Tobacco Chemistry. 73.* 4,6,8-Trihydroxy-11-capnosene-2,10-dione, a New Cembrane-Derived Bicyclic Diterpenoid from Tobacco

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Eklund, A.-M., Berg, J.-E. and Wahlberg, I., 1992. Tobacco Chemistry. 73. 4,6,8-Trihydroxy-11-capnosene-2,10-dione, a New Cembrane-Derived Bicyclic Diterpenoid from Tobacco. – Acta Chem. Scand. 46: 367–371.

A new diterpenoid containing a rare carbobicyclic cembrane-derived skeleton, the capnosane skeleton, has been isolated from flowers of Greek tobacco. It has been identified as (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*Z*)-4,6,8-trihydroxy-11-capnosene-2,10-dione (**1**) by spectral methods and X-ray analysis of the corresponding benzoate (**3**). A full account of the X-ray work is given.

Recent studies have disclosed the presence in tobacco of two diterpenoids having novel carbotricyclic basmane and virgane skeletons.[2,3] Both compounds are likely to arise via cyclization of appropriate parent cembranoids, a view that is substantiated by the fact that cembranoids are abundant and show rich structural diversity in tobacco.[4] We now report the isolation of a new diterpenoid (**1**) containing an unusual cembrane-derived carbobicyclic skeleton. It was obtained from an extract of flowers of Greek tobacco by repeated flash chromatography and HPLC.

Results

Structure elucidation. The new compound (**1**), $C_{20}H_{32}O_5$, formed a monoacetate (**2**), $C_{22}H_{34}O_6$, upon treatment with acetic anhydride and pyridine. An analysis of the spectral data of **2** revealed the presence of an isopropyl group (methyl doublets at δ 0.76 and 1.01 in the ^{1}H NMR spectrum), two methyl groups attached to fully substituted oxygen-carrying carbon atoms and one vinylic methyl group (methyl singlets at δ 1.34 and 1.45 and a methyl doublet at δ 1.85). These results are consonant with **1** having a diterpene structure.

The occurrence in acetate **2** of two oxo groups, of which one is α,β-unsaturated [IR absorption at 1729, 1693 and 1641 cm^{-1}; ^{13}C NMR signals at δ 201.2 (s) and 216.6 (s)], and of two tertiary hydroxy groups (OH-absorption in the IR spectrum; ^{13}C NMR singlets at δ 71.5 and 79.5) excluded a cembrane structure and demonstrated the new compound (**1**) to be carbobicyclic.

Extensive use was made of two-dimensional NMR spectroscopy in the structural elucidation work. Because of the limited amount (4.4 mg) of the acetate **2** at hand, inverse ^{13}C–^{1}H (HMQC) and inverse long-range ^{13}C–^{1}H (HMBC) shift correlation spectral methods, which have higher sensitivity than conventional methods, were applied. By using the results thus obtained together with those obtained from a double quantum filtered COSY spectrum, the structural units mentioned above were incorporated into structure **1** (without stereochemistry). In order to determine the relative stereochemistry, the benzoate **3**, which in contrast with the natural product **1** and the acetate **2** formed single crystals, was subjected to X-ray analysis (*vide infra*).

The results of the X-ray study, which are illustrated in Fig. 1, confirm that the new compound is a carbobicyclic diterpenoid possessing a five- and an eleven-membered

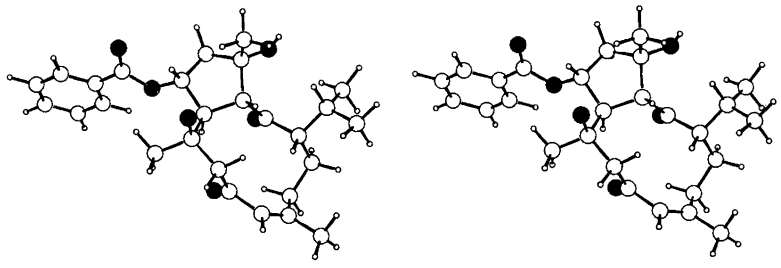

Fig. 1. A stereoscopic view of (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*Z*)-6-benzoyloxy-4,8-dihydroxy-11-capnosene-2,10-dione (**3**).

* For part 72, see Ref. 1.

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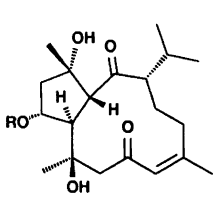
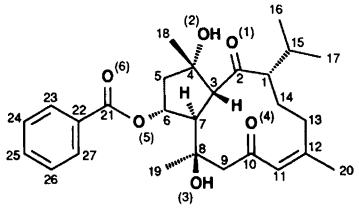


1 R=H
2 R=Ac



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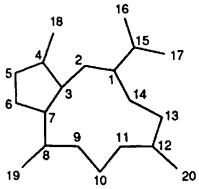

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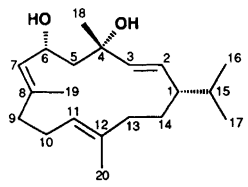

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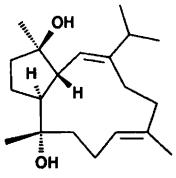

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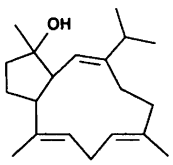

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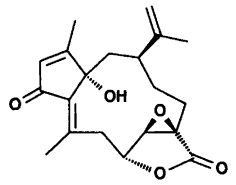

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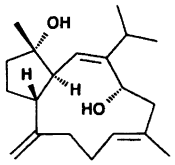

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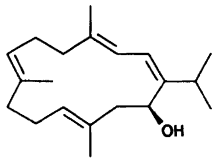

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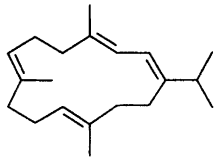

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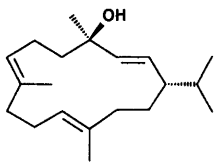

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ring, which are fused in a *trans* manner. By assigning the name capnosane (from καπνος, the Greek word for tobacco) to this rare skeleton (see below) and adopting the numbering system shown in **4**, the new compound is characterized as (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*Z*)-4,6,8-trihydroxy-11-capnosene-2,10-dione (**1**).‡

Biogenesis. Tobacco cembranoids, typified by the abundant diol **5**, commonly incorporate 2,3,7,8 and 11,12 double bonds and hydroxy substituents at C-4 and C-6.[4] In view of this, it is reasonable to assume that the new capnosane (**1**) is formed in tobacco via an intramolecular cyclization reaction connecting C-3 with C-7. It is noteworthy that if this process occurs with a 7,8-epoxide and does not proceed with epimerization at C-3 or C-7, the epoxide must have an unprecedented 7*S**,8*R**-configuration, that is *cis*-geometry.

The new capnosane is an addition to the small group of 3,7-cyclized cembranoids encountered in nature. This includes the unnamed compounds **6** and **7** isolated from an Australian *Cespitularia* species (soft coral)[5] and coralloidolide C (**8**) isolated from *Alcyonium coralloides,* a Mediterranean soft coral.[6]

Sarcophytol L (**9**), another 3,7-cyclized cembranoid, which was obtained by column chromatography of an extract of *Sarcophyton glaucum* (a soft coral), is probably an artefact formed by autooxidation of sarcophytol A (**10**).[7] Kobayashi *et al.*[8] have studied this process using not only **10** but also three geometrical isomers of **10** as starting material. They found that all four cembranoids give bicyclo[9.3.0]tetradecenes via epoxidation of the 3,4 double bond, isomerization to the 1,14-epoxide and an acid-induced transannular cyclization. The hydroxy group at C-14 is not a prerequisite, since cembrene-C (**11**) forms a 3,7-cyclized product on autooxidation. Isocembrol (**12**) also undergoes a transannular reaction to afford a 3,7-bicyclocembranoid via oxymercuration–demercuration.[9]

Crystallography. The final fractional atomic coordinates with estimated standard deviations and equivalent isotropic temperature factors for the non-hydrogen atoms in the benzoate **3** are listed in Table 1. Intramolecular bond lengths and bond angles, both with estimated standard deviations, are found in Tables 2 and 3, respectively, while selected non-bonded distances less than 3.5 Å and possible hydrogen bonds are given in Table 4. Crystal and experimental data are detailed in Table 5.

The maximum, minimum and mean values of the sp^3–sp^3 bonds are 1.573(8), 1.504(9) and 1.541(9) Å. The corresponding values for the sp^2–sp^3 and sp^2–sp^2 bonds are 1.540 (8), 1.496(8) and 1.510(8) Å and 1.464(8), 1.324(8) and 1.386(8) Å, respectively. The 11,12 double bond is of *cis*-geometry with a torsional angle [C(10)–C(11)–C(12)–C(13)] of −0.9(9)°.

‡ All tobacco cembranoids, for which absolute configurations have been determined, have a 1*S*-configuration. This configuration is therefore also assigned to the new capnosane.

Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors (A×100) for the non-hydrogen atoms and fixed isotropic temperature factors (U_{iso} = 5.0) for the hydrogen atoms in benzoate **3**.

	x	y	z	U_{eq}[a]
C(1)	1561(7)	−595(3)	3306(5)	3.7(1)
H(1)	3129(7)	−749(3)	3886(5)	
C(2)	977(7)	−4(3)	3997(5)	3.4(1)
C(3)	2887(7)	462(3)	4355(5)	3.5(1)
H(3)	4411(7)	242(3)	4127(5)	
C(4)	2456(8)	1062(3)	3461(5)	4.5(2)
C(5)	1598(9)	1515(3)	4484(6)	4.8(2)
H(5A)	−179(9)	1452(3)	4515(6)	
H(5B)	1908(9)	1980(3)	4174(6)	
C(6)	2904(8)	1368(3)	5913(6)	4.1(2)
H(6)	4508(8)	1598(3)	6015(6)	
C(7)	3060(7)	666(3)	5968(5)	3.4(1)
H(7)	1736(7)	453(3)	6468(5)	
C(8)	5134(7)	427(3)	6955(5)	4.1(2)
C(9)	5494(8)	−271(3)	6791(5)	4.4(2)
H(9A)	6850(8)	−408(3)	7594(5)	
H(9B)	5972(8)	−350(3)	5739(5)	
C(10)	3539(8)	−678(3)	6948(5)	4.2(2)
C(11)	3790(9)	−1318(3)	6387(6)	4.7(2)
H(11)	5357(9)	−1549(3)	6724(6)	
C(12)	2246(8)	−1618(3)	5528(5)	4.5(2)
C(13)	−21(9)	−1366(3)	4995(6)	4.8(2)
H(13A)	−1247(9)	−1726(3)	5010(6)	
H(13B)	−406(9)	−1000(3)	5695(6)	
C(14)	−149(9)	−1108(3)	3451(6)	4.9(2)
H(14A)	−1815(9)	−930(3)	3130(6)	
H(14B)	177(9)	−1478(3)	2747(6)	
C(15)	1956(8)	−482(3)	1726(5)	4.4(2)
H(15)	2906(8)	−63(3)	1717(5)	
C(16)	3332(10)	−1003(3)	1175(7)	5.9(2)
H(16A)	4812(10)	−1038(3)	1954(7)	
H(16B)	3827(10)	−936(3)	123(7)	
H(16C)	2361(10)	−1418(3)	1184(7)	
C(17)	−271(10)	−386(3)	722(6)	6.1(2)
H(17A)	−1304(10)	−63(3)	1207(6)	
H(17B)	−1054(10)	−831(3)	683(6)	
H(17C)	−88(10)	−239(3)	−352(6)	
C(18)	4660(11)	1282(3)	2980(7)	6.1(2)
H(18A)	5922(11)	1384(3)	3871(7)	
H(18B)	4267(11)	1691(3)	2356(7)	
H(18C)	5290(11)	936(3)	2315(7)	
C(19)	4965(9)	590(3)	8505(6)	5.5(2)
H(19A)	3496(9)	424(3)	8937(6)	
H(19B)	5072(9)	1080(3)	8626(6)	
H(19C)	6448(9)	381(3)	9074(6)	
C(20)	2808(10)	−2229(3)	4926(8)	6.3(2)
H(20A)	1453(10)	−2550(3)	4657(8)	
H(20B)	4137(10)	−2446(3)	5630(8)	
H(20C)	3446(10)	−2083(3)	3959(8)	
C(21)	2305(9)	2118(3)	7687(6)	4.7(2)
C(22)	1053(8)	2246(3)	8889(5)	4.4(2)
C(23)	1763(11)	2729(3)	9827(6)	6.2(2)
H(23)	3228(11)	2995(3)	9676(6)	
C(24)	547(13)	2861(3)	10943(7)	7.3(2)
H(24)	1091(13)	3231(3)	11665(7)	
C(25)	−1318(14)	2528(4)	11166(7)	7.4(3)
H(25)	−2233(14)	2637(4)	12049(7)	
C(26)	−1995(11)	2054(3)	10246(6)	6.3(2)
H(26)	−3467(11)	1792(3)	10406(6)	
C(27)	−834(9)	1915(3)	9126(6)	5.0(2)
H(27)	−1397(9)	1543(3)	8416(6)	
O(1)	−882(5)	100(2)	4298(4)	4.7(1)
O(2)	829(9)	945(3)	2244(5)	6.9(2)
H(O2)	1331(105)	1007(32)	1643(72)	
O(3)	7127(5)	727(2)	6602(4)	5.3(1)
O(4)	1845(6)	−517(2)	7424(4)	5.4(1)
O(5)	1744(5)	1576	7086(4)	4.6(1)
O(6)	3614(9)	2456(3)	7253(6)	9.2(1)

[a] U_{eq} was estimated as $\frac{1}{3}\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$.

Table 2. Bond lengths (Å) with esds in benzoate **3**.

C(2)–C(1)	1.508(8)	C(14)–C(1)	1.539(9)
C(15)–C(1)	1.555(8)	C(3)–C(2)	1.540(8)
O(1)–C(2)	1.208(6)	C(4)–C(3)	1.562(8)
C(7)–C(3)	1.573(8)	C(5)–C(4)	1.518(9)
C(18)–C(4)	1.530(9)	O(2)–C(4)	1.430(8)
C(6)–C(5)	1.504(9)	C(7)–C(6)	1.539(8)
O(5)–C(6)	1.453(7)	C(8)–C(7)	1.547(8)
C(9)–C(8)	1.553(9)	C(19)–C(8)	1.518(9)
O(3)–C(8)	1.441(7)	C(10)–C(9)	1.496(8)
C(11)–C(10)	1.510(9)	O(4)–C(10)	1.215(7)
C(12)–C(11)	1.324(8)	C(13)–C(12)	1.496(9)
C(20)–C(12)	1.506(10)	C(14)–C(13)	1.552(10)
C(16)–C(15)	1.536(9)	C(17)–C(15)	1.550(9)
C(22)–C(21)	1.464(8)	O(5)–C(21)	1.337(7)
O(6)–C(21)	1.189(7)	C(23)–C(22)	1.408(9)
C(27)–C(22)	1.386(8)	C(24)–C(23)	1.385(10)
C(25)–C(24)	1.375(11)	C(26)–C(25)	1.378(10)
C(27)–C(26)	1.371(8)		

Table 3. Bond angles (deg) with esds in benzoate **3**.

C(14)–C(1)–C(2)	113.0(5)	C(15)–C(1)–C(2)	110.4(5)
C(15)–C(1)–C(14)	112.7(5)	C(3)–C(2)–C(1)	117.0(4)
O(1)–C(2)–C(1)	122.4(5)	O(1)–C(2)–C(3)	120.6(5)
C(4)–C(3)–C(2)	111.8(5)	C(7)–C(3)–C(2)	110.7(4)
C(7)–C(3)–C(4)	105.6(5)	C(5)–C(4)–C(3)	104.6(5)
C(18)–C(4)–C(3)	109.5(5)	C(18)–C(4)–C(5)	111.1(5)
O(2)–C(4)–C(3)	109.3(5)	O(2)–C(4)–C(5)	111.9(5)
O(2)–C(4)–C(18)	110.3(5)	C(6)–C(5)–C(4)	104.3(5)
C(7)–C(6)–C(5)	105.5(5)	O(5)–C(6)–C(5)	111.5(5)
O(5)–C(6)–C(7)	108.7(5)	C(6)–C(7)–C(3)	104.7(5)
C(8)–C(7)–C(3)	115.7(5)	C(8)–C(7)–C(6)	113.4(5)
C(9)–C(8)–C(7)	112.6(5)	C(19)–C(8)–C(7)	110.6(5)
C(19)–C(8)–C(9)	110.7(5)	O(3)–C(8)–C(7)	109.6(5)
O(3)–C(8)–C(9)	107.1(4)	O(3)–C(8)–C(19)	105.9(5)
C(10)–C(9)–C(8)	117.0(5)	C(11)–C(10)–C(9)	113.7(5)
O(4)–C(10)–C(9)	124.7(5)	O(4)–C(10)–C(11)	121.5(5)
C(12)–C(11)–C(10)	125.5(6)	C(13)–C(12)–C(11)	123.9(6)
C(20)–C(12)–C(11)	119.8(6)	C(20)–C(12)–C(13)	116.1(6)
C(14)–C(13)–C(12)	112.5(5)	C(13)–C(14)–C(1)	113.2(5)
C(16)–C(15)–C(1)	111.1(5)	C(17)–C(15)–C(1)	112.3(5)
C(17)–C(15)–C(16)	110.7(5)	O(5)–C(21)–C(22)	111.7(5)
O(6)–C(21)–C(22)	125.1(6)	O(6)–C(21)–O(5)	123.2(6)
C(23)–C(22)–C(21)	119.0(6)	C(27)–C(22)–C(21)	122.4(5)
C(27)–C(22)–C(23)	118.6(6)	C(24)–C(23)–C(22)	119.1(7)
C(25)–C(24)–C(23)	121.6(7)	C(26)–C(25)–C(24)	118.9(6)
C(27)–C(26)–C(25)	120.8(7)	C(26)–C(27)–C(22)	121.0(6)
C(21)–O(5)–C(6)	118.7(5)		

Application of the ring-puckering concept of Cremer and Pople[10] to the benzoate **3** shows that $Q(2)$ = 0.378(5), $\varphi(2)$ = 78.23(68)° and that the five-membered ring is almost an envelope conformation. The eleven-membered ring has the puckering parameters $Q(2)$ = 0.660(5), $\varphi(2)$ = 151.7(5)°, $Q(3)$ = 0.567(5), $\varphi(3)$ = 148.4(6)°, $Q(4)$ = 1.111(6), $\varphi(4)$ = 262.2(3)°, $Q(5)$ = 0.417(5), $\varphi(5)$ = 179.9(8)° and the total puckering amplitude Q = 1.462(5). The atoms C(2), C(3) and C(7) to C(12) are in a crown-type conformation, while the atoms C(13), C(14) and C(1) are in a twisted conformation. The dihedral angle formed between the

Table 4. Selected non-bonded distances (Å) and possible hydrogen bonds.

Intramolecular			
O(1)–O(2)	2.955	O(1)–O(4)	3.453
O(5)–O(6)	2.225		
Intermolecular			
O(5)–O(3[a])	3.323	O(3)–O(1[b])	2.947
C(20)–O(6[c])	3.230	C(26)–O(2[d])	3.390
O(1)–C(9[e])	3.495		

Key to symmetry operations relating designated atoms to reference atoms at (*x, y, z*):
[a] $-1+x, y, z$; [b] $1+x, y, z$; [c] $1-x, -1/2+y, 1-z$; [d] $x, y, 1+z$; [e] $-1+x, y, z$.

Table 5. Crystal and experimental data for the benzoate **3**.

Formula	$C_{27}H_{36}O_6$
Formula weight	456.58
Space group	$P2_1$
Unit cell dimensions	$a = 6.006(1), b = 21.875(3)$ $c = 9.416(2)$ Å, $\beta = 97.35(1)$
Unit cell volume, *V*	1226.90(42) Å^3
Formula units per unit cell, *Z*	2
Calculated density, D_x	1.2359 g cm^{-3}
Radiation	Mo K_α
Wavelength, λ	0.71069 Å
Linear absorption coefficient	0.804 cm^{-1}
Temperature, *T*	293(1) K
Crystal shape	Prismatic
Crystal size	0.06×0.11×0.41 mm
Diffractometer	Siemens/Stoe AED 2
Determination of unit cell	
Number of reflections used	11
θ-range	10.0–25.0°
Intensity data collection	
Maximum sin(θ)/λ	0.59 Å^{-1}
Range of *h, k* and *l*	0–7, 0–26 and 0–11
Standard reflections	3
Intensity instability	< 6 %
Internal *R* value	0.037
Number of unique reflections	1462
Number of observed reflections	2225
Criterion for significance	$F > 6.06\sigma(F)$
Structure refinement	
Minimization of	$\Sigma\, w\Delta F^2$
Anisotropic thermal parameters	All non-hydrogen atoms
Isotropic thermal parameters	Hydrogen atoms
Number of refined parameters	316
Weighting scheme	$[\sigma^2(F)+0.0050\lvert F\rvert^2]^{-1}$
Final *R* for observed refls.	0.044
Final *wR* for observed refls.	0.057
Final *wR* for all 2225 refls.	0.066
Final $(\Delta/\sigma)_{max}$	0.24
Final $\Delta\varrho_{min}$ and $\Delta\varrho_{max}$	−0.21 and 0.15 e Å^{-3}

least-squares planes through the *trans*-fused five- and eleven-membered rings is 36.06(14)°.

An intramolecular hydrogen bond may be present between the oxo group at C(2) and the hydroxy hydrogen at C(4), the distance between acceptor and donor being 2.955 Å. There are two possible intermolecular hydrogen bonds: O(3)···O(1) of 2.947 Å and O(5)···O(3) of 3.323 Å.

Experimental

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter and IR spectra on a Perkin-Elmer FT-IR 1725X spectrometer. For other instrumental details see Ref. 11.

Isolation. Fraction 65C (0.57 g), obtained from an extract (200 g) of flowers of Greek *Nicotiana tabacum*,[12] was separated by repeated flash chromatography (silica gel; hexane–EtOAc gradient) followed by HPLC using a column packed with Spherisorb 5 CN and EtOAc as the eluent to give 21.5 mg of (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*Z*)-4,6,8-trihydroxy-11-capnosene-2,10-dione (**1**), which had m.p. 183–186 °C; $[\alpha]_D$ −12.9° (*c* 0.17, CH_3OH); (Found: $M^{+\cdot}$ 352.2273. Calc. for $C_{20}H_{32}O_5$ 352.2250); IR (KBr): 3417, 1689 and 1643 cm^{-1}; ^{1}H NMR (CD_3OD): δ 0.69 (d, *J* 6.7 Hz)/1.03 (d, *J* 6.9 Hz) (H-16/H-17), 1.29 (d, *J* 0.5 Hz, H-18), 1.50 (d, *J* 0.9 Hz, H-19), 1.75 (d, *J* 1.3 Hz, H-20), 1.92 (dd, *J* 6.1 and −11.7 Hz, H-5a), 2.22 (dd, *J* 9.2 and −11.7 Hz, H-5b), 2.62 (dd, *J* 0.6 and −19.0 Hz, H-9a), 2.65 (dd, *J* 5.9 and 6.8 Hz, H-7), 3.01 (br d, *J* −19.0 Hz, H-9b), 3.08 (dd, *J* 0.8 and 5.9 Hz, H-3), 4.20 (ddd, *J* 6.1, 6.8 and 9.2 Hz, H-6) and 6.15 (br s, H-11); MS [*m/z* (%, composition)]: 352 (*M*, 0.3), 334 (3), 316 (2, $C_{20}H_{28}O_3$), 291 (1, $C_{18}H_{27}O_3$), 273 (1, $C_{18}H_{25}O_2$), 247 (2, $C_{16}H_{23}O_2$), 205 (2, $C_{14}H_{21}O$), 177 (3, $C_{11}H_{13}O_2$), 165 (3, $C_{10}H_{13}O_2$), 153 (18, $C_{10}H_{17}O$), 140 (11, $C_9H_{16}O$ and $C_8H_{12}O_2$), 123 (7, $C_8H_{11}O$ and C_9H_{15}), 109 (13, C_7H_9O and C_8H_{13}), 95 (31, C_6H_7O), 82 (17, C_5H_6O), 69 (18, C_5H_9 and C_4H_5O), 55 (21, C_4H_7 and C_3H_3O) and 43 (100, C_2H_3O and C_3H_7).

Preparation of (1S,3R*,4S*,6R*,7R*,8R*,11Z)-6-acetoxy-4,8-dihydroxy-11-capnosene-2,10-dione* (**2**). Treatment of 5.0 mg of **1** with 0.2 ml of acetic anhydride in 0.4 ml of pyridine for 6 h at room temperature followed by work-up and purification by HPLC (Spherisorb 5; hexane–EtOAc 30:70) gave 4.4 mg of acetate **2**, which had m.p. 147.0–148.5 °C; $[\alpha]_D$ +4.1° (*c* 0.44, $CHCl_3$); (Found: $[M-60]^{+\cdot}$ 334.2133. Calc. for $C_{20}H_{30}O_4$ 334.2144); IR ($CHCl_3$): 3680, 3602, 3461, 1729, 1693, 1641 and 1252 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.76 (d, *J* 6.8 Hz)/1.01 (d, *J* 6.8 Hz) (H-16/H-17), 1.34 (s, H-18), 1.45 (s, H-19), 1.85 (d, *J* 1.3 Hz, H-20), 1.94 (dd, *J* 4.6 and −13.8 Hz, H-5a), 2.07 (s, OCOC*H*$_3$), 2.17 (dd, *J* 7.5 and −13.8 Hz, H-5b), 2.59 (d, *J* −17.1 Hz, H-9a), 2.78 (d, *J* −17.1 Hz, H-9b), 2.92 (dd, *J* 5.9 and 8.6 Hz, H-7), 3.23 (d, *J* 8.6 Hz, H-3), 5.27 (ddd, *J* 4.6, 5.9 and 7.5 Hz, H-6) and 5.98 (br s, H-11); ^{13}C NMR ($CDCl_3$): δ 17.0/22.3 (C-16/C-17), 20.7 (C-14), 21.4 (OCO*C*H$_3$), 25.0 (C-20), 26.0 (C-15), 27.2 (C-18), 28.0 (C-19), 29.3 (C-13), 47.9 (C-5), 51.9 (C-9), 57.8 (C-1), 58.5 (C-7), 59.0 (C-3), 71.5 (C-8), 73.8 (C-6), 79.5 (C-4), 130.2 (C-11), 151.7 (C-12), 170.6 (O*C*OCH$_3$), 201.2 (C-10), and

216.6 (C-2); MS [*m/z* (%)]: 334 (0.6, *M*−60), 316 (1), 291 (0.7), 273 (2), 237 (1), 205 (3), 153 (14), 123 (6), 109 (10), 95 (13), 82 (14), 69 (12), 55 (10) and 43 (100).

Preparation of (1S,3R*,4S*,6R*,7R*,8R*,11Z)-6-benzoyloxy-4,8-dihydroxy-11-capnosene-2,10-dione* (**3**). A solution of 5.4 mg of **1** in 1.5 ml of pyridine was treated with 12 µl of benzoyl chloride at room temperature for 3 h. Work-up and separation by HPLC (Spherisorb 5, hexane–EtOAc 75:25) gave 1.7 mg of the 6-*O*-benzoyl derivative **3**, which had m.p. 193.0–195.5 °C; $[\alpha]_D$ +16.0° (*c* 0.10, $CHCl_3$); IR ($CHCl_3$): 3692, 3602, 3483, 1712, 1697, 1640 and 1283 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.77 (d, *J* 6.8 Hz)/1.03 (d, *J* 6.8 Hz) (H-16/H-17), 1.38 (s, H-18), 1.49 (s, H-19), 1.86 (d, *J* 1.3 Hz, H-20), 2.10 (dd, *J* 5.3 and −13.5 Hz, H-5a), 2.31 (dd, *J* 7.3 and −13.5 Hz, H-5b), 2.68 (d, *J* −17.4 Hz, H-9a), 2.80 (d, *J* −17.4 Hz, H-9b), 3.10 (br s, OH), 3.13 (dd, *J* 6.2 and 8.5 Hz, H-7), 3.30 (d, *J* 8.5 Hz, H-3), 5.50 (ddd, *J* 5.3, 6.2 and 7.3 Hz, H-6), 6.01 (q, *J* 1.3 Hz, H-11) and 7.4–7.6 (m, $OCOC_6H_5$); MS [*m/z* (%)]: 456 (*M*, 0.1), 334 (1), 316 (0.8), 291 (0.4), 273 (0.8), 237 (0.6), 205 (0.7), 153 (7), 123 (9), 109 (10), 105 (64), 95 (16), 82 (19), 77 (48), 69 (16), 55 (19) and 43 (100).

X-Ray crystallography. The unit-cell parameters were refined from the θ values of 11 reflections (θ range 10–25°). The symmetry and systematic extinction of the X-ray reflections were consistent with the space group $P2_1$ or $P2_1/m$. The intensities were corrected for Lorentz and polarisation effects, but no correction was made for absorption (0.804 cm^{-1}). The intensities for three standard reflections (1 0 2, $\bar{1}$ 4 $\bar{2}$ and $\bar{2}$ $\bar{2}$ $\bar{1}$) were monitored every hour; the total deterioration of intensity was < 6 %.

The positions of all non-hydrogen atoms were obtained by direct methods using the SHELXS86 program.[13] One of the two hydroxy hydrogens was located from difference electron density maps. All non-hydroxy hydrogens were geometrically placed with a distance of 1.08 Å to the adjacent carbon atom. The structure was refined by the full-matrix least-squares techniques using the SHELX76 program[14] minimizing $\Sigma w(|F_o|-|F_c|)^2$. Anisotropic thermal parameters were used for the non-hydrogen atoms, while all hydrogen atoms were refined with all isotropic thermal factors constrained to a common value of 0.05 $Å^2$. All calculations were carried out on a C220 Convex computer.

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References

1. Olsson, E., Eklund, A.-M. and Wahlberg, I. *Acta Chem. Scand. 45* (1991) 92.
2. Wahlberg, I., Eklund, A.-M., Nishida, T., Enzell, C. R. and Berg, J.-E. *Tetrahedron Lett. 24* (1983) 843.
3. Uegaki, R., Fujimori, T., Ueda, N. and Ohnishi, A. *Phytochem. 26* (1987) 3029.
4. Wahlberg, I. and Enzell, C. R. *Nat. Prod. Rep. 4* (1987) 237.
5. Bowden, B. F., Coll, J. C., Gulbis, J. M., Mackay, M. F. and Willis, R. H. *Aust. J. Chem. 39* (1986) 803.
6. D'Ambrosio, M., Guerriero, A. and Pietra, F. *Helv. Chim. Acta 72* (1989) 1590.
7. Kobayashi, M. and Osabe, K. *Chem. Pharm. Bull. 37* (1989) 1192.
8. Kobayashi, M. and Nakano, E. *J. Org. Chem. 55* (1990) 1947.
9. Shevtsov, S. A., Raldugin, V. A., Bagryanskaya, I. Yu., Gatilov, Yu. V. and Pentegova, V. A. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* (1984) 102.
10. Cremer, D. and Pople, J. A. *J. Am. Chem. Soc. 97* (1975) 1358.
11. Wahlberg, I., Arndt, R., Nishida, T. and Enzell, C. R. *Acta Chem. Scand., Ser. B 40* (1986) 123.
12. Wahlberg, I., Eklund, A.-M., Nordfors, K., Vogt, C., Enzell, C. R. and Berg, J.-E. *Acta Chem. Scand., Ser. B 42* (1988) 708.
13. Sheldrick, G. M. SHELXS86 In: Sheldrick, G. M., Kruger, C. and Goddard, R., Eds., *Crystallographic Computing 3,* Oxford University Press, Oxford, 1985, pp. 175–189.
14. Sheldrick, G. M. SHELX76: *A Program for crystal structure determination,* University of Cambridge, England.

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