, forming infinite chains in the ⟨100⟩ direction [symmetry code: (i) −2−x, $\frac{1}{2}$+y, −1−z; (ii) −1−x, $\frac{1}{2}$+y, −1−z].

(1)   (2)

(3)   (4)
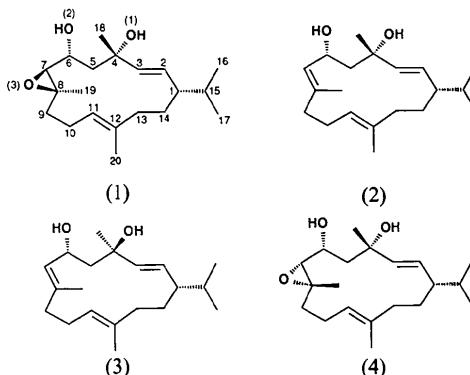
Experimental. The isolation of 3.7 mg of (1) from a chloroform extract of flowers of Greek tobacco has been described previously (Wahlberg, Eklund, Vogt, Enzell & Berg, 1986). A single crystal was obtained by recrystallization from a mixture of hexane and