Configuration, Conformation, and Reactivity of Highly Functionalized Eunicellane Diterpenes Isolated from the Gorgonians *Eunicella cavolinii* and *Eunicella singularis* from Marseille

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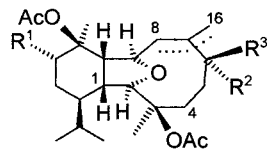
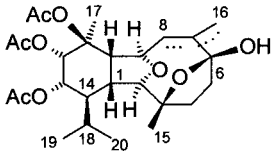
Eunicellane diterpenes with a C(7)=C(16) ($\Delta^{7,16}$; see **17**–**19**), (*Z*)-C(7)=C(8) ((7*Z*)$\Delta^{7,8}$; see **20**–**23**), and (*Z*)-C(6)=C(7) ((6*Z*)$\Delta^{6,7}$; see **10**) bond, an uncommon feature in the case of extensive functionalization at the cyclohexane ring and the latter exhibiting uncommon configurations, were isolated from the gorgonian *Eunicella cavolinii* from Marseille (*Figs. 5* and *2*). The gorgonian *Eunicella singularis* (= *Eunicella stricta*) from the same area gave (7*Z*)$\Delta^{7,8}$, $\Delta^{7,16}$, and (6*E*)$\Delta^{6,7}$ analogs **24**, **25**, and **13**, respectively (*Fig. 5* and *Scheme*). The (6*E*)$\Delta^{6,7}$ moiety of **13** – characterized by a slow 180° conformational flipping (*Fig. 3*) that results in broadening of NMR signals – makes the macrocycle highly strained. This may explain the spontaneous conversion of **13** to the 6-methoxy-7-hydroxy derivative **14** in the presence of MeOH at −20° in the dark (*Scheme*). The isomeric, deacylated analogue **10** showed only little broadening of NMR signals and proved stable, in accordance with the less strained nature of this compound (*Fig. 4*).

1. Introduction. – Gorgonians and alcyonarians are a rich source of 2,11-cyclized cembrane diterpenes, which bear an O-bridge between C(2) and C(9) at the ten-membered carbocycle, like in **1**–**6**[1]), or additional O-bridges, like in **7**–**9** and other examples (*Fig. 1*) [1]. Although these compounds have often been given trivial names related to the source organism or the collection site, we refer to them as eunicellane diterpenes from the first reported compound in this class, eunicellin (**1**) [2]. This should facilitate recognizing the chemical class to which these compounds belong.

We disclose here new eunicellanes that are unusual for both extensive functionalization at the cyclohexane moiety and, in cases, a high oxidation level at the macrocycle, which embodies either a C(7)=C(16) ($\Delta^{7,16}$), (*Z*)-C(7)=C(8) ((7*Z*)$\Delta^{7,8}$), (*Z*)-C(6)=C(7) ((6*Z*)$\Delta^{6,7}$), or (*E*)-C(6)=C(7) ((6*E*)$\Delta^{6,7}$) bond. The latter induces a high strain that allowed us to better understand both the conformational behavior and the reactivity of terpenoids in this family. These compounds were isolated from two gorgonians from the eastern coast of Marseille. Thus, during a re-examination of solvent extracts from *Eunicella cavolinii*, which had already given massileunicellins

[1]) For convenience, we have adopted the eunicellane numbering [1], except for systematic names (see *Exper. Part*).





1 $\Delta^{7,16}$, $R^1 = R^3 = AcO$, $R^2 = H$

2 $\Delta^{7,16}$, $R^1 = H$, $R^2, R^3 = O$

3 $\Delta^{7,8}$, $R^1 = H$, $R^2, R^3 = O$

4 $\Delta^{7,16}$, $R^1 = AcO$, $R^2, R^3 = O$

5 $\Delta^{7,16}$, $R^1 = AcO$, $R^2 = H$, $R^3 = OH$

6 $\Delta^{7,8}$, $R^1 = AcO$, $R^2, R^3 = O$

7 $\Delta^{7,16}$

8 $\Delta^{7,8}$

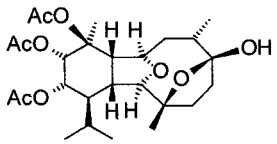


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Fig. 1. *Eunicellane diterpenes* **1** *and* **7**–**9** *previously isolated from the gorgonian* Eunicella singularis *and* **2**–**6** *from various* Eunicella *spp.*

A–C (**7**–**9**)[2]) (*Fig. 1*), we have now isolated the new eunicellanes **10** (*Fig. 2*) and **17**–**23** (*Fig. 5*). The other gorgonian, *Eunicella singularis* (= *Eunicella stricta*), has now given the new eunicellanes **13** (*Scheme*), **24**, and **25** (*Fig. 5*), besides the known analogs eunicellin (**1**) (reported from the same gorgonian species from the Banyuls-sur-Mer coast in NW Mediterranean) [2]), palmonine D (**2**), and palmonine E (**3**) (reported from *Eunicella verrucosa* from southern Spain [3]), as well as labiatin B (**4**), labiatin C (**5**)[3]) [4], and labiatin D (**6**) [5] (reported from *Eunicella labiata* from the coasts of Senegal) (*Fig. 1*).

2. Results and Discussion. – 2.1. *(6Z)* vs. *(6*E*) Configuration of the Eunicellanes.* The structure of the new eunicellane diterpene **10** (*Fig. 2*) was deduced from FAB-MS ($[M+H]^+$ at *m/z* 481), HR-EI-MS ($[M-AcOH]^+$ at *m/z* 420), and fully assigned NMR spectra (*Table 1*), which confirmed the composition and gave the connectivity

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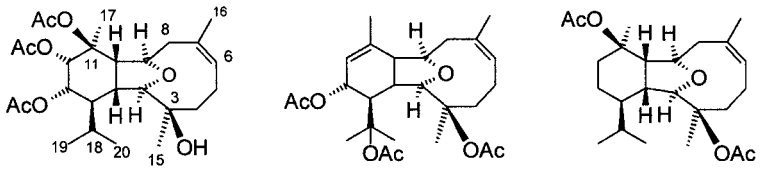
[2]) The structural formulae depicting the configuration for massileunicellins A–C (**7**–**9**) reported in [1] are erroneous, not corresponding to the correct one in Fig. 2 of [1], which accounts for all experimental data. Present structural formulae for **7**–**9** indicating the configuration imply that C(1), C(3), C(8), and C(10) point toward, while O–C(2), H–C(2), and H–C(9) point away from, the observer, in agreement with Fig. 2 of [1]. This type of stereochemical representation is adopted here also for all O-bridged diterpenes in this family, which were previously reported by other authors (*vide infra*) by a different, less explicit, representation. It should also be noticed that, due to a misprint, (9*R**) in the systematic names for massileunicellins A–C in [1] should be read (9*S**).

[3]) The relative configurations for labiatin C (**5**) [4] are assumed here to be the same as for all other eunicellanes. Moreover, labiatin E, recently isolated from the same gorgonian [5], must be viewed – in our present mode of depicting structural formulae[2]) – with α-oriented C(6)–OH.

and the relative configurations. In particular, NOE experiments established that the sp^3 C-atoms of **10** have the same configuration as the corresponding C-atoms of the massileunicellins A–C (**7**–**9**) [1]. The (6*Z*) configuration for **10** is based on δ(C(16)) 27.38 (in $CDCl_3$), a value typical for a deshielded Me C-atom at a trisubstituted C=C bond and in accordance with δ(C(16)) 28.87 reported for eunicellane **11**, previously isolated from the gorgonian *Muricella* sp. from south Korean waters [6]. All (6*E*) eunicellane diterpenes so far isolated – including the new **13** (see below, *Table 2*) isolated from *E. singularis* – are characterized by δ(C(16)) values comprised between 18 and 21 ppm[4])[5]). These conclusions find further support from related families of diterpenoids, where the methyl C-atom at the trisubstituted C=C bond with (*Z*)-configuration resonates downfield with respect to the (*E*)-isomer. This is the case for the asbestinanes, which have the same O-bridged macrocycle of the eunicellanes [11a], the briaranes, where there is no O-bridge [11b], and the xenicanes, where the macrocycle is nine-membered [11c]. The configuration of analogs, which are only known in the (*Z*) configuration, was assigned by X-ray diffraction data; these analogs showed consistently relatively low-field δ(C(16)) resonances[6]). This is the case of briaranes called stecholides [11d] and of certain other briaranes [11e].



10 **11** **12**

Fig. 2. *New (6Z)-$\Delta^{6,7}$-eunicellane diterpene* **10** *isolated from the gorgonian* Eunicella cavolinii *from the coast of Marseille and analogs* **11** *and* **12**, *previously reported from the gorgonians* Muricella *sp. from Korean waters and* E. cavolinii *from the Bay of Naples*, respectively

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[4]) Other eunicellanes depicted in the (6*Z*) configuration [7] should be viewed in the (6*E*) configuration, as originally described. This is the case of cladiellin [8] and related metabolites [9a], ophirin [9b], calicophirin B and its 13-deacetoxy derivative [6], lithophinins A–E [9c], 3-acetoxy-2,12-bis(butanoyloxy)cladiell-8-ene-4,11-diol [9d], and 12,13-diacetoxycladiella-2,6-dien-11-ol [9e]. The only firmly established (6*Z*)-eunicellane diterpene reported before our present work was **11**, isolated from the gorgonian *Muricella* sp. [6], and the (6*E*) configuration, which was erroneously attributed to it in a review article [10], should be corrected accordingly.

[5]) Eunicellane **13** is not suited to configurational studies by ^{1}H-NMR because of very broad signals. However, the lack of any NOE between H–C(6) and Me(16) is consistent with (6*E*) configuration, as deduced from ^{13}C-NMR data.

[6]) The (6*Z*) configuration for the eunicellane diterpene **12**, reported from *Eunicella cavolinii* of the Bay of Naples [12], was also deduced from ^{13}C-NMR data: the δ(C(16)) value, 20.32 ppm in $CDCl_3$, was deemed to support the (6*Z*) configuration [12] in comparison with ophirin, a (6*E*)-eunicellane characterized by δ(C(16)) 18.3 in the same solvent and whose configuration was confirmed by X-ray diffraction analysis [9b]. Actually, since the NMR data for the Bay of Naples eunicellane [12] best fit the (6*E*) configuration, this compound corresponds to the known acetoxycladiellin, isolated from the alcyonarian *Cladiella* sp. from the Great Barrier Reef [8], and structure **12** should be dismissed.

Table 1. *NMR Spectral Data* ($CDCl_3$) *for Compound* **10**. δ in ppm, J in Hz.

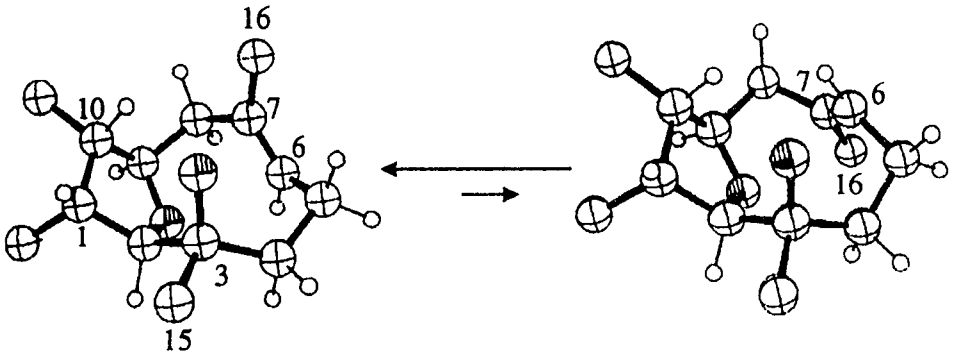
	δ(H)[a])	δ(C)[b])	NOE[c])	HMBC[d])
H–C(1)	2.26 (*dd*, *J*(1,14) = 12.2, *J*(1,10) = 7.1)	43.77 (*d*)	H–C(2), H–C(10), H–C(13)	C(11), C(14), CH_3CO
H–C(2)	3.85 (*s*)	91.02 (*d*)	H–C(14), 3 H–C(15)	C(4), C(11)
C(3)	–	74.94 (*s*)		
CH_2(4)	2.05 (*m*);	36.86 (br. *t*)		
CH_2(5)	3.20 (*m*), 1.98 (*m*)	28.03 (br. *t*)		
H–C(6)	5.88 (br. *dd*, *J*(6,5a) = 5.8, *J*(6,5b) = 11.4)	128.99 (*d*)	3 H–C(16)	
C(7)	–	136.45 (*s*)		
CH_2(8)	3.00 (*m*, H_α), 1.90 (*m*, H_β)	44.23 (br. *t*)	H–C(6), H–C(9), 3 H–C(16)	
H–C(9)	4.57 (br. *dt*, *J*(9,10) = 10.0, *J*(9,8α) ≈ *J*(9,8β) = 3.2)	78.11 (br. *d*)	3 H–C(17)	C(1), C(3), C(11), C(12), C(14)
H–C(10)	3.17 (*dd*, *J*(10,9) = 10.0, *J*(10,1) = 7.1)	43.77 (*d*)	H–C(1)	
C(11)	–	81.95 (*s*)		
H–C(12)	5.35 (*d*, *J*(12,13) = 2.9)	72.94 (*d*)	H–C(13)	
H–C(13)	5.26 (*dd*, *J*(13,14) = 11.8, *J*(13,12) = 2.9)	69.82 (*d*)		C(1), C(12)
H–C(14)	1.84 (br. *t*, *J*(14,13) ≈ *J*(14,1) = 11.8)	38.61 (*d*)	H–C(1), 3 H–C(16)	
Me(15)	0.97 (*s*)	21.15 (*q*)[e])	H–C(2)	C(2)
Me(16)	1.99 (br. *s*)	27.38 (br. *q*)	H–C(6)	C(6), C(7)
Me(17)	1.59 (*s*)	21.00 (*q*)[e])		C(12)
H–C(18)	1.60 (*m*)	29.02 (*d*)		
Me(19)	0.84 (*d*, *J*(19,18) = 6.9)	15.32 (*q*)		
Me(20)	1.03 (*d*, *J*(20,18) = 6.9)	24.15 (*q*)		C(14), C(19)
AcO	2.12, 2.05, 1.96 (all *s*)	169.93, 169.71, 169.49 (all *s*); 22.54, 21.19, 20.90 (all *q*)[e])		

[a]) Partial sharpening was observed for H–C(5) (3.12 (br. *dd*, *J* = 13.4, 5.5 Hz), H–C(6), H_α–C(8) (3.00 (br. *d*, *J* = 15.0 Hz), and H–C(9) at 40°. [b]) Partial sharpening was observed for C(4) ($w_{1/2}$ = 4.5 Hz), C(5) ($w_{1/2}$ = 6.4 Hz), C(8) ($w_{1/2}$ = 5.5 Hz), C(9) ($w_{1/2}$ = 5.4 Hz), and C(16) ($w_{1/2}$ = 6.0 Hz) at 40°. [c]) NOE Enhancement observed for the indicated H-atom(s) by irradiation of the proton(s) listed on the same row. [d]) Heterocorrelation of the indicated C-atom(s) with the proton(s) listed on the same row. [e]) Data may be interchanged.

2.2. *Conformational Behavior of (6*E*)- and (6*Z*)-Eunicellanes.* Broad ^{1}H-NMR signals at room temperature in $CDCl_3$ for the (6*E*)-eunicellane **13**[7]) suggest slow conformational motions. Nearly all deshielded ^{1}H-NMR signals (from +40° to −70°) of **13** indicated that the change from slow to fast motions occurs in a restricted temperature interval, close to 0°. The ^{13}C-NMR spectra of **13** taken at room temperature showed mostly broadened signals ($w_{1/2}$ = 8–15 Hz), except for C(2) and

7) Broad ^{1}H-NMR signals at 25°, and sharpening of the signals on raising the temperature to 80°, were previously reported, as an isolated example, for a (6*E*)-eunicellane diterpene called acetoxycladiellin [8]. This observation, along with the presence of ^{1}H-NMR *m*s instead of sharp patterns reported for analogs [9b–d][12], may suggest that slow conformational motions are the rule for eunicellanes that bear a C=C bond of (6*E*) configuration.

the isopropyl and acetoxy C-atoms. The ^{13}C-NMR spectra recorded between $+50$ and $-10°$ revealed that the shift from slow to fast motions occurs near to room temperature, likely because of a larger $\Delta\delta$ for corresponding C-atoms in the two conformers than for protons in the ^{1}H-NMR spectra. For these conformational processes of **13**, we roughly estimated an activation barrier of 13 ± 1 kcal/mol, which is typical of a *trans*-cyclodecene [13]. Neither low-temperature ($-70°$) ^{1}H-NMR spectra nor ^{13}C-NMR spectra revealed distinct conformers. These were simulated by molecular-mechanics (MM) calculations as the partners of an equilibrium (see *Fig. 3*) involving the flipping of the (*E*)−C(6)=C(7)−Me(16) unit of a conformer with Me(16) *cis* to AcO−C(3) (major conformer **13a**) and a conformer with Me(16) *trans* to AcO−C(3) (minor conformer **13b**). Calculated *J* values and interproton distances for conformer **13a** are in accordance with the values observed from ^{1}H-NMR spectra (*Table 2*). In particular, the coupling pattern $J(9,10) = 9.8$, $J(9,8\alpha) = 6.0$, and $J(9,8\beta) = 1.0$ Hz calculated for the H−C(9) *ddd* of **13a** fits nicely the observed ($-10°$) *dd* at δ(H) 4.40 with $J = 9.7$ and 5.9 Hz. In line with these conclusions, the minor conformer **13b** does not contribute appreciably to the observed *J* values (the calculated *J* for the H−C(9) *ddd*, $J(9,10) = 10.4$, $J(9,8\alpha) = 8.6$, and $J(9,8\beta) = 3.2$ Hz, diverge considerably from the observed values).



13a (partial structure) **13b** (partial structure)

Fig. 3. *ORTEP-Type representation of the portions involved in slow conformational motions of the energy-minimized conformers* **13a** *and* **13b**. From MM calculations for the whole molecule **13** in agreement with NMR data. For simplicity AcO = O.

The MM calculations for **13a** and **13b** suggest that *a*) **a**-type conformers are more stable than **b**-type conformers (by 0.71, 1.12, or 4.11 kcal/mol strain energy, according to the force field used, *i.e.* MMX, parameterized MMX [14], or MM3, resp.); *b*) the dihedral angle C(5)−C(6)−C(7)−C(8) for both types of conformers is *ca.* 150°, which is considerably smaller than the value 170° calculated for a hypothetical ten-membered ring compound deriving from the **a**-type conformer by removal of the O-bridge[8]); *c*) adjacent

[8]) A value of 150° is in the range observed for *trans*-cyclooctenes [11c], implying that the *trans* C=C bond causes much strain in **13**.

Table 2. *NMR Assignments* ($CDCl_3$) *for Compounds* **13**, **24**, *and* **25**. δ in ppm, J in Hz.

	13[a])		**24**		**25**	
Position	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
H–C(1)	40.72 (*d*)	2.18 (*dd*, *J* = 11.6, 6.7)	41.18 (*d*)	2.32 (*dd*, *J* = 11.4, 7.4)	40.6 (*d*)	2.24 (*dd*, *J* = 11.6, 7.5)
H–C(2)	90.25 (*d*)	3.63 (br. *s*)	89.31 (*d*)	3.71 (*d*, *J* = 5.1)	90.15 (*d*)	3.60 (*s*)
C(3)	86.39 (*s*)	–	85.59 (*s*)	–	73.96 (*s*)	–
CH_2(4)	34.01 (*t*)	2.05–2.25 (*m*)	29.32 (*t*)	1.80 (*m*), 2.15 (*m*)	34.78 (*t*)[a])	1.65 (*m*), 1.90(*m*)
CH_2(5)	25.71 (*t*)	2.10 (*m*), 2.30 (*m*)	30.04 (*t*)	1.80 (*m*), 2.00 (*m*)	31.81 (*t*)[a])	1.85 (*m*), 2.00 (*m*)
H–C(6)	132.46 (*d*)	5.31 (br. *d*, *J* = 10.9)	76.43 (*d*)	6.33 (*dd*, *J* = 10.9, 3.0)	76.40 (*d*)	5.18 (br. *d*, *J* = 7.3)
C(7)	124.11 (*s*)	–	134.08 (*s*)	–	146.30 (*s*)	–
CH_2(8) or H–C(8)	43.27 (*t*)	2.52 (*dd*, *J* = 14.0, 5.9, H_α), 2.20 (*m*, H_β)	128.32 (*d*)	5.23 (br. *s*)	41.16 (*t*)	3.11 (*dd*, *J* = 14.1, 5.6, H_α), 2.45 (*d*, *J* = 14.1, H_β)
H–C(9)	76.50 (*d*)	4.40 (*dd*, *J* = 9.7 5.9)	78.66 (*d*)	4.89 (*ddq*, *J* = 10.5, 5.7, 2.3)	77.83 (*d*)	4.54 (*dd*, *J* = 10.6, 5.6)
H–C(10)	43.63 (*d*)	3.35 (*dd*, *J* = 9.7, 6.7)	49.03 (*d*)	3.46 (*dd*, *J* = 10.5, 7.4)	44.38 (*d*)	3.24 (*dd*, *J* = 10.6, 7.5)
C(11)	81.08 (*s*)	–	81.90 (*s*)	–	80.87 (s)	–
H–C(12)	73.80 (*d*)	5.00 (br. *s*)	74.02 (*d*)	5.44 (*m*)	73.46 (*d*)	5.13 (br. *s*)
CH_2(13)	22.83 (*t*)	1.68 (*m*)	22.58 (*t*)	1.75 (*m*), 1.67 (*m*)	22.86 (*t*)	1.70 (*m*)
H–C(14)	37.06 (*d*)	1.56 (*m*)	36.20 (*d*)	1.56 (*m*)	35.97 (*d*)	1.57 (*m*)
Me(15)	22.28 (*q*)	1.60 (br. *s*)	22.24 (*q*)[a])	1.53 (*s*)	27.31 (*q*)	1.20 (*s*)
Me(16) or CH_2(16)	20.33 (*q*)	1.85 (br. *s*)	18.19 (*q*)	1.63 (*t*, *J* = 1.9)	119.24 (*t*)	5.54 (*s*), 5.34 (*s*)
Me(17)	22.57 (*q*)	1.61 (*s*)	22.74 (*q*)[a])	1.53 (*s*)	22.61 (*q*)	1.55 (*s*)
H–C(18)	27.35 (*d*)	1.80 (*m*)	27.10 (*d*)	1.90 (*m*)	27.38 (*d*)	1.95 (*m*)
Me(19)	15.09 (*q*)	0.78 (*d*, *J* = 6.8)	14.90 (*q*)	0.89 (*d*, *J* = 6.8)	14.86 (*q*)	0.76 (*d*, *J* = 6.8)
Me(20)	21.41 (*q*)	0.88 (*d*, *J* = 6.8)	21.21 (*q*)[b])	0.93 (*d*, *J* = 6.8)	21.53 (*q*)[b])	0.89 (*d*, *J* = 6.8)
AcO	[c])	2.06, 2.00, 1.99 (all *s*)	[d])	2.07, 2.02, 1.98, 1.95 (all *s*)	[e])	2.07, 2.00, 1.99 (all *s*)

[a]) Recorded at $-10°$. [b]) Data in the same column can be interchanged. [c]) 170.58, 169.88, 169.54 (all *s*); 22.50, 21.48, 21.20 (all *q*). [d]) 170.31, 170.09, 170.03 (× 2) (all *s*); 23.16, 21.97[a]), 21.53, 21.21 (all *q*). [e]) 170.58, 169.67, 169.65 (all *s*); 21.59[b]), 21.42, 21.27 (all *q*).

dihedral angles along the nine-membered oxamacrocycle take opposite signs, except for the couple of adjacent dihedral angles C(9)–O–C(2)–C(3)/O–C(2)–C(3)–C(4) in conformer **a** and for the three couples of dihedral angles C(9)–O–C(2)–C(3)/O–C(2)–C(3)–C(4), C(3)–C(4)–C(5)–C(6)/C(4)–C(5)–C(6)–C(7), and C(6)–C(7)–C(8)–C(9)/C(7)–C(8)–C(9)–C(10) in conformer **b**, suggesting that the protons at C(4), C(5), and C(8) are eclipsed in the disfavored conformer **b**. The body of these observations can be rationalized by a conformational equilibrium where the concentration of the minor conformer **b**, too low for direct NMR observation, is sufficient to induce detectable line broadening.

Broad ^{1}H-NMR signals at room temperature were also observed for the protons at or near the olefinic moiety in compound **10**, like 3 H–C(16), 2 H–C(8), and H–C(6), which are much too broad for allylic coupling only. Partial sharpening of these ^{1}H signals was observed on raising the temperature to 40° (*Table 1*), whereas considerable

broadening of the ^{13}C signals for C(5), C(8), and C(16), and a less-marked broadening for those from C(4) and C(9) ($w_{1/2} = 14$ and 8 Hz, resp.), were observed at room temperature. MM Calculations (see *Fig. 4*) are in agreement with a modest broadening of the NMR signals that may be attributed to a limited conformational freedom for the O-bridged (6*Z*) ring, which contrasts with the flexibility of the corresponding (6*E*) stereoisomer [11c].

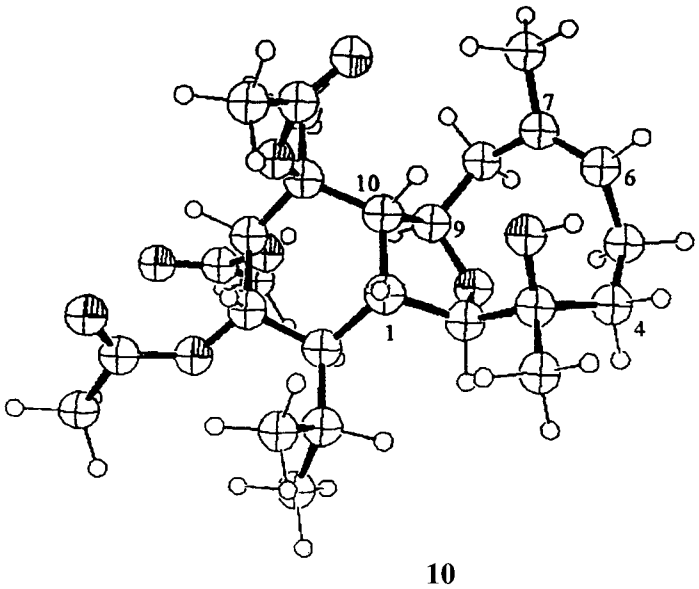


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Fig. 4. *ORTEP-Type representation of the energy-minimized conformation of the eunicellane diterpene* **10**. From MM calculations in agreement with NMR data.

MM Calculations indicated that *a*) the conformer of **10** shown in *Fig. 4* is favored with respect to the one resulting from 180° flipping of the C=C bond (by strain energy 0.81 or 4.69 kcal/mol, according to the force field used, *i.e.* MMX or MM3, resp.); *b*) the favored conformer nicely accounts for the observed *J* couplings and inter-proton distances[9]); *c*) the dihedral angle C(5)–C(6)–C(7)–C(8) for the favored conformer is close to 0° (MMX force field).

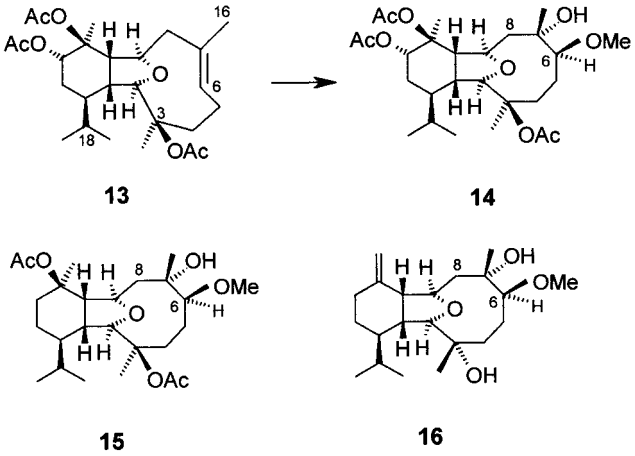
2.3. *Reactivity of (6*E*)-Eunicellanes.* On storage in $CDCl_3$/MeOH at −20° in the dark, compound **13** underwent a spontaneous, albeit slow transformation into **14** (*Scheme*). Structure **14** is supported by a close matching of its MeO–C(6)–C(7)–OH NMR data with those of palmonine A (**15**), previously isolated from *Eunicella verrucosa* [3], and by a comparison with sclerophytin F methyl ether (**16**), isolated from

[9]) In particular, the *J* couplings calculated for H–C(6) and H–C(9) of the favored conformer as *dd* ($J(6,5a) = 10.2$ and $J(6,5b) = 4.6$ Hz) and *ddd* ($J(9,10) = 9.5$, $J(9,8\alpha) = 4.0$ and $J(9,8\beta) = 2.7$ Hz), respectively, nicely fit the data observed at room temperature (5.88 (br. *dd*, $J = 5.8$, 11.4 Hz) and 4.57 (br. *dt*, $J = 10.0$, 3.2 Hz)), while the corresponding patterns calculated for to disfavored conformer (*dd* ($J(6,5a) = 8.0$ and $J(6,5b) = 5.6$ Hz) and *ddd* ($J(9,10) = 8.6$, $J(9,8\alpha) = 4.2$ and $J(9,8\beta) = 11.2$ Hz)) disagree with the observed patterns.

the alcyonarian *Sclerophytum capitalis* [15]. Moreover, the β-oriented MeO–C(6) and α-oriented OH–C(7) in compound **14** are supported by both NOE enhancements between H–C(6) and OH–C(7) and the lack of any effect between H–C(6) and Me–C(7) (*Exper. Part*). The mechanism of the transformation **13** → **14** is unclear, however.

While an intermediate 6,7-*exo*-epoxide of **13** is conceivable[10][11], its nucleophilic opening by MeOH [20] from the less hindered face of the (6*E*) C=C bond does not account for the observed configuration at C(6) and C(7) of **14**. We can only offer a tentative rationalization of these observations within this reactivity scheme by hypothesizing *a*) formation of an intermediate epoxide by preferential *exo*-attack at the most abundant conformer of **13**, to account for formation of a single diastereoisomer **14**, and *b*) anchimeric assistance by the C(2)–O–C(9) heteroatom [8] to the stabilization of a carbonium ion at C(6) that undergoes MeOH attack from the least hindered side to give the *cis*-diol monomethyl ether with the configuration shown in **14**. MM3 Calculations for these hypothetical intermediates suggested the 6,7-*exo*-epoxide derived from **13a** to be much more stable than either the corresponding 6,7-*endo*-epoxide or the 6,7-*exo*-epoxide derived from **13b**.

Scheme. *Spontaneous Addition of MeOH to the Strained (6*E*)-Eunicellane Diterpene* **13** (see *Exper. Part*), *isolated from the gorgonian* Eunicella singularis *from the coast of Marseille*



It is relevant to this concern that strained *trans*-cycloalkenes are more prone to epoxidation than relatively unstrained *cis*-cycloalkenes [21]. This may explain why **10** was recovered unaltered after storage under conditions similar to, and for longer times than, those that led to a nearly complete transformation of **13** to **14**. Only the latter

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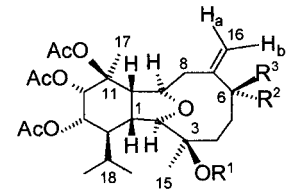
[10]) Autoepoxidation of *trans*-unsaturated nine-membered-ring compounds, either from atmospheric oxygen or peroxides in trace amounts in the standard, nominally peroxide-free Et_2O used, was already observed – though not reported – during our studies of xeniolide diterpenes [11c]. Autoepoxidation reactions have also been observed for both synthetic *trans*-cycloalkenes in contact with air [16] and acetylcoriacenone on brief storage in cold $CDCl_3$ [17].

[11]) Bridgehead olefins or *trans*-cycloalkenes undergo electrophilic attack at the C=C bond from preferentially the outside of the ring system, such as in the epoxidation by 3-chloroperbenzoic acid of *trans* C=C bonds in eleven- [18] and nine-membered rings [19].

process involves a substantial release of strain on changing from the (6*E*)-unsaturated to the saturated eunicellane.

In this light, the transformation **13** → **14** suggests that also palmonine A (**15**) [3] and sclerophytin F methyl ether (**16**) [15] may be artifacts from the isolations. Further in this vein, also eunicellane diterpenes that carry a β-oriented OH–C(6) group and an α-oriented OH–C(7) group, like sclerophytins C–F [7a] and other ones isolated from a *Cladiella* sp. [7c], might derive from nucleophilic attack by H_2O at the epoxide center of biogenetic precursors. The latter find precedents in eunicellanes bearing a 6,7-epoxide group isolated from gorgonians, like solenopodins A–C from *Solenopodium stechei* [11d].

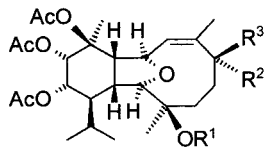
2.4. *Highly Oxidized Eunicellanes.* Among the eunicellanes isolated from *Eunicella cavolinii* from Marseille, massileunicellins A–C (**7**–**9**) [1][2]) are unusual for a second O-bridge and extensive functionalization at the cyclohexane ring. The latter feature is found in eunicellanes **17**–**23** too (*Fig. 5*). Their structures are supported by protonated molecular ions in FAB-MS, fragment ions from loss of AcOH in EI-MS spectra (*Exper. Part*), and NMR spectra, which showed the presence of different substituents at C(3) and C(6), the exocyclic methylidene group for **17**–**19** (*Table 3*), and the (6*Z*)-endocyclic C=C bond for **20**–**23**.



17 R^1 = Ac, R^2 = H, R^3 = AcO

18 R^1 = R^2 = H, R^3 = AcO

19 R^1 = Ac, R^2, R^3 = O

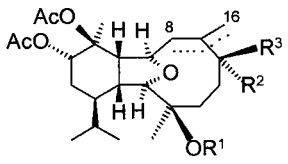


20 R^1 = Ac, R^2 = H, R^3 = AcO

21 R^1 = R^2 = H, R^3 = AcO

22 R^1 = Ac, R^2 = H, R^3 = OH

23 R^1 = Ac, R^2, R^3 = O



24 $\Delta^{7,8}$, R^1 = Ac, R^2 = H, R^3 = AcO

25 $\Delta^{7,16}$, R^1 = R^2 = H, R^3 = AcO

Fig. 5. *New $\Delta^{7,16}$- and $\Delta^{7,8}$-eunicellane diterpenes isolated from the gorgonians* Eunicella cavolinii (see **17**–**23**) *and* Eunicella singularis (see **24** and **25**) *from the coast of Marseille*

Table 3. *^{13}C-NMR Data* ($CDCl_3$) *for Eunicellane Diterpenes* **17**–**23**. δ in ppm.

	17	**18**	**19**	**20**	**21**	**22**	**23**
C(1)	41.69 (*d*)	41.49 (*d*)	43.14 (*d*)	41.83 (*d*)	41.20 (*d*)	42.73 (*d*)	43.28 (*d*)
C(2)	90.22 (*d*)	91.08 (*d*)	90.55 (*d*)	91.10 (*d*)	91.65 (*d*)	93.25 (*d*)	91.21 (*d*)
C(3)	84.49 (*s*)	73.79 (*s*)	84.15 (*s*)	84.05 (*s*)	71.10 (*s*)	84.39 (*s*)	83.51 (*s*)
C(4)	29.00 (*t*)	31.79 (*t*)[a]	33.43 (*t*)	33.85 (*t*)	36.54 (*t*)	30.80 (*t*)[a]	33.99 (*t*)
C(5)	32.09 (*t*)	34.88 (*t*)[a]	35.23 (*t*)	37.55 (*t*)	30.60 (*t*)	31.38 (*t*)[a]	37.59 (*t*)
C(6)	76.09 (*d*)	76.11 (*d*)	205.50 (*s*)	71.84 (*d*)[a]	73.86 (*d*)	71.73 (*d*)	211.18 (*s*)
C(7)	145.45 (*s*)	146.92 (*s*)	147.97 (*s*)	133.83 (*s*)	135.65 (*s*)	137.18 (*s*)	138.38 (*s*)
C(8)	40.71 (*t*)	41.00 (*t*)	41.36 (*t*)	127.84 (*d*)	129.14 (*d*)	125.90 (*d*)	124.74 (*d*)
C(9)	78.59 (*d*)	78.23 (*d*)	78.27 (*d*)	78.92 (*d*)	78.81 (*d*)	78.46 (*d*)	77.64 (*d*)
C(10)	43.52 (*d*)	43.64 (*d*)	46.85 (*d*)	49.51 (*d*)	51.49 (*d*)	48.45 (*d*)	47.73 (*d*)
C(11)	82.03 (*s*)	81.96 (*s*)	81.53 (*s*)	82.83 (*s*)	81.47 (*s*)	81.98 (*s*)	81.58 (*s*)
C(12)	72.59 (*d*)	72.75 (*d*)	72.52 (*d*)	74.34 (*d*)[a]	74.59 (*d*)	72.60 (*d*)	72.67 (*d*)
C(13)	69.43 (*d*)	69.60 (*d*)	69.52 (*d*)	70.20 (*d*)	71.44 (*d*)	69.27 (*d*)	69.43 (*d*)
C(14)	40.12 (*d*)	39.92 (*d*)	38.77 (*d*)	37.89 (*d*)	37.20 (*d*)	39.80 (*d*)	38.47 (*d*)
C(15)	22.50 (*q*)[a]	27.34 (*q*)	22.61 (*q*)[a]	22.60 (*q*)	28.04 (*q*)	22.65 (*q*)[b]	22.57 (*q*)[a]
C(16)	118.99 (*t*)	119.49 (*t*)	119.69 (*t*)	19.43 (*q*)	18.45 (*q*)	19.10 (*q*)	19.10 (*q*)
C(17)	22.45 (*q*)[a]	21.37 (*q*)[b]	21.14 (*q*)[b]	21.22 (*q*)[b]	22.23 (*q*)[a]	21.15 (*q*)[c]	21.15 (*q*)[b]
C(18)	27.51 (*d*)	27.91 (*d*)	28.68 (*d*)	29.18 (*d*)	29.95 (*d*)	29.47 (*d*)	28.76 (*d*)
C(19)	15.29 (*q*)	15.18 (*q*)	15.17 (*q*)	15.02 (*q*)	14.20 (*q*)	15.63 (*q*)	15.14 (*q*)
C(20)	24.07 (*q*)	24.07 (*q*)	23.99 (*q*)	23.62 (*q*)	23.46 (*q*)	23.97 (*q*)	23.96 (*q*)
AcO	[d]	[e]	[f]	[g]	[h]	[k]	[i]

[a][b][c]) Data in the same column can be interchanged. [d]) 170.62, 169.90, 169.74, 169.62, 169.39 (all *s*); 22.38[a]), 21.40 (× 2), 21.18, 20.98 (all *q*). [e]) 170.57, 169.89, 169.63, 169.55 (all *s*); 22.53, 21.39[b]), 21.17, 20.98 (all *q*). [f]) 169.96, 169.88, 169.66, 169.54 (all *s*); 22.56[a]), 22.16, 21.08[b]), 20.97 (all *q*). [g]) 170.32, 169.99, 169.95, 169.89, 169.85 (all *s*); 22.60, 21.99[b]), 21.22, 20.95[b]), 20.46 (all *q*). [h]) 170.23, 169.88 (× 2), 169.75 (all *s*); 22.59[a]), 21.23, 20.95, 20.42 (all *q*). [k]) 170.14, 169.92, 169.71, 169.54 (all *s*); 21.73[b]), 21.18[c]), 20.95, 20.76 (all *q*). [i]) 170.27, 169.88, 169.64, 169.44 (all *s*); 22.49[a]), 21.81, 21.15, 20.94[b]) (all *q*).

β-Orientation of the OH group in compound **22**[12]) (*Exper. Part*) is supported by both its ^{1}H-NMR signal (δ 5.82(*d*)) indicating H-bonding with AcO–C(3)[13]), and acetylation of **22** with Ac_2O/pyridine to give a compound identical to natural **20** (superimposable ^{1}H-NMR signals and coelution on HPLC (*Si60*, hexane/i-PrOH 92 : 8)).

Eunicellanes **24** and **25** from *Eunicella singularis*, like eunicellin (**1**) from the same gorgonian [2] and labiatin B (**4**) and C (**5**) from *Eunicella labiata* [4] (*Fig. 1*), are less

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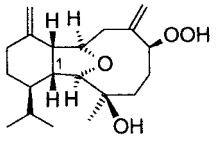
12) The 6-*O*-benzoyl derivative of **22** was prepared with intent to establish the absolute configuration by chiral exciton coupling between the allylic C=C bond and the benzoate chromophore, in analogy with the case of litophynin C [9c]. However, the data for the 6-*O*-benzoyl derivative of **22** could not be analyzed by the classical model of the allylic benzoate rule [23] because the CD and UV spectra are shifted with respect to one another (UV(EtOH): 229 (12000), 276 (1500) nm. CD ($\Delta\varepsilon$): 240 (+1.2), 229 (+0.0), 202 (−6.8) nm).

13) Another, more polar eunicellane diterpene was also isolated from *E. cavolinii*, albeit in too small an amount for a complete NMR assignment. Partial spectral data (*Exper. Part*) suggest the structure of an OH–C(3) analog of **23**, thus posing its candidacy as a biogenetic precursor of massileunicellin B (**8**). In fact, this new isolate underwent a *ca.* 50% transformation into **8** on storage in $CDCl_3$ solution. The groups OH–C(3) and C(6)=O in this putative biogenetic intermediate are favorably positioned for intramolecular cyclization to give the massileunicellin hemiketal. It is relevant to this concern that all known eunicellanes of the type suggested here for this new isolate are esterified at the OH–C(3) group, like **19**, **23**, **25**, and other examples [3–5][7c].

extensively functionalized at the cyclohexane ring than **7**–**9** from *E. cavolinii*. These compounds differ by their oxidation level at the macrocycle, however (NMR and MS data in *Table 2* and *Exper. Part*).

Conceivably, eunicellanes **24** and **25** arise from enzymatic oxidation of olefinic precursors to give allylic hydroperoxides, which undergo either reduction to hydroxy derivatives or rearrangement. This is supported by the isolation of cladiellaperoxide (**26**) from the alcyonarian *Cladiella sphaeroides* [24] and of both allohimachalane (**27**) and hemiketal **28** from a Chinese angiosperm, *Illicium tsangii* [25a]. However, the facile formation of allylic hydroperoxides from **27** in the presence of molecular oxygen under light, followed by rearrangement reactions in $CDCl_3/H^+$ to give **28** and ring-opened products [25b], has also be taken into account. Thus, these may be viewed either as spontaneous reactions *in vivo* – due to the proneness of the precursors for reactions of this type – or artifact processes of the isolation. Eunicellanes highly oxidized at the macrocycle pose the same dilemma since suitable C(6)=C(7) olefinic precursors, including also compounds **10** and **13**, have been identified [6][8][9][12]. Any answer to these questions is left to biosynthetic and synthetic experimentation.



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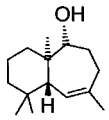

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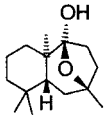

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We thank *M. Rossi* and *A. Sterni* for skilled technical help with the isolation of products and with mass spectra, respectively, and *MURST* and *CNR*, Roma, for financial support.

Experimental Part

General. See [1]. Moreover, yields of isolated natural products are given on the basis of raw-extract weight, while yields for reactions are given on the basis of reacted substrate. Prep. HPLC: t_R in min, UV monitoring at 215 nm and flow 5 ml min^{-1}. NMR: $CDCl_3$ as solvent at 25° probe temp., unless otherwise stated; ^{13}C,^1H assignments by inverse detection shift correlation experiments, except for **20** and **24**, which were assigned by general spectral analogy with similar compounds. Optical rotation data: $CHCl_3$.

Collection and Isolations. Chromatographic fractions of workup of *Eunicella cavolinii* extracts follow from [1]. *Frs.* 9–12 were subjected to reversed-phase FC (*RP-18*, gradient H_2O/MeCN): 18 fractions, of which *Fr.* 9 was subjected to reversed-phase HPLC (*RP-18*, MeOH/H_2O 3:2): peak eluates at t_R 8.5 and 9.8; the first eluate was subjected in turn to HPLC (*CN*, hexane/i-PrOH 85:15, flow 1 ml min^{-1}): pure **18** (t_R 8.5; 1.9 mg, 0.010%), **23** (t_R 10.5; 2.3 mg, 0.013%), **19** (t_R 11.8; 1.9 mg, 0.010%); the latter eluate under similar HPLC conditions gave **21** (t_R 8.2; 1.3 mg, 0.007%) and **22** (t_R 9.2; 2.6 mg, 0.014%). *Frs. 4–8* and *10* from reversed-phase FC were combined and subjected to HPLC (*CN*, hexane/i-PrOH 9:1): peak eluates at t_R 6.5 (further purified by reversed-phase HPLC (*RP-18*, MeOH/H_2O 3:1): **10** (t_R 12.5; 2.9 mg, 0.016%)), t_R 9.5 (further purified by reversed-phase HPLC (*RP-18*, MeOH/H_2O 4:1): **20** (t_R 8.0; 0.9 mg, 0.005%)), and t_R 11.8 (further purified by reversed-phase HPLC (*RP-18*, MeOH/H_2O 82:12): **17** (t_R 6.3; 6.2 mg, 0.034%)). *Frs. 14–18* from FC (*Si-60*) were combined and subjected to HPLC (*CN*, hexane/i-PrOH 4:1): a more polar, 3-hydroxy analogue of compound **23** (t_R 9.0; trace amounts). *Eunicella singularis* (38M) was collected on July 15, 1981, at both the Triperie cave and at 200 m distance from this, in caves next to Cape Morgiou, depths 12–17 m. This gorgonian species was immediately soaked in 95% EtOH (2 l); after several days, the slurry was filtered and evaporated to give an oily residue (32 g) that was stored at –20° in the dark until July 1997, when it was subjected to FC (*Si-60*, gradient hexane/AcOEt/MeOH): 26 fractions of 50 ml each. *Frs. 6–16* were combined and subjected to reversed-phase FC (*RP-18*, gradient H_2O/MeCN): 4 fractions that were subjected to reversed-phase HPLC (*RP-18*, MeCN/H_2O 4:1):

labiatin B (**4**)/labiatin D (**6**) 2:1 (t_R 4.0; 18.4 mg, 0.05%) and **13** (t_R 8.0; 18.2 mg, 0.05%). Other eluates, corresponding to UV absorption peaks in a t_R range from 4 to 6, were evaporated and subjected to reversed-phase HPLC (*RP-18*, MeCN/H_2O 65:35): peak eluate at t_R 6.2 (further subjected to reversed-phase HPLC (*RP-18*, H_2O/MeCN 55:45): **25** (t_R 11.6; 3.2 mg, 0.01%), labiatin C (**5**; t_R 12.7; 4.2 mg, 0.013%)), palmonine D (**2**)/palmonine E (**3**) 4:1 (t_R 10.3; 5.0 mg, 0.015%), eunicellin (**1**; t_R 12.3; 10.2 mg, 0.03%), and **24** (t_R 13.8; 0.9 mg, 0.004%). This gorgonian species was recollected on July 22, 1997, at slightly to the inner side of Triperie cave, in between the two sites of the 1981 collection described above, at depths 12–15 m, and immediately soaked in propanol (3 l). After a couple of weeks the slurry was filtered and evaporated: a TLC comparison gave results identical to those of the 1981 collection.

*(1*R*,2*R*,3*R*,6*Z*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R**)-Eunicellane* **10** (= *(1*S*,2*S*,3*S*,4*R*,4a*R*,5*R*,6*R*,9*Z*,12*R*,12a*S*)-1,2,3,4,4a,5,6,7,8,11,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,3,6-tetrol 1,2,3-Triacetate*; **10**). $[\alpha]_D^{25} = +37$ ($c = 0.1$). NMR: *Table 1*. HR-EI-MS: 420.2509 ± 0.0030 ($C_{24}H_{36}O_6^{+\cdot}$; calc. 420.2512). FAB-MS (3-nitrobenzyl alcohol): 481 (0.3, $[M+H]^+$).

*(1*R*,2*R*,3*R*,6*E*,9*R*,10*S*,11*S*,12*S*,14*S**)-Eunicellane* **13** (= *(1*S*,2*S*,4*S*,4a*R*,5*R*,6*R*,9*E*,12-R*,12a*S*)-1,2,3,4,4a,5,6,7,8,11,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,6-triol 1,2,6-Triacetate*; **13**). ^{1}H-NMR: 2.20 (*m*, H–C(1), H_β–C(8)); 2.10 (*m*, H_a–C(4), H_a–C(5)); 2.30–2.40 (*m*, H_b–C(4), H_b–C(5)); 3.63 (br. *s*, H–C(2)); 5.31(*m*, H–C(6)); 2.52 (*dd*, $J_{gem} = 14.0$, $J(8\alpha,9) = 5.9$, H_α–C(8)); 4.40 (*m*, H–C(9)); 3.35 (*dd*, $J(10,1) = 6.7$, $J(10,9) = 9.7$, H–C(10)); 5.00 (br. *s*, H–C(12)); 1.70 (*m*, H–C(13)); 1.60 (*m*, H–C(14)); 1.44 (br. *s*, 3 H–C(15)); 1.85 (br. *s*, 3 H–C(16)); 1.61 (*s*, 3 H–C(17)); 1.78 (*m*, H–C(18)); 0.77 (*d*, $J(19,20) = 6.8$, 3 H–C(19)); 0.90 (*d*, $J(20,19) = 6.8$, 3 H–C(20)); 2.06, 2.00, 1.99 (3*s*, 3 Ac). NMR (–10°): *Table 2*. EI-MS: 464 (0.1, $M^{+\cdot}$), 404 (1, $[M - AcOH]^{+\cdot}$), 344 (1.8), 302 (2), 284 (4), 43 (100). HR-EI-MS: 404.2556 ± 0.0030 ($C_{24}H_{36}O_5^{+\cdot}$; calc. 404.2563). FAB-MS (3-nitrobenzyl alcohol): 465 (0.3, $[M+H]^+$).

Conversion of Eunicellane **13** *to* **14.** On storage for several months in a solvent mixture containing MeOH and $CDCl_3$ at –20° in the dark, **13** was almost completely converted into **14**, which was purified by reversed-phase HPLC (*RP-18*, MeCN/H_2O 8:2; t_R 4.5): 8.0 mg (98%) of **14**. $[\alpha]_D^{25} = +56$ ($c = 0.2$). ^{1}H-NMR: 2.13 (*m*, H–C(1)); 3.57 (*s*, H–C(2)); 2.66 (*dd*, $J_{gem} = 13.6$, $J(4,5) = 9.0$, H_β–C(4)); 1.78 (*m*, H_α–C(4)); 1.67 (*dd*, $J_{gem} = 13.6$, $J(5,4) = 8.7$, H–C(5)); 1.35 (*m*, H–C(5)); 4.07 (br. *d*, $J(6,5) = 6.2$, H–C(6)); 1.85 (*m*, 2 H–C(8)); 4.49 (*q*, $J(9,8) \approx J(9,10) = 7.2$, H–C(9)); 3.46 (*t*, $J(10,1) = J(10,9) = 7.2$, H–C(10)); 5.15 (br. *s*, H–C(12)); 1.68 (*m*, H–C(13)); 1.50 (*m*, H–C(14)); 1.41 (br. *s*, 3 H–C(15)); 1.12 (*s*, 3 H–C(16)); 1.53 (*s*, 3 H–C(17)); 1.78 (*m*, H–C(18)); 0.81 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 0.91 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.08, 2.00, 2.07, 1.99 (4*s*, 4 Ac); 3.33 (*s*, MeO); 2.41 (br. *s*, OH, exchangeable with D_2O). 1D-NOE: 3.57 (H–C(2)) → H_α–C(4), H–C(9), H–C(14), 3 H–C(15); 4.07 (H–C(6)) → MeO, OH–C(7); 4.49 (H–C(9)) → H_α–C(8), 3 H–C(17); 3.46 (H–C(10)) → H–C(1); 1.41 (3 H–C(15)) → H–C(2); 2.41 (OH) → H–C(6), 3 H–C(16), MeO. ^{13}C-NMR: 41.60 (*d*, C(1)); 90.48 or 90.22 (*d*, C(2)); 86.19 (*s*, C(3)); 36.40 (*t*, C(4)); 26.41 (*t*, C(5)); 90.22 or 90.48 (*d*, C(6)); 76.11 (*s*, C(7)); 46.80 (*t*, C(8)); 75.75 (*d*, C(9)); 50.09 (*d*, C(10)); 81.21 (*s*, C(11)); 72.78 (*d*, C(12)); 22.80 (*t*, C(13)); 35.71 (*d*, C(14)); 22.73 (*q*, C(15)); 23.11 (*q*, C(16)); 23.10 (*q*, C(17)); 28.51 (*d*, C(18)); 15.44 (*q*, C(19)); 23.70 (*q*, C(20)); 170.50, 169.90, 169.71 (3*s*, 3 AcO); 22.22, 21.33, 20.70 (3*q*, AcO); 56.79 (*q*, MeO). EI-MS: 495 (1.5, $[M - OH]^{+\cdot}$), 494 (3.8, $[M - H_2O]^+$), 481 (1, $[M - MeO]^+$), 453 (1.6), 452 (4, $[M - AcOH]^{+\cdot}$), 392 (9), 43 (100). HR-EI-MS: 494.2877 ± 0.0030 ($C_{27}H_{42}O_8^{+\cdot}$; calc. 494.2879).

*(1*R*,2*R*,3*R*,6*S*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R**)-Eunicellane* **17** (= *(1*S*,2*S*,3*S*,4*R*,4a*R*,5*R*,6*R*,9*S*,12*R*,12a*S*)-Tetradecahydro-1,6-dimethyl-4-(1-methylethyl)-10-methylidene-5,12-epoxybenzocyclodecene-1,2,3,6,9-pentol 1,2,3,6,9-Pentacetate*; **17**). $[\alpha]_D^{25} = -40$ ($c = 0.4$). ^{1}H-NMR: 2.22 (*dd*, $J(1,10) = 7.4$, $J(1,14) = 11.4$, H–C(1)); 3.63 (*s*, H–C(2)); 2.17, 1.85 (2 *m*, 2 H–C(4)); 2.05, 1.85 (2 *m*, 2 H–C(5)); 5.13 (*dd*, $J(6,5a) = 11.6$, $J(6,5b) = 4.3$, H–C(6)); 3.09 (*dd*, $J_{gem} = 14.0$, $J(8\alpha,9) = 4.4$, H_α–C(8)); 2.40 (*d*, $J_{gem} = 14.0$, H_β–C(8)); 4.60 (*dd*, $J(9,10) = 10.6$, $J(9,8\alpha) = 4.4$, H–C(9)); 3.35 (*dd*, $J(10,9) = 10.6$, $J(10,1) = 7.4$, H–C(10)); 5.32 (br. *d*, $J(12,13) = 2.9$, H–C(12)); 5.30 (*dd*, $J(13,12) = 2.9$, $J(13,14) = 11.8$, H–C(13)); 1.84 (*t*, $J(14,1) = J(14,13) = 11.8$, H–C(14)); 1.56 (*s*, 3 H–C(15)); 5.26 (*s*, H_a–C(16)); 5.41 (*s*, H_b–C(16)); 1.56 (*s*, 3 H–C(17)); 1.76 (*m*, H–C(18)); 0.82 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 1.03 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.11, 2.07, 1.97, 1.92 (3*s*, 3 Ac). 1D-NOE: 5.32 (H–C(12)) → H–C(13); 5.26 (H_a–C(16)) → H_b–C(16), H_β–C(8); 3.35 (H–C(10) → H–C(1), 3 H–C(17); 3.09 (H_α–C(8)) → H–C(9); 2.40 (H_β–C(8)) → H–C(10); 2.22 (H–C(1)) → H–C(10)), H–C(13); 1.56 (3 H–C(15) and 3 H–C(17)) → H–C(2), H–C(9), H–C(10), H–C(12). ^{13}C-NMR: *Table 3*. EI-MS: 537 (0.3), 521 (7, $[M - AcO]^+$), 520 (10, $[M - AcOH]^{+\cdot}$), 477 (1), 461 (3), 460 (3), 418 (29), 417 (2), 401 (6), 400 (9), 358 (6), 357 (3), 341 (3), 340 (3), 316 (4), 315 (4), 281 (4), 280 (4), 43 (100). FAB-MS (3-nitrobenzyl alcohol): 581 (0.3, $[M+H]^+$).

*(1*R*,2*R*,3*R*,6*S*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R**)-Eunicellane* **18** (= *(1*S*,2*S*,3*S*,4*R*,4a*R*,5*R*,6*R*,9*S*,12*R*,12a*S*)-Tetradecahydro-1,6-dimethyl-4-(1-methylethyl)-10-methylidene-5,12-epoxybenzocyclodecene-

1,2,3,6,9-pentol 1,2,3,9-Tetracetate; **18**). $[\alpha]_D^{25} = -41$ ($c = 0.4$). ^{1}H-NMR: 2.26 (*dd*, $J(1,10) = 7.2$, $J(1,14) = 11.8$, H–C(1)); 3.62 (*s*, H–C(2)); 2.17, 1.85 (2 *m*, 2 H–C(4)); 2.05, 1.72 (2 *m*, 2 H–C(5)); 5.16 ('*t*', $J = 7.8$, H–C(6)); 3.13 (*dd*, $J_{gem} = 13.8$, $J(8\alpha,9) = 5.0$, H_α–C(8)); 2.42 (*d*, $J_{gem} = 13.8$, H_β–C(8)); 4.60 (*dd*, $J(9,10) = 10.6$, $J(9,8\alpha) = 5.0$, H–C(9)); 3.27 (*dd*, $J(10,9) = 10.6$, $J(10,1) = 7.2$, H–C(10)); 5.31 (br. *d*, $J(12,13) = 3.0$, H–C(12)); 5.26 (*dd*, $J(13,12) = 3.0$, $J(13,14) = 11.8$, H–C(13)); 1.84 (*t*, $J(14,1) = J(14,13) = 11.8$, H–C(14)); 1.22 (*s*, 3 H–C(15)); 5.32 (*s*, H_a–C(16)); 5.53 (*s*, H_b–C(16)); 1.55 (*s*, 3 H–C(17)); 1.78 (*m*, H–C(18)); 0.80 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 1.02 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.08 (9 H); 2.07, 1.96 (5*s*, 5 Ac). 1D-NOE: 5.32 (H_a–C(16) → H_b–C(16), H_β–C(8); 3.62 (H–C(2)) → 3 H–C(15), H–C(14); 3.27 (H–C(10)) → H–C(1), 3 H–C(17); 1.22 (3 H–C(15)) → H–C(2); 1.55 (3 H–C(17)) → H–C(9), H–C(10), H–C(12). ^{13}C-NMR: *Table 3*. EI-MS: 479 (1.3); 478 (1, $[M - AcOH]^{+\bullet}$), 477 (1), 419 (1), 418 (1), 376 (1), 358 (4), 359 (1), 316 (4), 299 (2), 298 (3), 43 (100). HR-EI-MS: 478.2564 ± 0.0030 ($C_{26}H_{38}O_8^{+\bullet}$; calc. 478.2566). FAB-MS (3-nitrobenzyl alcohol): 539 (0.3, $[M + H]^+$).

*(1*R*,2*R*,3*R*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R*)-Eunicellane* **19** (=*(1S*,2S*,3S*,4R*,4aR*,5R*,6R*,12-R*,12aS*)-Tetradecahydro-1,6-dimethyl-4-(1-methylethyl)-10-methylidene-9-oxo-5,12-epoxybenzocyclodecene-1,2,3,6-tetrol 1,2,3,6-Tetracetate*; **19**). $[\alpha]_D^{25} = +16$ ($c = 0.4$). ^{1}H-NMR: 2.19 (*dd*, $J(1,10) = 7.5$, $J(1,14) = 11.6$, H–C(1)); 3.59 (*s*, H–C(2)); 2.17, 2.04 (2 *m*, 2 H–C(4)); 2.64 (*m*, 2 H–C(5)); 2.94 (*dd*, $J_{gem} = 13.5$, $J(8\alpha,9) = 4.9$, H_α–C(8)); 2.72 (*dd*, $J_{gem} = 13.5$, $J(8\beta,9) = 7.3$, H_β–C(8)); 4.35 (*ddd*, $J(9,10) = 9.7$, $J(9,8\alpha) = 4.9$, $J(9,8\beta) = 7.3$, H–C(9)); 3.63 (*dd*, $J(10,9) = 9.7$, $J(10,1) = 7.5$, H–C(10)); 5.26 (br. *s*, H–C(12)); 5.25 (br. *d*, $J(13,14) = 11.6$, H–C(13)); 1.75 (*t*, $J(14,1) = J(14,13) = 11.6$, H–C(14)); 1.41 (*s*, 3 H–C(15)); 5.27 (*s*, H_a–C(16)); 5.57 (br. *s*, H_b–C(16)); 1.56 (*s*, 3 H–C(17)); 1.78 (*m*, H–C(18)); 0.80 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 1.02 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.11, 2.07, 1.97, 1.92 (4*s*, 4 Ac). 1D-NOE: 2.94 (H_α–C(8)) → H–C(9); 3.63 (H–C(10)) → H–C(1), H–C(12); 1.75 (H–C(14)) → H–C(2), 3 H–C(15). ^{13}C-NMR: *Table 3*. EI-MS: 477 (1.5), 476 (4, $[M - AcOH]^{+\bullet}$), 417 (3), 416 (9), 374 (1), 356 (6), 297 (3), 296 (5), 43 (100). HR-EI-MS: 476.2405 ± 0.0030 ($C_{26}H_{36}O_8^{+\bullet}$; calc. 476.2410). FAB-MS (3-nitrobenzyl alcohol): 537 (1.3, $[M + H]^+$). MS (3-nitrobenzyl alcohol): 537 (1.3, $[M + H]^+$).

*(1*R*,2*R*,3*R*,6*S*,7*Z*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R*)-Eunicellane* **20** (=*(1S*,2S*,3S*,4R*,4aR*,5R*,6R*,9S*,10Z,12R*,12aS*)-1,2,3,4,4a,5,6,7,8,9,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,3,6,9-pentol 1,2,3,6,9-Pentacetate*; **20**). $[\alpha]_D^{25} = +7$; $[\alpha]_{546} = +15$ ($c = 0.08$). ^{1}H-NMR: 2.22 (*dd*, $J(1,10) = 7.5$, $J(1,14) = 11.6$, H–C(1)); 3.66 (*s*, H–C(2)); 2.10–1.70 (series of *m*, 2 H–C(4), 2 H–C(5)); 6.36 (br. *d*, $J(6,5) = 10.9$, H–C(6)); 5.25 (br. *s*, H–C(8)); 4.89 (br. *d*, $J(9,10) = 6.7$, H–C(9)); 3.56 (*t*, $J(10,9) = J(10,1) = 7.5$, H–C(10)); 5.49 (br. *s*, H–C(12)); 5.29 (*dd*, $J(13,12) = 2.9$, $J(13,14) = 10.6$, H–C(13)); 1.75 (*m*, H–C(14)); 1.49 (*s*, 3 H–C(15)); 1.65 (br. *s*, 3 H–C(16)); 1.59 (*s*, 3 H–C(17)); 1.80 (*m*, H–C(18)); 0.91 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 1.02 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.11, 2.04, 2.02, 1.99, 1.95 (5*s*, 5 Ac). 1D-NOE: 5.25 (H–C(8)) → 3 H–C(16). ^{13}C-NMR: *Table 3*. EI-MS: 580 (0.2, $M^{+\bullet}$), 521 (5), 520 (5), 477 (2), 461 (4), 418 (3), 401 (2), 358 (6), 341 (2), 43 (100). HR-EI-MS: 520.2661 ± 0.0030 ($C_{28}H_{40}O_9^{+\bullet}$; calc. 520.2672), 477.2476 ± 0.0030 ($C_{26}H_{37}O_8^+$; calc. 477.2488).

*(1*R*,2*R*,3*R*,6*S*,7*Z*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R*)-Eunicellane* **21** (=*(1S*,2S*,3S*,4R*,4aR*,5R*,6R*, 9S*,10Z,12R*,12aS*)-1,2,3,4,4a,5,6,7,8,9,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,3,6,9-pentol 1,2,3,9-Tetracetate*; **21**). $[\alpha]_D^{25} = -24$ ($c = 0.1$). ^{1}H-NMR: 2.37 (br. *dd*, $J(1,10) = 7.2$, $J(9,14) = 11.4$, H–C(1)); 3.79 (br. *s*, H–C(2)); 2.15–1.80 (series of *m*, 2 H–C(4), 2 H–C(5)); 6.37 (*m*, H–C(6)); 5.30 (br. *s*, H–C(8)); 4.94 (br. *d*, $J(9,10) = 7.2$, H–C(9)); 3.17 (*t*, $J(10,9) = J(10,1) = 7.2$, H–C(10)); 5.67 (*d*, $J(12,13) = 3.1$, H–C(12)); 5.28 (*dd*, $J(13,14) = 10.5$, $J(13,12) = 3.1$, H–C(13)); 1.80 (*m*, H–C(14)); 1.22 (*s*, 3 H–C(15)); 1.70 (br. *s*, 3 H–C(16)); 1.59 (*s*, 3 H–C(17)); 1.65 (*m*, H–C(18)); 0.91 (*d*, $J(19,20) = 6.9$, 3 H–C(19)); 1.02 (*d*, $J(20,19) = 6.9$, 3 H–C(20)); 2.10, 2.04, 2.03, 1.99 (4*s*, 4 Ac). 1D-NOE: 3.79 (H–C(2)) → 3 H–C(15); 5.30 (H–C(8)) → 3 H–C(17); 4.94 (H–C(9)) → H–C(8), 3 H–C(17); 1.22 (3 H–C(15)) → H–C(2); 1.70 (3 H–C(16)) → H–C(8); 1.59 (3 H–C(17)) → H–C(9), H–C(12), H–C(13). ^{13}C-NMR: *Table 3*. EI-MS: 479 (3); 478 (6, $[M - AcOH]^{+\bullet}$), 419 (7), 418 (4), 359 (7), 358 (6), 299 (4), 298 (4), 43 (100). HR-EI-MS: 478.2563 ± 0.0030 ($C_{26}H_{38}O_8^{+\bullet}$; calc. 478.2566). FAB-MS (3-nitrobenzyl alcohol): 539 (0.6, $[M + H]^+$).

*(1*R*,2*R*,3*R*,6*S*,7*Z*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R*)-Eunicellane* **22** (=*(1S*,2S*,3S*,4R*,4aR*,5R*,6R*,9S*,10Z,12R*,12aS*)-1,2,3,4,4a,5,6,7,8,9,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,3,6,9-pentol 1,2,3,6-Tetracetate*; **22**). $[\alpha]_D^{25} = -9$ ($c = 0.2$). ^{1}H-NMR: 2.14 (*dd*, $J(1,10) = 7.5$, $J(1,14) = 11.6$, H–C(1)); 3.63 (*s*, H–C(2)); 2.20–1.70 (series of *m*, 2 H–C(4), 2 H–C(5)); 4.05 (*dd*, $J(6,5) = 8.2$, $J(6,OH) = 12.2$, H–C(6)); 5.29 (br. *s*, H–C(8)); 4.94 (br. *d*, $J(9,10) = 8.4$, H–C(9)); 3.66 (*dd*, $J(10,1) = 7.5$, $J(10,9) = 8.4$, H–C(10)); 5.36 (*d*, $J(12,13) = 2.7$, H–C(12)); 5.29 (*dd*, $J(13,12) = 2.7$, $J(13,14) = 11.8$, H–C(13)); 1.81 (*t*, $J(14,1) = J(14,13) = 11.8$, H–C(14)); 1.44 (*s*, 3 H–C(15)); 1.76 (br. *s*, 3 H–C(16)); 1.60 (*s*, 3 H–C(17));

1.67 (*m*, H–C(18)); 0.87 (*d*, *J*(19,20) = 6.9, 3 H–C(19)); 1.06 (*d*, *J*(20,19) = 6.9, 3 H–C(20)); 2.12, 2.07, 1.98, 1.97 (4*s*, 4 Ac); 5.84 (*d*, *J*(OH,6) = 12.2, OH–C(6), disappeared on addition of D_2O, while the 4.05 *dd* changed to a *d*, *J* = 8.2). 1D-NOE: 4.05 (H–C(6)) → 3 H–C(16); 5.29 (H–C(8)) → H–C(6), H–C(10), 3 H–C(17); 1.44 (3 H–C(15)) → H–C(2); 1.76 (3 H–C(16)) → H–C(8); 1.60 (3 H–C(17)) → H–C(9), H–C(13). ^{13}C-NMR: *Table 3*. EI-MS: 479 (1.4), 478 (4, $[M - AcOH]^{+\bullet}$), 419 (3), 418 (7), 359 (2), 358 (5), 299 (4), 298 (3), 43 (100). HR-EI-MS: 478.2564 ± 0.0030 ($C_{26}H_{38}O_8^{+\bullet}$; calc. 478.2566). FAB-MS (3-nitrobenzyl alcohol): 539 (0.6, $[M + H]^+$).

*(1*R*,2*R*,3*R*,7*Z*,9*R*,10*S*,11*S*,12*S*,13*S*,14*R*)-Eunicellane* **23** (= *(1*S*,2*S*,3*S*,4*R*,4a*R*,5*R*,6*R*,10*Z*,12*R*,12a*S*)-1,2,3,4,4a,5,6,7,8,9,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-9-oxo-5,12-epoxybenzocyclodecene-1,2,3,6-tetrol 1,2,3,6-Tetracetate*; **23**). $[\alpha]_D^{25} = -23$ (*c* = 0.2). ^{1}H-NMR: 2.26 (*dd*, *J*(1,10) = 7.2, *J*(1,14) = 11.8, H–C(1)); 3.72 (*s*, H–C(2)); 2.20 (*m*, 2 H–C(4)); 2.64 (*ddd*, J_{gem} = 12.4, *J* = 7.4, 2.3, H_a–C(5)); 2.43 (*dt*, J_{gem} = 12.4, *J* = 2.3, H_b–C(5)); 5.35 (br. *s*, H–C(8)); 4.91 (br. *d*, *J*(9,10) = 10.8, H–C(9)); 3.61 (br. *dd*, *J*(10,9) = 10.8, *J*(10,1) = 7.2, H–C(10)); 5.28 (*d*, *J*(12,13) = 3.0, H–C(12)); 5.25 (*dd*, *J*(13,12) = 3.0, *J*(13,14) = 11.8, H–C(13)); 1.81 (*m*, H–C(14)); 1.41 (*s*, 3 H–C(15)); 1.81 (*d*, *J*(16,8) = 1.7, 3 H–C(16)); 1.60 (*s*, 3 H–C(17)); 1.80 (*m*, H–C(18)); 0.84 (*d*, *J*(19,20) = 6.9, 3 H–C(19)); 1.03 (*d*, *J*(20,19) = 6.9, 3 H–C(20)); 2.08, 2.07, 2.05, 1.97 (4 *s*, 4 Ac). 1D-NOE: 3.72 (H–C(2)) → H–C(14), 3 H–C(15), H–C(18); 5.35 (H–C(8)) → 3 H–C(16); 4.91 (H–C(9)) → H–C(8), 3 H–C(17); 3.61 (H–C(10)) → H–C(1), H–C(8), H–C(9), 3 H–C(17); 1.41 (3 H–C(15) → H–C(1), H–C(2); 1.60 (3 H–C(17)) → H–C(9), H–C(12). ^{13}C-NMR: *Table 3*. EI-MS: 477 (3), 476 (10, $[M - AcOH]^{+\bullet}$), 417 (1), 416 (3), 357 (2), 356 (4), 296 (1), 43 (100). HR-EI-MS: 476.2406 ± 0.0030 ($C_{26}H_{36}O_8^{+\bullet}$; calc. 476.2410). FAB-MS (3-nitrobenzyl alcohol): 537 (1.5, $[M + H]^+$).

3-Hydroxy Analogue of **23**. ^{1}H-NMR: 2.35 (*dd*, *J* (1,10) = 7.8, *J*(1,14) = 11.4, H–C(1)); 377 (*s*, H–C(2)); 2.20–1.70 (series of *m*, 2 H–C(4), 2 H–C(5), H–C(18)); 5.39 (*quint.*, *J*(8,16) ≈ *J*(8,9) = 1.5, H–C(8)); 4.93 (*m*, H–C(9)); 3.14 (*t*, *J*(10,9) ≈ *J*(10,1) = 7.8, H–C(10)); 5.61 (*d*, *J* (12,13) = 3.0, H–C(12)); 5.22 (*dd*, *J* (13,12) = 3.0, *J*(13,14) = 11.8, H–C(13)); 1.82 (*t*, *J*(14,1) = *J*(14,13) = 11.8, H–C(14)); 1.14 (*s*, 3 H–C(15)); 1.84 (br. *s*, 3 H–C(16)); 1.56 (*s*, 3 H–C(17)); 0.87 (*d*, *J*(19,20) = 6.9, 3 H–C(19)); 1.05 (d, *J*(20,19) = 6.9, 3 H–C(20)); 2.07, 2.03, 1.98 (3*s*, Ac). 1D-NOE: 3.77 (H–C(2)) → 3 H–C(15); 5.39 (H–C(8)) → 3 H–C(16); 4.93 (H–C(9)) → 3 H–C(17); 3.14 (H–C(10)) → H–C(1), 3 H–C(17); 5.22 (H–C(13)) → H–C(1), 3 H–C(17); 1.14 (3 H–C(15)) → H–C(1), H–C(2). ^{13}C-NMR: 128.24 (*d*); 94.66 (*d*); 81.60 (*s*); 78.70 (*d*); 71.85 (*s*); 71.47 (*d*); 69.15 (*d*); 51.37 (*d*); 41.81 (*d*); 40.09 (*d*); 33.37 (*t*); 29.55 (*t*); 28.51 (*d*); 26.39, 21.16, 21.06, 20.98, 20.95, 20.73, 15.67 (7*q*); no other signal could be detected. EI-MS: 494 (0.2, $M^{+\bullet}$), 434 (1.2, $[M - AcOH]^{+\bullet}$), 374 (0.8), 315 (3), 314 (1.5), 43 (100).

*(1*R*,2*R*,3*R*,6*S*,7*Z*,9*R*,10*S*,11*S*,12*S*,14*R*)-Eunicellane* **24** (= *(1*S*,2*S*,4*R*,4a*R*,5*R*,6*R*,9*S*,10*Z*,12*R*,12a*S*)-1,2,3,4,4a,5,6,7,8,9,12,12a-Dodecahydro-1,6,10-trimethyl-4-(1-methylethyl)-5,12-epoxybenzocyclodecene-1,2,6,9-tetrol 1,2,6,9-Tetracetate*; **24**). [α]: no reliable value available at any wavelength because of low molar rotation and small amounts of material. NMR: *Table 2*. 1D-NOE: 1.63 (3 H–C(16)) → H–C(8). EI-MS: 463 (2), 462 (3, $[M - AcOH]^{+\bullet}$), 419 (5), 403 (7), 402 (1.4), 360 (4), 342 (1.5), 43 (100). HR-EI-MS: 462.2616 ± 0.0030 ($C_{26}H_{38}O_7^{+\bullet}$; calc. 462.2617), 419.2423 ± 0.0030 ($C_{24}H_{35}O_6^+$; calc. 419.2434). FAB-MS (3-nitrobenzyl alcohol): 463 (3.9, $[M - AcOH + H]^+$).

*(1*R*,2*R*,3*R*,6*S*,9*R*,10*S*,11*S*,12*S*,14*R*)-Eunicellane* **25** (= *(1*S*,2*S*,4*R*,4a*R*,5*R*,6*R*,9*S*,12*R*,12a*S*)-Tetradecahydro-1,6-dimethyl-4-(1-methylethyl)-10-methylidene-5,12-epoxybenzocyclodecene-1,2,6,9-tetrol 1,2,9-Triacetate*; **25**). $[\alpha]_D^{25} = -13$ (*c* = 0.2). NMR: *Table 2*. 1D-NOE: 3.60 (H–C(2)) → H–C(14), 3 H–C(15); 4.54 (H–C(9)) → H–C(8α), 5.54 (H_a–C(16)) → H_b–C(16); 5.34 (H_b–C(16)) → H_a–C(16). EI-MS: 420 (2, $[M - AcOH]^{+\bullet}$), 361 (1.6), 360 (2.6), 342 (2), 300 (5), 299 (2), 43 (100). FAB-MS (3-nitrobenzyl alcohol): 481 (0.3, $[M + H]^+$).

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