

Tobacco Chemistry. 83.† Four New Cyclized Cembranoids from Tobacco

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Four new cyclized cembranoids have been isolated from an extract of flowers of Greek tobacco. They have been identified as the carbobicyclic capnosanoids (1*S**,2*R**,3*S**,4*S**,6*R**,7*R**,8*R**,11*R**)-2,11:8,11-diepoxy-12(20)-capnosene-4,6-diol (**1**) and (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*S**)-8,11-epoxy-4,6-dihydroxy-12(20)-capnosene-2-one (**2**) and the carbotricyclic basmanoids (1*R**,2*S**,3*R**,4*S**,7*S**,8*S**,11*R**,12*S**)-1,3-epoxy-4,8-dihydroxybasman-6-one (**3**) and the corresponding (7*R**,8*R**,11*S**)-isomer (**4**) by spectral methods, 2D-NMR techniques being particularly useful. The crystal structures of **1** and **3** have been determined and are described. The biogenesis of the new compounds is discussed.

Diterpenoids assumed to arise by carbon–carbon bond closures across the macrocyclic ring of a preformed cembrane precursor are commonly classified as cyclized cembranoids. Compounds of this type are plentiful and characteristic metabolites of termites and certain marine organisms, e.g., soft corals, where they co-occur with cembranoids.² Tobacco has also emerged as a source of cyclized cembranoids. Three compounds have been reported, the carbobicyclic capnosanoid **5**,³ the carbotricyclic basmanoid **6**⁴ and the carbotricyclic virganoid **7**.⁵ While a few capnosanoids are encountered among the constituents of soft corals,² compounds having a basmane or a virgane skeleton have so far only been found in tobacco. The basmanoid **6** has been the target of synthetic studies^{6,7} and a synthesis of racemic **6** has recently been described.^{8,9} A total synthesis of racemic **7** has also been reported.^{10,11}

We now report the isolation by HPLC of four new cyclized cembranoids, the capnosanoids **1** and **2** and the basmanoids **3** and **4**, from an extract of flowers of Greek tobacco.

Results

Structure elucidation. The first new compound (**1**, C₂₀H₃₂O₄) contains an isopropyl group and two methyl groups attached to fully substituted oxygen-carrying

carbon atoms (three-proton doublets at δ 0.82 and 0.99 and three-proton singlets at δ 1.22 and 1.41 in the ¹H NMR spectrum) and a 1,1-disubstituted double bond [¹H NMR signals at δ 4.81 and 4.97; ¹³C NMR: δ 109.4 (t) and 149.5 (s)]. Since the IR spectrum displayed hydroxy bands but was devoid of carbonyl absorption, these results suggest that **1** is a tetracyclic diterpenoid.

DQCOSY, HMQC and HMBC experiments were used to assign the ¹H and ¹³C NMR spectra and to establish the carbon–carbon connectivity of the carbon skeleton. This analysis led to the identification of **1** as a carbobicyclic capnosanoid (see Table 1). The ring junction protons, H-3 and H-7, appear as doublets of doublets at δ 1.78 and 3.04, respectively in the ¹H NMR spectrum. H-6, carrying a hydroxy group, shows coupling to the hydroxy proton resonating at δ 1.77 and gives rise to a ddd at δ 4.06. A tertiary hydroxy group, whose hydroxy proton resonates at δ 1.70, is attached to C-4.

The elemental composition requires that the remaining two oxygen atoms in the capnosanoid **1** form part of two ring systems. One of these ring systems was identified as a 2,11-epoxy bridge with the aid of the HMBC spectrum, which showed a correlation between H-2 and C-11. The latter carbon atom, which is deshielded and resonates at δ 110.6, was evidently also part of the other epoxy bridge extending to C-8 (δ 84.8). Compound **1** was hence identified as 2,11:8,11-diepoxy-12(20)-capnosene-4,6-diol.

Information on the relative stereochemistry was provided by NOE difference spectroscopy (Table 2). Thus,

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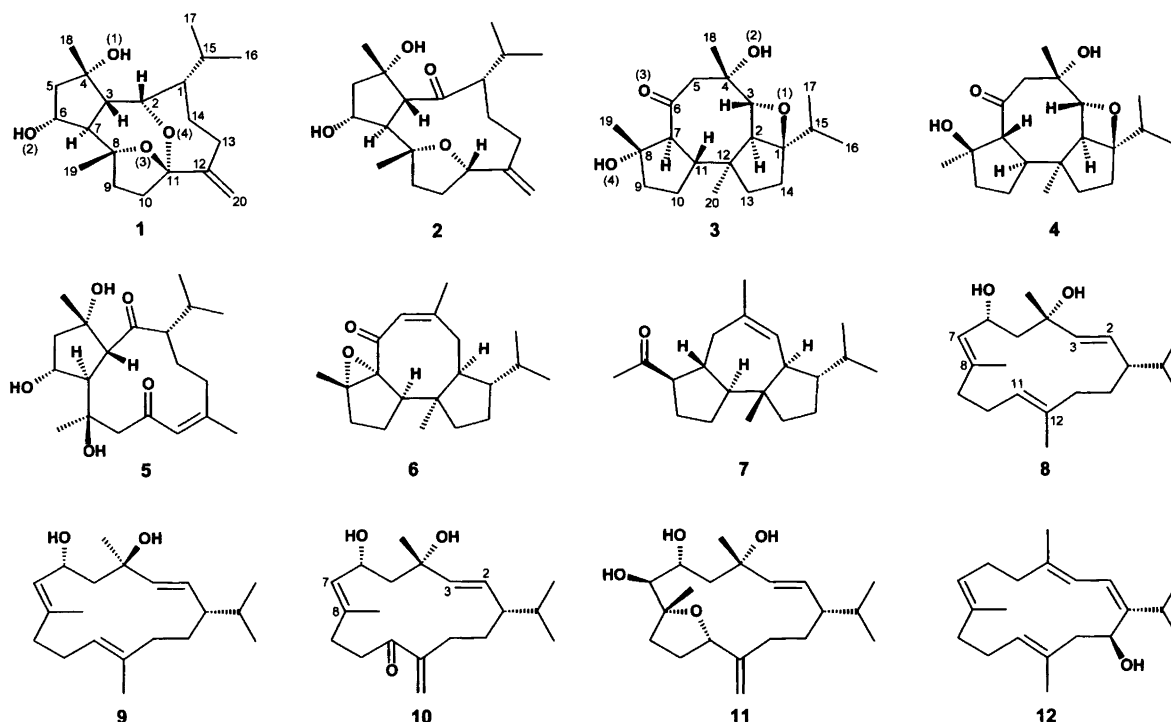


Table 1. HMBC Correlations for compounds 1-4.

| Compound | | 1 | 2 | 3 | 4 |
|----------|---------------------------------------|-----------------------------------|---|----------------------------------|---|
| Atom | | | | | |
| C-1 | H-16, H-17, H-2, H-3 | H-13a, H-13b, H-14b, H-16, H-17 | H-2, H-13a, H-14ab, H-15, H-16, H-17 | H-2, H-13a, H-14b, H-16, H-17 | |
| C-2 | H-1, H-3, H-7 | H-3, H-7 | H-3, H-13a, H-14ab, H-20 | H-13a, H-20 | |
| C-3 | H-1, H-7, H-18 | H-5b, H-6, H-7, H-18, 4-OH | H-2, H-5a, H-5b, H-18 | H-2, H-5a, H-5b, H-18 | |
| C-4 | H-2, H-5a, H-18 | H-3, H-5b, H-6, H-7, H-18, 4-OH | H-2, H-3, H-5a, H-5b, H-18 | H-2, H-3, H-5a, H-5b, H-18, 4-OH | |
| C-5 | H-18 | H-18, 4-OH, 6-OH | H-7, H-18, 4-OH | H-18, 4-OH | |
| C-6 | H-5a, H-5b, H-7 | H-5b, H-7, 6-OH | H-5a, H-5b, H-7 | H-5a, H-5b, H-7 | |
| C-7 | H-9a, H-9b, H-19 | H-3, H-5b, H-9a, H-9b, H-19 | H-5a, H-9ab, H-10ab, H-11, H-19 | H-5a, H-5b, H-19 | |
| C-8 | H-3, H-7, H-9a, H-19 | H-3, H-6, H-7, H-10ab, H-19 | H-7, H-9ab, H-10ab, H-19 | H-7, H-19 | |
| C-9 | H-19, H-10a, H-10b, H-7 | H-7, H-10ab, H-19 | H-10ab, H-19 | H-19 | |
| C-10 | H-9a, H-9b | H-9a, H-9b | H-9ab, H-11 | | |
| C-11 | H-2, H-9b, H-10a, H-13b, H-20a, H-20b | H-9b, H-10ab, H-13a, H-20a, H-20b | H-9ab, H-10ab, H-20 | H-7, H-20 | |
| C-12 | H-13b | H-13a, H-13b, H-14b, H-20a, H-20b | H-3, H-7, H-10ab, H-11, H-13b, H-14ab, H-20 | H-3, H-7, H-14b, H-20 | |
| C-13 | H-1, H-20a, H-20b | H-11, H-14b, H-20a, H-20b | H-2, H-11, H-14ab, H-20 | H-2, H-20 | |
| C-14 | | H-13a, H-13b | H-2, H-13a, H-13b, H-15 | H-2 | |
| C-15 | H-2, H-16, H-17 | H-1, H-16, H-17 | H-2, H-16, H-17 | H-2, H-16, H-17 | |
| C-16 | H-17 | H-17 | H-15, H-17 | H-15, H-17 | |
| C-17 | H-16, H-1 | H-1, H-16 | H-15, H-16 | H-15, H-16 | |
| C-18 | H-3, H-5b | H-3 | H-5a, H-5b | H-5a, H-5b | |
| C-19 | H-7 | H-7, H-9a | H-9ab | H-7 | |
| C-20 | H-13b | H-11, H-13a, H-13b | H-2, H-11, H-13a, H-13b | H-2, H-11 | |

Table 2. Selected NOE data using NOE difference spectroscopy^a or NOESY^b for compounds 1–4.

| Irradiated signal | Compound | | | |
|-------------------|------------------------------|----------------------------|------------------|--------------------------------------|
| | 1 ^a | 2 ^b | 3 ^a | 4 ^b |
| H-1 | | H-3, H-14a, H-15 | | |
| H-2 | H-7, H-18, 4-OH | | | H-5b, H-11, H-15, H-17, H-20, 4-OH |
| H-3 | | H-1, H-5a, H-18, H-19 | H-5b, H-11, H-18 | H-5a, H-7, H-13b, H-18 |
| H-6 | H-3, H-5b, H-19 | H-5a, H-19 | | |
| H-7 | H-2, H-5a, H-9b, H-10a, 6-OH | H-9b, H-13a, 6-OH | | H-3, H-5a, H-9b, H-10a, H-13b, 8-OH |
| H-11 | | | | H-2, H-5b, H-9a, H-10b, H-19, H-20 |
| H-15 | | | | H-2, H-14a, H-16, H-17, H-20, 4-OH |
| H-18 | H-2, H-3, H-5b, H-15, 4-OH | H-3, H-5a, H-15 | H-3, H-5a, H-5b | H-3, H-5a, H-5b, 4-OH |
| H-19 | H-3, H-6, H-9a | H-3, H-5a, H-6, H-9a, H-11 | H-5b | H-5a, H-5b, H-9a, H-11, 8-OH |
| H-20a/H-20 | H-13b, H-20b | H-13b, H-14a, H-20b | H-2, H-7 | H-2, H-10b, H-11, H-13a, H-14a, H-15 |
| H-20b | H-10b, H-20a | H-11, H-20a | | |

enhancements were observed between H-2 and the C-4 hydroxy proton and H-7 and between H-7 and the C-6 hydroxy proton and H-5a. These results suggested that H-2, H-5a, H-7 and the hydroxy groups at C-4 and C-6 are located on the same face of the carbocyclic ring system, e.g., the α -face. The NOEs between H-6 and H-3, H-5b and H-19 and those between H-18 and H-3 and H-5b would then allocate all these protons to the β -face. Since unambiguous evidence for the orientation of the isopropyl group was not provided by the NOE experiments due to overlap of signals, single crystals of **1** were subjected to X-ray analysis (*vide infra*). The results of that study confirmed the structural assignment made and demonstrated that the relative stereochemistry is (1*S**,2*R**,3*S**,4*S**,6*R**,7*R**,8*R**,11*R**).

The second new compound (**2**, C₂₀H₃₂O₄) is also a diterpenoid of the capnosane class. It was identified as (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*S**)-8,11-epoxy-4,6-dihydroxy-12(20)-capnosene-2-one with the aid of spectral methods. Thus, the carbon-carbon connectivity of the carbobicyclic skeleton was elucidated by DQCOSY, HMQC and HMBC experiments. Particularly useful were the correlations in the HMBC spectrum between C-4 and H-3, H-5b and H-18, between C-8 and H-7 and H-19, between C-19 and H-7 and H-9a, between C-12 and the protons attached to C-13 and C-20 and between C-20 and H-11 and H-13ab, since they linked the structural fragments identified from the DQCOSY spectrum across the intervening quaternary C-4, C-8 and C-12.

The allocation of the oxo group to C-2 followed from the observation of a correlation between this carbon atom and H-3 in the HMBC spectrum. The oxo group, which gives rise to an absorption band at 1671 cm⁻¹, is evidently strongly hydrogen-bonded to the hydroxy group at C-4. This view is substantiated by the fact that C-2 is deshielded and resonates at δ 225.4 in the ¹³C NMR spectrum. Deshielding is also shown by the hydroxy proton which appears at δ 6.27 in the ¹H NMR spectrum and is correlated with C-3, C-4 and C-5 in the HMBC spectrum.

H-6, the proton under the secondary hydroxy group

in **2**, resonates at δ 3.80 and is coupled to the hydroxy proton at δ 4.18, to H-7 at δ 2.51 and to H-5a at δ 1.62. The identification of the remaining oxygen atom as an epoxide extending from C-8 to C-11 followed from the chemical shifts of C-8 and C-11, δ 83.2 and 83.7, respectively, and from the chemical shift value of H-11, δ 4.36.^{12,13}

The stereostructure of **2** was studied with the aid of the NOESY spectrum. This contained cross-peaks between H-1 and H-3, between H-3 and H-18 and H-19 and between H-19 and H-6, suggesting that these protons are located on the same face of the molecule, e.g., the β -face. H-3, H-6, H-18 and H-19 show NOE effects with H-5a, while H-5b exhibits an NOE with the proton of the hydroxy group attached to C-6. There is also a strong NOE effect between this hydroxy proton and H-7. As a consequence, H-5b, the hydroxy group at C-6 and H-7 are allocated to the α -face of the molecule. The presence of a cross-peak due to long-range coupling between H-7 and H-19 in the DQCOSY spectrum supports the proposed *trans*-relationship between H-7 and H-19. H-11 was assigned a β -orientation because of its NOE with H-19. These results were used to establish the relative configuration of **2** as (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*S**).

It was suggested by the elemental composition, C₂₀H₃₂O₄, and by the presence of an isopropyl group and three methyl groups [three-proton signals at δ 0.84 (s), 0.87 (d), 0.93 (d), 1.20 (s) and 1.31 (s) in the ¹H NMR spectrum] that the third new compound (**3**) is a diterpenoid. Furthermore, since **3** contains an oxo group (IR band at 1671 cm⁻¹; ¹³C NMR signal at δ 213.8) and is devoid of double bonds, it must have a tetracyclic structure.

The DQCOSY, HMQC and HMBC spectra contained a wealth of structural information and allowed the identification of **3** as a carbocyclic basmane. The correlations in the HMBC spectrum between C-1 and H-2, H-13, H-14 and H-15, between C-4 and H-2, H-3, H-5ab and H-18, between C-6 and H-5ab and H-7, between C-8 and H-7, H-9ab, H-10ab and H-19 and

between C-12 and H-3, H-7, H-11, H-13b and H-20 were particularly helpful in this assignment.

In addition to C-6, which bears the oxo group, four carbon atoms in **3**, C-1, C-3, C-4 and C-8 (δ 96.7, 81.1, 73.9 and 80.9, respectively) are evidently oxygen-carrying. Of these, C-1, because of its chemical shift value, was deduced to be part of an ether-ring extending to C-3 and thus forming a four-membered ring. The remaining two oxygen atoms in **3** are accounted for by hydroxy groups (IR bands at 3590 and 3410 cm^{-1}). Hence, **3** was formulated as a 1,3-epoxy-4,8-dihydroxybasman-6-one.

Since the steric information provided by NOE difference spectroscopy did not suffice for an unambiguous stereochemical assignment, single crystals of **3** were submitted to X-ray analysis. The results obtained confirm the structural formulation made and demonstrate that the configuration of **3** is (1*R**,2*S**,3*R**,4*S**,7*S**,8*S**,11*R**,12*S**).

The fourth new compound (**4**), $\text{C}_{20}\text{H}_{32}\text{O}_4$, was provisionally identified as a 1,3-epoxy-4,8-dihydroxybasman-6-one isomeric with **3** by comparison of their spectral data. This assignment was corroborated by a detailed analysis of the 2D-NMR spectra of **4** which established the carbon-carbon connectivities of this carbocyclic compound (see Table 1).

The allocation of the oxo group (IR band at 1671 cm^{-1}) to C-6 (δ 214.1) was based on the observation of correlations between this carbon atom and H-5ab (δ 2.57 and 2.63) and H-7 (δ 2.96) in the HMBC spectrum. The hydroxy-carrying C-4 and C-8, resonating at δ 74.4 and 82.0, respectively, in the ^{13}C NMR spectrum, were, *inter alia*, correlated with H-18 (δ 1.29) and H-19 (δ 1.15), respectively. In addition, the HMBC spectrum showed a cross-peak between C-4 and a hydroxy proton giving rise to a singlet at δ 2.48.

The presence of the four-membered ether ring extending from C-1 (δ 95.1) to C-3 (δ 80.9) was supported by correlations in the HMBC spectrum between these two carbon atoms and H-2 (δ 2.90), between C-1 and H-16/H-17 (δ 0.90/1.06) and between C-3 and H-5ab.

The stereostructure of **4** was determined by a NOESY experiment (Table 2). NOE interactions were observed between H-3 and H-5a, H-7, H-13b and H-18 and between H-7 and H-5a, H-13b and the proton of the hydroxy group attached to C-8. Hence, these protons are all located on the same face of the molecule, e.g., the β -face. The NOE responses between H-2 and H-5b, H-11, H-20 and the proton of the hydroxy group linked to C-4 and that between H-11 and H-19 were used to assign these protons to the α -face of the molecule. The large coupling constant, 12.0 Hz, between H-7 and H-11 showed that these two protons are antiparallel and confirmed that they are directed toward opposite faces of the molecule. The isopropyl group was assigned an α -orientation on the basis of the NOE interactions between H-15 and H-2, H-20 and the proton of the hydroxy group linked to C-4. These results established the relative configuration at all asymmetric centers and

identified **4** as (1*R**,2*S**,3*R**,4*S**,7*R**,8*R**,11*S**,12*S**)-1,3-epoxy-4,8-dihydroxybasman-6-one.

Biogenesis. Tobacco is a rich source of cembranoids, some eighty compounds having been isolated to date. These are typified by the abundant diols **8** and **9** which incorporate 2,3, 7,8 and 11,12 double bonds and hydroxy substituents at C-4 and C-6.¹⁴ The new diterpenoids (**1–4**) are evidently structurally related to the tobacco cembranoids.

The capnosanoids **1** and **2** are formally generated by intramolecular cyclization reactions connecting C-3 with C-7 in a parent cembranoid, e.g., **8**. The ketal **1** may arise from the 11-oxocembranoid **10**¹⁵ which is a tobacco constituent. Epoxidation of the 2,3 or the 7,8 double bond, acid-induced carbon-carbon bond closures across C-3 and C-7 followed by ketal formation are the proposed steps to **1**. The capnosanoid **2** may be generated from the 8,11-epoxide **11**, another tobacco cembranoid,¹⁶ via epoxidation, acid-induced cyclization and oxidation.

The validity of the proposed biogenetic routes is supported by results from previous studies. These have shown that sarcophytol A (**12**), a 14-hydroxycembranoid of marine origin, as well as three geometric isomers of **12** undergo acid-induced transannular reactions following epoxidation to give bicyclo[9.3.0]tetradecenes.¹⁷ Attempts to prepare capnosanoids related to the new tobacco constituents **1** and **2** from appropriate tobacco cembranoids via epoxidation and acid-induced catalysis were, however, unsuccessful.

The biogenesis of the new basmanoids (**3**, **4**) requires carbon-carbon bond closures between C-2 and C-12 and between C-7 and C-11 in a parent cembranoid. The biogenesis must also encompass oxygenation at C-1 and/or C-3, structural features so far unprecedented among the tobacco cembranoids.

Crystallography. The capnosanoid **1** crystallizes with one molecule in the asymmetric unit. Final fractional coordinates, intramolecular bond lengths and bond angles, with estimated standard deviations, are listed in Tables 3–5. Crystal and experimental data are given in Table 9. Figure 1 is a stereoscopic drawing of the molecule.

There are two long intramolecular hydrogen bonds: O(1)–O(2) of 3.419(3) Å and O(1)–O(4) of 3.420(3) Å. Two intermolecular hydrogen bonds were found, these being: O(1ⁱ)–O(2), 2.803(3) Å and O(1ⁱⁱ)–O(4), 2.857(3) Å [symmetry codes (i) $x-0.5, -0.5-y, -z$ and (ii) $0.5+x, -0.5-y, -z$].

The basmanoid **3** crystallizes with two molecules, A and B, in the asymmetric unit. Final fractional coordinates are presented in Table 6, and intramolecular bond lengths and bond angles, both with estimated standard deviations, are listed in Tables 7 and 8. Crystal and experimental data are given in Table 9. Figure 2 is a stereoscopic drawing of basmanoid **3**.

Four intramolecular hydrogen bonds were found: O(1A)–O(2A) of 2.901(6) Å, O(1B)–O(2B) of

Table 3. Final fractional coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($\times 10^2 \text{ \AA}$) for the non-hydrogen atoms in capnosanoid 1.

| Atom | x | y | z | U_{eq}^a |
|-------|----------|----------|----------|-------------------|
| C(1) | -4524(3) | -5458(2) | 449(2) | 4.15(8) |
| C(2) | -3661(3) | -4305(2) | 395(1) | 3.23(7) |
| C(3) | -1996(3) | -4500(2) | 405(2) | 3.28(7) |
| C(4) | -1133(3) | -4020(2) | -269(2) | 3.59(8) |
| C(5) | 406(3) | -4111(3) | 22(2) | 3.89(8) |
| C(6) | 347(3) | -3871(3) | 874(2) | 4.14(9) |
| C(7) | -1260(3) | -3889(2) | 1061(2) | 3.41(8) |
| C(8) | -1670(3) | -4351(3) | 1854(2) | 3.76(8) |
| C(9) | -1783(4) | -3311(3) | 2393(2) | 4.98(10) |
| C(10) | -3259(4) | -2788(3) | 2185(2) | 5.43(11) |
| C(11) | -4027(3) | -3771(3) | 1747(2) | 4.11(8) |
| C(12) | -5542(3) | -4091(3) | 1960(2) | 4.86(10) |
| C(13) | -6076(4) | -5227(3) | 1632(2) | 5.53(11) |
| C(14) | -6026(3) | -5303(3) | 780(2) | 4.90(10) |
| C(15) | -4565(4) | -6067(3) | -333(2) | 5.99(11) |
| C(16) | -5629(5) | -5489(5) | -881(2) | 7.87(16) |
| C(17) | -4870(6) | -7378(4) | -270(3) | 9.6(2) |
| C(18) | -1345(4) | -4644(3) | -1014(2) | 5.20(10) |
| C(19) | -792(4) | -5390(3) | 2137(2) | 4.99(10) |
| C(20) | -6373(5) | -3386(5) | 2373(3) | 7.80(16) |
| O(1) | -1520(2) | -2791(2) | -359(1) | 4.07(6) |
| O(2) | 894(3) | -2744(2) | 1088(1) | 5.71(8) |
| O(3) | -3152(2) | -4774(2) | 1823(1) | 3.79(6) |
| O(4) | -4092(2) | -3438(2) | 949(1) | 3.53(6) |

$$^a U_{\text{eq}} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

Table 4. Bond lengths (\AA) in capnosanoid 1.

| | | | |
|-------------|----------|-------------|----------|
| C(2)–C(1) | 1.541(5) | C(14)–C(1) | 1.528(6) |
| C(15)–C(1) | 1.554(7) | C(3)–C(2) | 1.567(6) |
| O(4)–C(2) | 1.451(4) | C(4)–C(3) | 1.544(6) |
| C(7)–C(3) | 1.521(6) | C(5)–C(4) | 1.527(6) |
| C(18)–C(4) | 1.517(6) | O(1)–C(4) | 1.452(4) |
| C(6)–C(5) | 1.542(6) | C(7)–C(6) | 1.533(6) |
| O(2)–C(6) | 1.430(5) | C(8)–C(7) | 1.554(6) |
| C(9)–C(8) | 1.526(6) | C(19)–C(8) | 1.522(6) |
| O(3)–C(8) | 1.463(4) | C(10)–C(9) | 1.543(7) |
| C(11)–C(10) | 1.539(7) | C(12)–C(11) | 1.505(6) |
| O(3)–C(11) | 1.408(4) | O(4)–C(11) | 1.471(4) |
| C(13)–C(12) | 1.502(7) | C(20)–C(12) | 1.335(7) |
| C(14)–C(13) | 1.520(7) | C(16)–C(15) | 1.538(8) |
| C(17)–C(15) | 1.522(8) | | |

3.041(6) \AA , O(2B)–O(3B) of 2.969(6) \AA and O(3B)–O(4B) with a distance of 3.203(7) \AA . There are four intermolecular hydrogen bonds, which build an infinite three-dimensional network: O(1A)–O(2B) of 2.794(5) \AA [symmetry code: $x-0.5, 0.5-y, 1-z$], O(2A)–O(4A) of 2.741(6) \AA [symmetry code: $0.5-x, -y, z-0.5$], O(2A)–O(4B) of 2.818(7) [symmetry code: $1-x, y-0.5, 1.5-z$] and O(4A)–O(2B) of 2.915(6) [symmetry code: $1-x, y-0.5, 1.5-z$].

Experimental

High performance liquid chromatography was carried out using a Waters 6000A or Delta Prep 3000 solvent delivery system, a Waters U6K injector and Waters R-401

Table 5. Bond angles (deg) in capnosanoid 1.

| | | | |
|-------------------|----------|-------------------|----------|
| C(14)–C(1)–C(2) | 113.8(3) | C(15)–C(1)–C(2) | 109.6(3) |
| C(15)–C(1)–C(14) | 111.9(4) | C(3)–C(2)–C(1) | 113.3(3) |
| O(4)–C(2)–C(1) | 113.1(3) | O(4)–C(2)–C(3) | 111.2(3) |
| C(4)–C(3)–C(2) | 117.1(3) | C(7)–C(3)–C(2) | 113.0(3) |
| C(7)–C(3)–C(4) | 101.5(3) | C(5)–C(4)–C(3) | 101.6(3) |
| C(18)–C(4)–C(3) | 116.5(3) | C(18)–C(4)–C(5) | 112.8(4) |
| O(1)–C(4)–C(3) | 107.3(3) | O(1)–C(4)–C(5) | 109.6(3) |
| O(1)–C(4)–C(18) | 108.7(3) | C(6)–C(5)–C(4) | 106.8(3) |
| C(7)–C(6)–C(5) | 104.2(3) | O(2)–C(6)–C(5) | 114.0(3) |
| O(2)–C(6)–C(7) | 107.6(3) | C(6)–C(7)–C(3) | 106.3(3) |
| C(8)–C(7)–C(3) | 115.6(3) | C(8)–C(7)–C(6) | 116.1(3) |
| C(9)–C(8)–C(7) | 109.0(3) | C(19)–C(8)–C(7) | 115.5(3) |
| C(19)–C(8)–C(9) | 115.6(4) | O(3)–C(8)–C(7) | 108.0(3) |
| O(3)–C(8)–C(9) | 102.3(3) | O(3)–C(8)–C(19) | 105.3(3) |
| C(10)–C(9)–C(8) | 102.1(3) | C(11)–C(10)–C(9) | 104.8(4) |
| C(12)–C(11)–C(10) | 118.9(4) | O(3)–C(11)–C(10) | 105.7(3) |
| O(3)–C(11)–C(12) | 108.8(3) | O(4)–C(11)–C(10) | 108.7(3) |
| O(4)–C(11)–C(12) | 105.5(3) | O(4)–C(11)–O(3) | 109.0(3) |
| C(13)–C(12)–C(11) | 114.9(4) | C(20)–C(12)–C(11) | 122.5(5) |
| C(20)–C(12)–C(13) | 122.5(5) | C(14)–C(13)–C(12) | 115.3(4) |
| C(13)–C(14)–C(1) | 114.8(4) | C(16)–C(15)–C(1) | 113.1(4) |
| C(17)–C(15)–C(1) | 112.1(5) | C(17)–C(15)–C(16) | 110.2(5) |
| C(11)–O(3)–C(8) | 106.5(3) | C(11)–O(4)–C(2) | 118.0(3) |

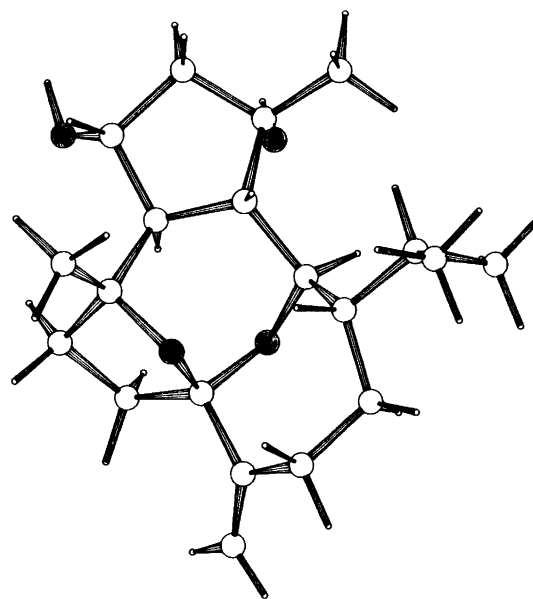


Fig. 1. Drawing of the capnosanoid 1.

or R-403 differential refractometers. Melting points, optical rotations and infrared spectra were recorded on a Leitz Wetzlar instrument, a Perkin-Elmer 241 polarimeter and a Perkin-Elmer FT-IR 1725X spectrometer, respectively. NMR spectra were obtained on a Varian UNITY 300 or a Varian UNITY 500 instrument and mass spectra on a Kratos MS 25 Stereo DS 55 SM/DS 55 S mass spectrometer-computer system.

Isolation. A chloroform extract (500 g) obtained from 5900 kg of flowers of Greek *Nicotiana tabacum* was initially fractionated into six fractions, 1 (92 g), 2 (120 g), 3 (43 g), 4 (72 g), 5 (207 g) and 6 (58 g) by flash

Table 6. Final fractional coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($\times 10^2 \text{ \AA}^2$) for the non-hydrogen atoms in basmanoid 3.

| Atom | x | y | z | U_{eq}^a |
|------------|---------|----------|----------|------------|
| Molecule A | | | | |
| C(1A) | 2167(4) | 1810(3) | 8832(4) | 4.62(20) |
| C(2A) | 2104(4) | 1051(3) | 9382(3) | 3.89(17) |
| C(3A) | 1519(4) | 631(3) | 8761(3) | 4.02(16) |
| C(4A) | 1872(4) | -203(3) | 8427(3) | 4.17(18) |
| C(5A) | 1927(5) | -877(3) | 9075(3) | 5.16(21) |
| C(6A) | 1200(5) | -751(3) | 9700(3) | 4.80(20) |
| C(7A) | 1476(4) | -276(3) | 10422(3) | 4.21(17) |
| C(8A) | 1230(5) | -715(4) | 11200(3) | 5.06(20) |
| C(9A) | 407(5) | -230(4) | 11509(4) | 5.96(24) |
| C(10A) | 631(5) | 674(4) | 11287(4) | 6.04(25) |
| C(11A) | 978(4) | 604(3) | 10444(3) | 4.48(17) |
| C(12A) | 1574(4) | 1325(3) | 10119(3) | 4.60(20) |
| C(13A) | 964(5) | 2054(4) | 9806(4) | 6.21(24) |
| C(14A) | 1578(5) | 2509(4) | 9208(4) | 5.62(21) |
| C(15A) | 3096(4) | 2081(4) | 8497(3) | 5.15(20) |
| C(16A) | 3799(5) | 2301(5) | 9108(4) | 7.83(28) |
| C(17A) | 2983(6) | 2813(4) | 7921(4) | 6.89(25) |
| C(18A) | 1250(5) | -512(4) | 7769(3) | 5.85(22) |
| C(19A) | 1059(6) | -1662(4) | 11163(4) | 7.04(27) |
| C(20A) | 2293(5) | 1627(4) | 10713(4) | 6.12(23) |
| O(1A) | 1623(3) | 1349(2) | 8240(2) | 4.78(12) |
| O(2A) | 2815(3) | -122(3) | 8166(2) | 5.13(15) |
| O(3A) | 405(4) | -1017(3) | 9621(3) | 7.51(19) |
| O(4A) | 1979(3) | -566(3) | 11728(2) | 5.86(16) |
| Molecule B | | | | |
| C(1B) | 3781(5) | 3623(4) | 2883(4) | 6.06(22) |
| C(2B) | 4225(4) | 3967(3) | 3641(4) | 4.96(21) |
| C(3B) | 4671(4) | 3103(3) | 3687(4) | 4.85(21) |
| C(4B) | 5698(5) | 3068(3) | 3811(4) | 5.04(20) |
| C(5B) | 5907(5) | 3320(4) | 4653(3) | 5.20(21) |
| C(6B) | 5669(4) | 4233(4) | 4835(3) | 5.00(21) |
| C(7B) | 4756(5) | 4505(4) | 5205(3) | 5.09(20) |
| C(8B) | 4831(5) | 4561(4) | 6101(4) | 6.00(24) |
| C(9B) | 3829(5) | 4731(6) | 6311(5) | 8.22(32) |
| C(10B) | 3251(5) | 4201(5) | 5758(5) | 7.80(28) |
| C(11B) | 3888(4) | 3996(4) | 5056(4) | 5.75(23) |
| C(12B) | 3469(4) | 4153(4) | 4236(4) | 5.63(23) |
| C(13B) | 2716(5) | 3506(4) | 4010(5) | 7.07(28) |
| C(14B) | 2758(5) | 3447(5) | 3107(5) | 7.17(28) |
| C(15B) | 3960(6) | 4042(5) | 2126(4) | 7.20(26) |
| C(16B) | 3614(6) | 4944(5) | 2079(6) | 9.65(35) |
| C(17B) | 3542(7) | 3515(6) | 1474(5) | 10.13(40) |
| C(18B) | 6063(5) | 2174(4) | 3644(5) | 7.10(24) |
| C(19B) | 5203(5) | 3771(4) | 6480(4) | 6.70(25) |
| C(20B) | 3103(5) | 5061(4) | 4135(5) | 7.41(28) |
| O(1B) | 4335(3) | 2851(2) | 2941(3) | 6.19(15) |
| O(2B) | 6196(3) | 3647(2) | 3331(2) | 5.20(14) |
| O(3B) | 6243(3) | 4779(3) | 4693(3) | 7.33(16) |
| O(4B) | 5378(3) | 5271(3) | 6332(3) | 7.17(18) |

$$^a U_{eq} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

chromatography over silica gel using a gradient of hexane-EtOAc-MeOH as the eluent. Fraction 3 (80 g) was separated further by flash chromatography (silica gel, hexane-EtOAc 1:1) and by HPLC (Prep Pak-500 Silica 15, hexane-EtOAc 70:30) into six fractions. One of these (5.1 g) was subjected to repeated HPLC using columns packed with Spherisorb 5 CN (hexane-EtOAc

Table 7. Bond lengths (\AA) in basmanoid 3.

| Molecule A | | | |
|---------------|-----------|---------------|-----------|
| C(2A)-C(1A) | 1.540(9) | C(14A)-C(1A) | 1.540(10) |
| C(15A)-C(1A) | 1.522(11) | O(1A)-C(1A) | 1.485(8) |
| C(3A)-C(2A) | 1.522(10) | C(12A)-C(2A) | 1.552(10) |
| C(4A)-C(3A) | 1.531(9) | O(1A)-C(3A) | 1.463(7) |
| C(5A)-C(4A) | 1.554(9) | C(18A)-C(4A) | 1.533(10) |
| O(2A)-C(4A) | 1.437(8) | C(6A)-C(5A) | 1.521(11) |
| C(7A)-C(6A) | 1.516(10) | O(3A)-C(6A) | 1.229(9) |
| C(8A)-C(7A) | 1.560(10) | C(11A)-C(7A) | 1.570(9) |
| C(9A)-C(8A) | 1.513(11) | C(19A)-C(8A) | 1.522(10) |
| O(4A)-C(8A) | 1.435(9) | C(10A)-C(9A) | 1.518(11) |
| C(11A)-C(10A) | 1.550(11) | C(12A)-C(11A) | 1.537(10) |
| C(13A)-C(12A) | 1.552(11) | C(20A)-C(12A) | 1.538(11) |
| C(14A)-C(13A) | 1.543(11) | C(16A)-C(15A) | 1.508(11) |
| C(17A)-C(15A) | 1.541(10) | | |
| Molecule B | | | |
| C(2B)-C(1B) | 1.562(11) | C(14B)-C(1B) | 1.550(13) |
| C(15B)-C(1B) | 1.494(11) | O(1B)-C(1B) | 1.465(9) |
| C(3B)-C(2B) | 1.516(10) | C(12B)-C(2B) | 1.530(11) |
| C(4B)-C(3B) | 1.497(10) | O(1B)-C(3B) | 1.439(8) |
| C(5B)-C(4B) | 1.545(11) | C(18B)-C(4B) | 1.539(10) |
| O(2B)-C(4B) | 1.433(8) | C(6B)-C(5B) | 1.520(11) |
| C(7B)-C(6B) | 1.526(11) | O(3B)-C(6B) | 1.223(8) |
| C(8B)-C(7B) | 1.562(11) | C(11B)-C(7B) | 1.512(11) |
| C(9B)-C(8B) | 1.515(12) | C(19B)-C(8B) | 1.514(12) |
| O(4B)-C(8B) | 1.431(8) | C(10B)-C(9B) | 1.524(13) |
| C(11B)-C(10B) | 1.559(11) | C(12B)-C(11B) | 1.567(12) |
| C(13B)-C(12B) | 1.544(11) | C(20B)-C(12B) | 1.543(11) |
| C(14B)-C(13B) | 1.573(13) | C(16B)-C(15B) | 1.517(13) |
| C(17B)-C(15B) | 1.530(12) | | |

80:20) and Lichrosorb 10 Diol (hexane-EtOAc 60:40) to give 63 mg of a crude sample of (1*S**,3*R**,4*S**,6*R**,7*R**,8*R**,11*S**)-8,11-epoxy-4,6-dihydroxy-12(20)-capnosene-2-one (**2**). Part of this material was purified further by HPLC (Spherisorb 5 and Spherisorb 5 CN, hexane-EtOAc 70:30) to give 4.8 mg of a homogeneous sample of **2**.

Fraction 5 (128 g) was separated by flash chromatography (silica gel, hexane-EtOAc gradient) into eight fractions, 51-58. Further separation of fraction 54 (16.8 g) by HPLC (Spherisorb 5, EtOAc; Spherisorb 5 CN, hexane-EtOAc 60:40; Lichrosorb 10 Diol, hexane-EtOAc 30:70) gave 4.9 mg of (1*S**,2*R**,3*S**,4*S**,6*R**,7*R**,8*R**,11*R**)-2,11:8,11-diepoxy-12(20)-capnosene-4,6-diol (**1**). Fraction 56 (28.0 g) was separated by HPLC (Spherisorb 5 CN, hexane-EtOAc 40:60) into six fractions, 561-566. Repetitive HPLC of fraction 562 (12.7 g) (Spherisorb 5 ODS, MeOH-H₂O 80:20 and acetonitrile-acetone-H₂O 32:23:45; Lichrosorb 10 Diol, hexane-EtOAc 20:80) gave 4.7 mg of (1*R**,2*S**,3*R**,4*S**,7*S**,8*S**,11*R**,12*S**)-1,3-epoxy-4,8-dihydroxybasman-6-one (**3**). (1*R**,2*S**,3*R**,4*S**,7*R**,8*R**,11*S**,12*S**)-1,3-Epoxy-4,8-dihydroxybasman-6-one (**4**, 4.4 mg) was isolated from fraction 57 (10.5 g) by HPLC using columns packed with Spherisorb 5 (EtOAc), Lichrosorb 10 Diol (hexane-EtOAc 10:90) and Spherisorb 5 CN (hexane-EtOAc 40:60).

It should be noted that the yields of compounds 1-4

Table 8. Bond angles (deg) in basmanoid 3.

| Molecule A | | | |
|----------------------|----------|----------------------|----------|
| C(14A)–C(1A)–C(2A) | 105.5(6) | C(15A)–C(1A)–C(2A) | 120.6(6) |
| C(15A)–C(1A)–C(14A) | 116.4(6) | O(1A)–C(1A)–C(2A) | 90.8(5) |
| O(1A)–C(1A)–C(14A) | 110.8(6) | O(1A)–C(1A)–C(15A) | 109.8(6) |
| C(3A)–C(2A)–C(1A) | 86.3(5) | C(12A)–C(2A)–C(1A) | 108.7(5) |
| C(12A)–C(2A)–C(3A) | 115.7(6) | C(4A)–C(3A)–C(2A) | 117.5(6) |
| O(1A)–C(3A)–C(2A) | 92.3(5) | O(1A)–C(3A)–C(4A) | 113.8(5) |
| C(5A)–C(4A)–C(3A) | 109.6(5) | C(18A)–C(4A)–C(3A) | 111.4(6) |
| C(18A)–C(4A)–C(5A) | 110.4(6) | O(2A)–C(4A)–C(3A) | 111.0(6) |
| O(2A)–C(4A)–C(5A) | 103.9(6) | O(2A)–C(4A)–C(18A) | 110.3(6) |
| C(6A)–C(5A)–C(4A) | 113.0(6) | C(7A)–C(6A)–C(5A) | 118.3(6) |
| O(3A)–C(6A)–C(5A) | 121.2(7) | O(3A)–C(6A)–C(7A) | 120.4(7) |
| C(8A)–C(7A)–C(6A) | 115.8(5) | C(11A)–C(7A)–C(6A) | 110.0(6) |
| C(11A)–C(7A)–C(8A) | 105.8(5) | C(9A)–C(8A)–C(7A) | 104.9(6) |
| C(19A)–C(8A)–C(7A) | 116.1(6) | C(19A)–C(8A)–C(9A) | 112.9(7) |
| O(4A)–C(8A)–C(7A) | 107.9(6) | O(4A)–C(8A)–C(9A) | 106.3(6) |
| O(4A)–C(8A)–C(19A) | 108.2(6) | C(10A)–C(9A)–C(8A) | 102.9(6) |
| C(11A)–C(10A)–C(9A) | 103.9(6) | C(10A)–C(11A)–C(7A) | 103.5(5) |
| C(12A)–C(11A)–C(7A) | 113.4(5) | C(12A)–C(11A)–C(10A) | 118.3(6) |
| C(11A)–C(12A)–C(2A) | 111.7(5) | C(13A)–C(12A)–C(2A) | 101.5(5) |
| C(13A)–C(12A)–C(11A) | 111.5(6) | C(20A)–C(12A)–C(2A) | 107.9(6) |
| C(20A)–C(12A)–C(11A) | 111.3(6) | C(20A)–C(12A)–C(13A) | 112.7(6) |
| C(14A)–C(13A)–C(12A) | 105.0(6) | C(13A)–C(14A)–C(1A) | 105.4(6) |
| C(16A)–C(15A)–C(1A) | 112.8(6) | C(17A)–C(15A)–C(1A) | 111.5(6) |
| C(17A)–C(15A)–C(16A) | 110.7(6) | C(3A)–O(1A)–C(1A) | 90.5(4) |
| Molecule B | | | |
| C(14B)–C(1B)–C(2B) | 104.0(7) | C(15B)–C(1B)–C(2B) | 120.9(6) |
| C(15B)–C(1B)–C(14B) | 117.7(7) | O(1B)–C(1B)–C(2B) | 90.6(5) |
| O(1B)–C(1B)–C(14B) | 110.6(6) | O(1B)–C(1B)–C(15B) | 109.7(7) |
| C(3B)–C(2B)–C(1B) | 84.4(5) | C(12B)–C(2B)–C(1B) | 110.1(6) |
| C(12B)–C(2B)–C(3B) | 116.2(6) | C(4B)–C(3B)–C(2B) | 117.4(6) |
| O(1B)–C(3B)–C(2B) | 93.5(5) | O(1B)–C(3B)–C(4B) | 116.9(6) |
| C(5B)–C(4B)–C(3B) | 108.7(6) | C(18B)–C(4B)–C(3B) | 110.2(6) |
| C(18B)–C(4B)–C(5B) | 110.5(7) | O(2B)–C(4B)–C(3B) | 112.8(6) |
| O(2B)–C(4B)–C(5B) | 106.6(6) | O(2B)–C(4B)–C(18B) | 108.0(6) |
| C(6B)–C(5B)–C(4B) | 113.5(6) | C(7B)–C(6B)–C(5B) | 123.4(6) |
| O(3B)–C(6B)–C(5B) | 118.6(7) | O(3B)–C(6B)–C(7B) | 118.0(7) |
| C(8B)–C(7B)–C(6B) | 112.0(6) | C(11B)–C(7B)–C(6B) | 119.5(6) |
| C(11B)–C(7B)–C(8B) | 104.9(6) | C(9B)–C(8B)–C(7B) | 100.6(7) |
| C(19B)–C(8B)–C(7B) | 114.2(6) | C(19B)–C(8B)–C(9B) | 112.4(8) |
| O(4B)–C(8B)–C(7B) | 111.2(6) | O(4B)–C(8B)–C(9B) | 108.5(7) |
| O(4B)–C(8B)–C(19B) | 109.5(6) | C(10B)–C(9B)–C(8B) | 105.8(7) |
| C(11B)–C(10B)–C(9B) | 106.5(6) | C(10B)–C(11B)–C(7B) | 104.1(6) |
| C(12B)–C(11B)–C(7B) | 112.9(6) | C(12B)–C(11B)–C(10B) | 116.7(6) |
| C(11B)–C(12B)–C(2B) | 107.9(6) | C(13B)–C(12B)–C(2B) | 101.7(6) |
| C(13B)–C(12B)–C(11B) | 113.3(7) | C(20B)–C(12B)–C(2B) | 110.3(7) |
| C(20B)–C(12B)–C(11B) | 112.5(7) | C(20B)–C(12B)–C(13B) | 110.5(6) |
| C(14B)–C(13B)–C(12B) | 105.3(7) | C(13B)–C(14B)–C(1B) | 106.0(7) |
| C(16B)–C(15B)–C(1B) | 114.2(8) | C(17B)–C(15B)–C(1B) | 109.8(7) |
| C(17B)–C(15B)–C(16B) | 110.2(8) | C(3B)–O(1B)–C(1B) | 90.8(5) |

given above are isolated yields from the fractions examined. They do not necessarily represent the concentrations of these compounds in tobacco flowers.

(1*S**, 2*R**, 3*S**, 4*S**, 6*R**, 7*R**, 8*R**, 11*R**)-2,11:8,11-Diepoxy-12(20)-capsosene-4,6-diol (**1**) had m.p. 197–199 °C; $[\alpha]_D^{25} -33^\circ$ (*c* 0.21, CHCl₃). IR (CHCl₃): 3592, 3425, 1122, 909 cm⁻¹. ¹H NMR (CDCl₃): δ 0.82 (d, *J* 6.8 Hz)/0.99 (d, *J* 6.8 Hz) (H-16/H-17), 1.22 (s, H-18), 1.41 (s, H-19), 1.70 (d, *J* 7.6 Hz, –OH on C-6), 1.73 (dt, *J* 8.0 and –11.7 Hz, H-9a), 1.77 (s, –OH on C-4) 1.78 (dd, *J* 4.1 and 13.0 Hz, H-3), 1.84 (dd, *J* 3.8

and –14.5 Hz, H-5a), 1.89 (br dt, *J* 3.2 and 8.8 Hz, H-1), 2.22 (dd, *J* 8.5 and –14.5 Hz, H-5b), 2.23 (ddd, *J* 2.5, 9.1 and –11.7 Hz, H-9b), 2.34 (br t, *J* –13.9, H-13a), 2.44 (ddd, *J* 8.0, 9.1 and –13.5 Hz, H-10a) 2.47 (ddd, *J* 3.1, 6.6 and –13.9 Hz, H-13b), 2.63 (ddd, *J* 2.5, 11.6 and –13.5 Hz, H-10b), 3.04 (dd, *J* 7.8 and 13.0 Hz, H-7), 3.82 (dd, *J* 4.1 and 8.8 Hz, H-2), 4.12 (ddd, *J* 3.8, 7.6 and 8.5 Hz, H-6), 4.81 (q, *J* 1.0 Hz, H-20a), 4.97 (t, *J* 1.3 Hz, H-20b). ¹³C NMR (CDCl₃): δ 15.9/22.3 (C-16/C-17), 21.4 (C-19), 24.3 (C-14), 26.7 (C-15), 27.5 (C-18), 34.5 (C-13), 37.0 (C-10), 41.0 (C-9), 52.0 (C-5), 53.5 (C-1), 57.8 (C-3), 59.6 (C-7), 71.3 (C-6), 74.7 (C-2),

Table 9. Crystal and experimental data for capnosanoid 1 and basmanoid 3.

| | 1 | 3 |
|---|---|---|
| Formula | C ₂₀ H ₃₂ O ₄ | 2(C ₂₀ H ₃₂ O ₄) |
| Formula weight | 336.47 | 670.92 |
| Space group | P2 ₁ 2 ₁ 2 ₁ | P2 ₁ 2 ₁ 2 ₁ |
| Unit cell dimensions/Å | a=9.3134(4) b=11.3699(14) c=17.7933(11) | a=14.4190(18) b=15.8566(11) c=17.3550(43) |
| Unit cell volume V/Å ³ | 1884.2(3) | 3968.0(1.1) |
| Formula units per unit cell, Z | 4 | 8 |
| Calculated density, D _x /g cm ⁻³ | 1.19 | 1.13 |
| Radiation | Cu Kα | Cu Kα |
| Wavelength, λ/Å | 1.54184 | 1.54184 |
| Linear absorption coefficient/cm ⁻¹ | 6.10 | 5.39 |
| Temperature, T/K | 293(1) | 293(1) |
| Crystal shape | Prismatic | Prismatic |
| Diffractometer | Siemens/Stoe AED 2 | Siemens/Stoe AED 2 |
| Determination of unit cell | | |
| Number of reflections used | 11 | 19 |
| θ-range/° | 10.0–25.0 | 10.0–25.0 |
| Intensity data collection | | |
| Maximum [sin(θ)/λ]/Å ⁻¹ | 0.61 | 0.56 |
| Range of h, k and l | 0–10, 0–13 and 0–21 | 0–16, 0–17 and 0–19 |
| Standard reflections | 3 | 3 |
| Intensity instability (%) | <2 | <3 |
| Number of collected reflections | 1980 | 3168 |
| Number of unique reflections | 1897 | 2872 |
| Number of observed reflections | 1705 | 2247 |
| Criterion for significance | F > 3σ(F) | F > 3σ(F) |
| Structure refinement | | |
| Minimization of | Σ ωΔF ² | Σ ωΔF ² |
| Anisotropic thermal parameters | | All non-hydrogen atoms |
| Isotropic thermal parameters | | Hydrogen atoms |
| Number of refined parameters | 230 | 440 |
| Weighting scheme | [σ ² (F) + 0.003 F ²] ⁻¹ | [σ ² (F) + 0.005 F ²] ⁻¹ |
| Final R for observed refls. | 0.051 | 0.061 |
| Final wR for observed refls. | 0.054 | 0.062 |
| Final wR for all refls. | 0.057 | 0.071 |
| Final (Δ/σ) _{max} | 0.132 | 0.002 |
| Final Δρ _{min} and Δρ _{max} /e Å ³ | –0.23 and 0.16 | –0.28 and 0.20 |
| GOF | 1.142 | 0.996 |

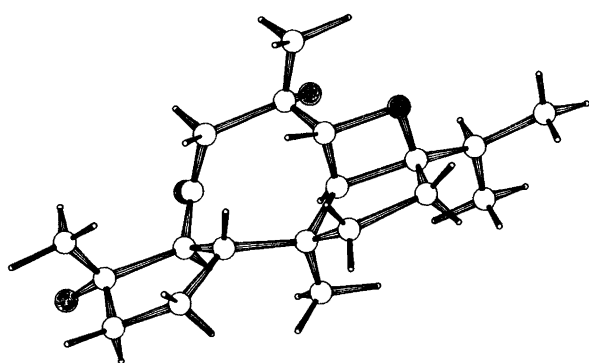


Fig. 2. Drawing of the basmanoid 3.

84.8 (C-8), 109.4 (C-20), 110.6 (C-11), 149.5 (C-12) (the C-4 signal, which overlapped a solvent peak at δ 77.2, was observed in the HMBC spectrum). MS [*m/z* (%): 336 (9, *M*), 193 (7), 167 (6), 152 (8), 137 (7), 135 (7), 133 (6), 123 (8), 121 (8), 109 (21), 95 (18), 81 (17), 69 (25), 55 (34), 43 (100).

(1*S**, 3*R**, 4*S**, 6*R**, 7*R**, 8*R**, 11*S**)-8,11-Epoxy-4,6-dihydroxy-12(20)-capnosene-2-one (**2**) was an oil and had [α]_D –14° (*c* 0.48, CHCl₃). (Found [*M*]⁺ 336.2329. Calc. for C₂₀H₃₂O₄: 336.2301). IR (CHCl₃): 3387, 3076, 1671, 1391, 1379, 1091 and 911 cm⁻¹. ¹H NMR (CDCl₃): δ 0.85 (d, *J* 6.8 Hz)/0.97 (d, *J* 6.8 Hz) (H-16/H-17), 1.24 (s, H-19), 1.30 (s, H-18), 2.51 (dt, *J* 1.5 and 9.3 Hz, H-7), 2.80 (d, *J* 9.3 Hz, H-3), 3.48 (ddd, *J* 2.7, 3.6 and 12.3 Hz, H-1), 3.80 (ddd, *J* 1.5, 5.6 and 11.5 Hz, H-6), 4.18 (d, *J* 11.5 Hz, –OH on C-6), 4.36 (t, *J* 7.7 Hz, H-11), 4.94 (t, *J* 1.3 Hz, H-20a), 5.06 (br s, H-20b) and 6.27 (d, *J* 2.0 Hz, –OH on C-4). ¹³C NMR (CDCl₃): δ 18.0/21.2 (C-16/C-17), 22.5 (C-19), 26.6 (C-18), 27.1 (C-13), 28.6 (C-15), 29.6 (C-14), 31.1 (C-10), 38.0 (C-9), 49.0 (C-5), 56.3 (C-1), 60.0 (C-3), 68.4 (C-7), 75.5 (C-6), 83.2 (C-4 and C-8), 83.7 (C-11), 115.4 (C-20), 149.8 (C-12) and 225.4 (C-2). MS [*m/z* (%): 336 (19, *M*), 318 (10, C₂₀H₃₀O₃), 300 (20, C₂₀H₂₈O₂), 275 (8, C₁₈H₂₇O₂), 221 (20, C₁₄H₂₁O₂), 193 (17), 189 (16), 165 (20), 149 (26), 137 (54), 121 (31), 109 (37), 95 (56), 93 (70), 81 (52), 69 (50), 55 (41) and 43 (100).

(1R*,2S*,3R*,4S*,7S*,8S*,11R*,12S*)-1,3-Epoxy-4,8-dihydroxybasman-6-one (**3**) had m.p. 122–123 °C; $[\alpha]_D -26^\circ$ (*c* 0.47, CHCl₃). (Found: M^+ 336.2264. Calc. for C₂₀H₃₂O₄: 336.2300). IR (CHCl₃): 3590, 3410, 1671, 1461, 1383 and 1367 cm⁻¹. ¹H NMR (CDCl₃): δ 0.84 (d, *J* 0.7 Hz, H-20), 0.87 (d, *J* 6.9 Hz)/0.93 (d, *J* 6.8 Hz) (H-16/H-17), 1.21 (s, H-19), 1.30 (s, H-18), 2.41 (dt, *J* 8.3 and 11.5 Hz, H-11), 2.48 (d, *J* -11.5 Hz, H-5a), 2.52 (dd, *J* 1.2 and 6.8 Hz, H-2), 2.65 (d, *J* 11.5 Hz, H-7), 2.66 (d, *J* -11.5 Hz, H-5b) and 4.45 (d, *J* 6.8 Hz, H-3). ¹³C NMR (CDCl₃): δ 16.9/17.0 (C-16/C-17), 17.4 (C-20), 23.1 (C-10), 25.1 (C-19), 25.3 (C-18), 32.5 (C-14), 35.7 (C-15), 38.1 (C-13), 41.7 (C-9), 43.4 (C-12), 48.6 (C-11), 51.3 (C-5), 53.1 (C-2), 68.1 (C-7), 73.9 (C-4), 80.9 (C-8), 81.1 (C-3), 96.7 (C-1) and 213.8 (C-6). MS [*m/z* (% composition)]: 336 (0.4, *M*), 318 (3, C₂₀H₃₀O₃), 300 (6, C₂₀H₂₈O₂), 278 (3, C₁₇H₂₆O₃), 275 (7, C₁₈H₂₇O₂), 260 (4, C₁₇H₂₄O₂), 257 (3, C₁₈H₂₅O), 183 (10), 165 (14), 153 (14), 135 (12), 123 (62), 107 (22), 95 (14), 81 (34), 71 (17), 55 (19) and 43 (100).

(1R*,2S*,3R*,4S*,7R*,8R*,11S*,12S*)-1,3-Epoxy-4,8-dihydroxybasman-6-one (**4**) was an oil and had $[\alpha]_D -18^\circ$ (*c* 0.52, CHCl₃). (Found: M^+ 336.2334. Calc. for C₂₀H₃₂O₄: 336.2300). IR (CHCl₃): 3597, 3490, 1703, 1671, 1459, 1380 and 1367 cm⁻¹. ¹H NMR (CDCl₃): δ 0.88 (d, *J* 0.8 Hz, H-20), 0.90 (d, *J* 6.9 Hz)/1.06 (d, *J* 6.8 Hz) (H-16/H-17), 1.15 (s, H-19), 1.29 (s, H-18), 2.48 (s, -OH), 2.57 (d, *J* -10.5 Hz, H-5a), 2.63 (d, *J* -10.5 Hz, H-5b), 2.90 (dd, *J* 1.4 and 7.0 Hz, H-2), 2.96 (d, *J* 12.0 Hz, H-7) and 4.59 (d, *J* 7.0 Hz, H-3). ¹³C NMR (CDCl₃): δ 16.0/18.4 (C-16/C-17), 23.8 (C-18), 24.4 (C-10), 25.7 (C-19), 26.1 (C-20), 30.9 (C-13), 34.9 (C-14), 36.9 (C-15), 40.3 (C-9), 44.3 (C-12), 49.5 (C-11), 53.6 (C-2 and C-5), 63.5 (C-7), 74.4 (C-4), 80.9 (C-3), 82.0 (C-8), 95.8 (C-1) and 214.1 (C-6). MS [*m/z* (% composition)]: 336 (0.2, *M*), 318 (1, C₂₀H₃₀O₃), 300 (3, C₂₀H₂₈O₂), 275 (3, C₁₈H₂₇O₂), 257 (2, C₁₈H₂₅O), 233 (2), 177 (3), 165 (3), 161 (3), 149 (5), 135 (7), 123 (26), 109 (11), 107 (11), 95 (14), 81 (19), 71 (15), 69 (16), 55 (18) and 43 (100).

X-Ray crystallography study. Single crystals of **1** and **3** were obtained by recrystallization from mixtures of ethyl acetate and hexane. The space group symmetry was determined from systematic absences and by the unit cell parameters found by the least-squares method from 11 (for **1**) and 19 (for **3**) centred reflections. The intensities of three test reflections 0 3 8, 3 4 2, 4 0 3 (for **1**) and 1 1 -2, 3 0 -1, 2 1 -1 (for **3**), remeasured every 60 min, showed <2% and <3% intensity instability, respectively. The intensities were scaled and corrected for Lorentz and polarization effects but no correction was made for absorption.

The positions of all non-hydrogen atoms in **1** and 25 of the 48 non-hydrogen atoms in **3** were obtained by

direct methods using the SHELXS86 program.¹⁸ The remaining non-hydrogen atoms in **3**, the hydroxy hydrogens in **1** and two of the hydroxy hydrogens in **3** (two were not found) were located from difference electron-density maps. All hydrogen atoms were geometrically placed and refined. Full matrix least-squares anisotropic refinement of the non-hydrogen parameters was applied using the SHELX76 program.¹⁹ The hydrogen parameters were refined with all isotropic temperature factors constrained to a common value and bond lengths restricted to 1.00 Å. The atomic scattering factors²⁰ used for non-hydrogen and hydrogen atoms were those included in SHELX76 program.

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