52. Slowly Interconverting Conformers of the Briarane Diterpenoids Verecynarmin B, C, and D, Isolated from the Nudibranch Mollusc *Armina maculata* and the Pennatulacean Octocoral *Veretillum cynomorium* of East Pyrenean Waters

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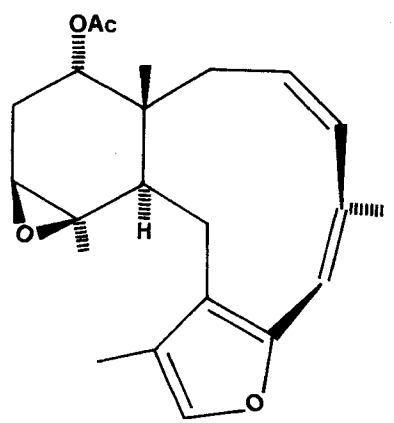
The novel briarane diterpenoids verecynarmin B (= (−)-(1*R**,10*S**,11*R**,4*E*,12*Z*)-briara-4,7,12,17-tetraen-14-one; (−)-**4**); verecynarmin C (= (−)-(1*R**,10*R**,11*S**,4*E*,12*Z*)-11-hydroxybriara-4,7,12,17-tetraen-14-one; (−)-**5**); and verecynarmin D (= (−)-(1*R**,10*R**,11*R**,4*E*,12*E*)-13-chloro-11-hydroxybriara-4,7,12,17-tetraen-14-one; (−)-**6**) are reported here as constituents of both the Mediterranean nudibranch mollusc *Armina maculata* (RAFINESQUE) and its prey, the pennatulacean octocoral *Veretillum cynomorium* (PALLAS). The structural assignments rest mainly on (*i*) establishing that these briaranes occur in solution as two stable conformers which interconvert slowly (*ca.* 10 times per second at r.t. according to dynamic NMR) by 180° flipping of the C(4)=C(5) group in the ten-membered ring *(Scheme 1)*; (*ii*) deriving, for both conformers, $^1H,^1H$ coupling constants from 1D spectra, as well as $^1H,^1H$, $^{13}C,^1H$, and $^{13}C,^{13}C$ correlations from 2D experiments; (*iii*) subjecting the briaranes to SeO_2 oxidation at the C(16) methyl group with isomerization at the C(4)=C(5) bond to give, in each case, only one observable molecular species as shown by NMR spectroscopy *(Scheme 2)*.

1. Introduction. – Recently, we have described verecynarmin A ((−)-**1**), the first briarane diterpenoid isolated from a mollusc, the nudibranch *Armina maculata* of East Pyrenean waters [1]. The origin of the compound was traced to the mollusc's prey, the octocoral *Veretillum cynomorium* [1], which belongs to an order, the Pennatulacea, tropical members of which have already given several briaranes [2].



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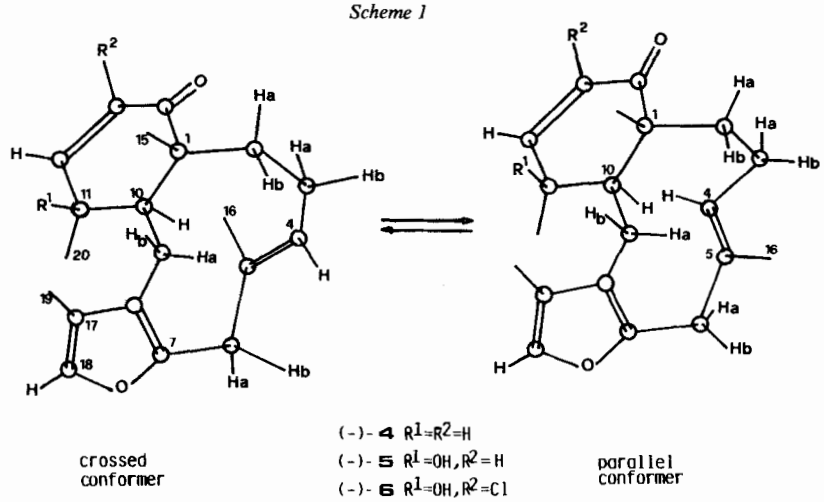
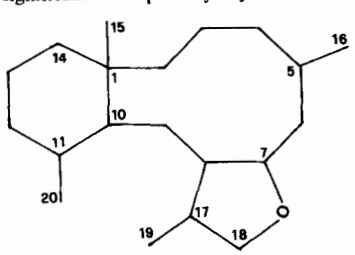
We report here on three related briaranes, verecynarmin B ((−)-**4**), C ((−)-**5**), and D ((−)-**6**), isolated from the same mollusc and sea pen[1]), which undergo unusually slow conformational changes; one of them, atypically, bears a Cl-atom at the six-membered ring.

2. Results and Discussion. – Three *Ehrlich*-reactive compounds of *A. maculata*, one less polar (verecynarmin B ((−)-**4**)) and two more polar (verecynarmin D ((−)-**6**) and C ((−)-**5**)) than verecynarmin A ((−)-**1**) [1], are now isolated. Their ^{13}C-NMR spectra are complex and, in each case, difficult to attribute to a single kind of molecule; however, failure to change the ^{13}C-NMR spectra on extensive HPLC leads to the assumption that they are single compounds existing in slowly interconverting forms.

Scheme 1



[1]) Like with (−)-**1** in previous work [1], we use here for simplicity the briarane nomenclature and numbering of formula **2**. For retrieval purposes, the IUPAC nomenclature and numbering of formula **3** may be used whereby the names of verecynarmin B ((−)-**4**), C ((−)-**5**), and D ((−)-**6**) are (−)-(8a*R**,12*R**,12a*S**,5*E*,10*Z*)-7,8,8a,12,12a,13-hexahydro-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-*b*]furan-9(4*H*)-one, (−)-(8a*R**,12*S**,12a*R**,5*E*,10*Z*)-7,8,8a,12,12a,13-hexahydro-12-hydroxy-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-*b*]furan-9(4*H*)-one, and (−)-(8a*R**,12*R**,12a*R**,5*E*,10*E*)-10-chloro-7,8,8a,12,12a,13-hexahydro-12-hydroxy-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-*b*]furan-9(4*H*)-one, respectively. No absolute configuration significance is implied by any of the structural formulae of this paper.



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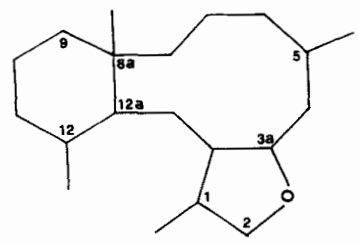

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IUPAC numbering

2.1. *The Gross Structure.* It will become apparent that the structural assignments require complementary information from all three verecynarmins though, owing to its higher abundance, which more than compensates for its lower stability, the more detailed NMR data are obtained with verecynarmin D ((−)-**6**).

The ^{13}C-NMR spectrum of (−)-**6** consists of 40 resonances with each one of 20 stronger signals accompanied by a weaker signal. The two series of stronger and weaker signals are listed in *Table 1* under the headings 'crossed conformer' and 'parallel conformer', respectively; this implies that we are thinking of two equilibrium conformers of (−)-**6** which slowly interconvert on the NMR time scale. In fact, line broadening is observed on raising the temperature in $(CD_3)_2SO$ solution until the stronger and the weaker ^{1}H-NMR signals of each couple coalesce at 82 ± 3°.

The MS of (−)-**6** has the base peak at *m/z* 348 with the isotopic composition for a Cl-atom; in accordance with all NMR evidence, this has to be taken as the molecular ion.

As verecynarmin B ((−)-**4**) and C ((−)-**5**) show similar spectra, except for lack of the Cl-atom, the structural analysis of all these compounds requires a complete analysis of the spectra for both conformers. To this end, focussing the attention on (−)-**6**, we proceed along four steps. We first analyze ^{1}H,^{1}H couplings *(Table 2)* and COSY ^{1}H,^{1}H correlations [3], securing the fragment from H–C(10) to 2 H–C(2) along the ten-membered ring for both the crossed and the parallel conformer (*Scheme 1*, (−)-**6**).

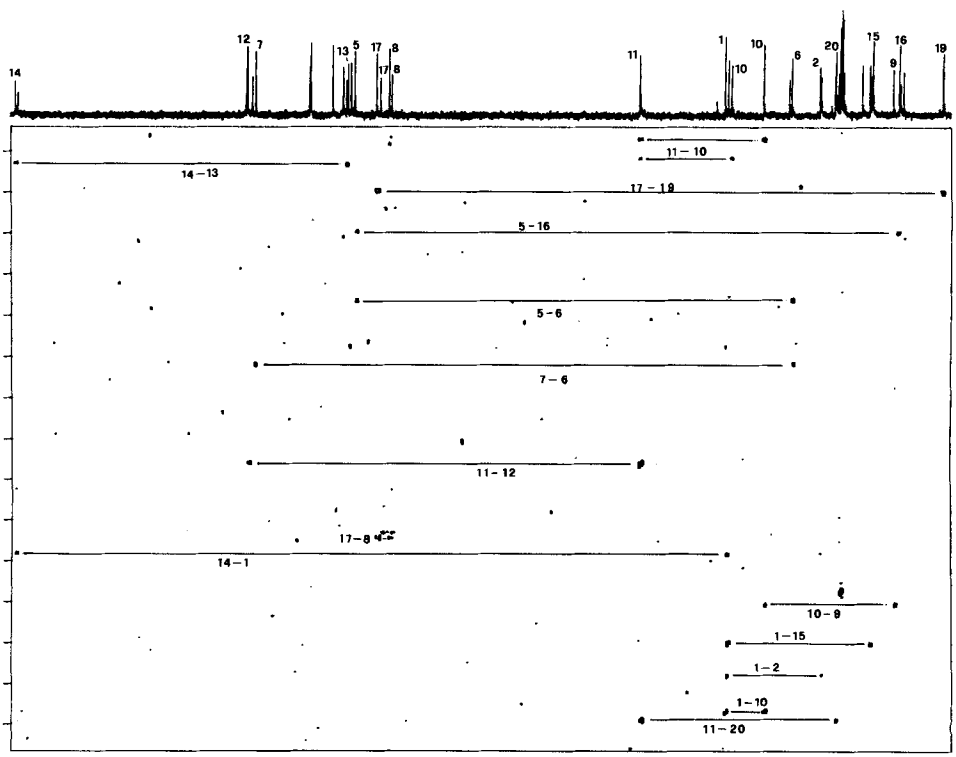


Fig. 1. *^{13}C,^{13}C Double-quantum coherence contour plot for verecynarmin D* ((−)-**6**). The 1D ^{13}C-NMR spectrum is shown along the abscissa scale.

With both (−)-**6** conformers, H–C(10) is strongly coupled to H_b–C(9) and weakly coupled to H_a–C(9), the latter bearing also a homoallylic coupling to 2 H–C(6), while H_b–C(6) is long-range coupled to H–C(18). Typically for β-methyl-substituted furans [1], H–C(18) shows a J of 1.3 Hz with Me(19). That the 2 H–C(6) resonate at quite low field for a CH_2 group (*ca.* 3.2 ppm) cannot be accounted for by bonding of C(6) to only a furan ring; deshielding by the C(4)=C(5) system is also suggested. In fact, H_a–C(6) is coupled to Me(16), which is coupled to H–C(4). The fragment from C(10) to C(4) can be further extended up to C(2) on the basis of COSY maps for the crossed conformer: H–C(4) is correlated to 2 H–C(3)[2]) which is correlated to both H_a–C(2) and H_b–C(2).

The second step in the structural analysis of verecynarmin D is to assign the H-bearing C-atoms from one-bond $^{13}C,^{1}H$ correlations [4] (δ(C) column in *Table 1* for (−)-**6**), and in the next step, the fragment C(12)–C(11)(C(20))–C(10)(C(9))–C(1)(C(2))-(C(15))–C(14)–C(13) is established by $^{13}C,^{13}C$ double-quantum coherence experiments [5] *(Fig. 1)* which confirm also the fragments C(16)–C(5)–C(6)–C(7) and C(19)–C(17)–C(8)[3]).

The fourth step of the structural analysis of verecynarmin D ((−)-**6**) concerns the $^{13}C,^{1}H$ long-range correlations [4] *(Table 1)* which establish the fragment H–C(12)–C(12)–C(13). This supports the cyclohexenone portion of (−)-**6**, which was already implied by both typical ^{13}C-NMR resonances *(Table 1)* and UV absorption at

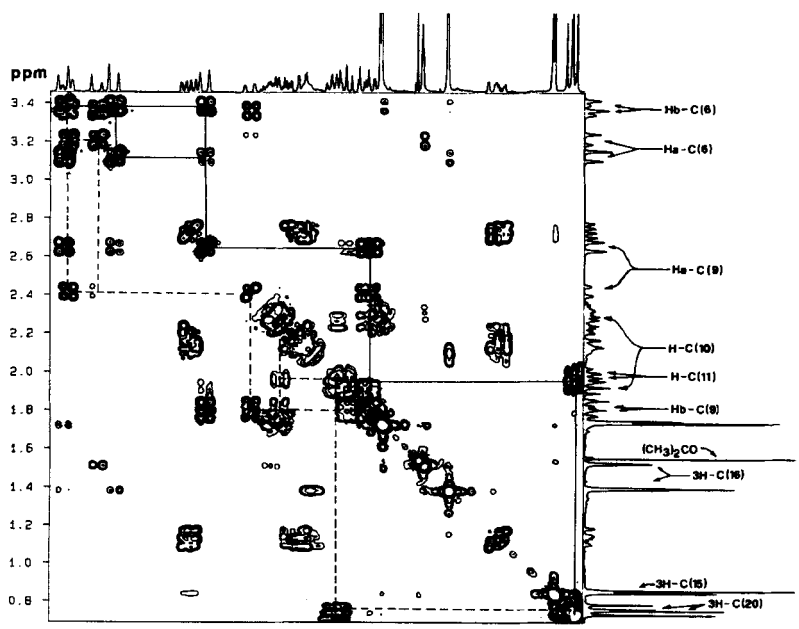


Fig. 2. *High-field COSY contour plot for verecynarmin B* ((−)-**4**). The 1D, ^{1}H-NMR spectrum is shown along both sides of the plot. Continuous and dashed lines joining the contour maps are for the crossed and the parallel conformer, respectively.

[2]) The attribution of the superimposed at 1.90–2.05 ppm signals to 2 H–C(3) firmly rests on $^{13}C,^{1}H$ hetero-correlations.

[3]) This experiment has been carried out at the limits of the potency of modern NMR instrumentation due to scarce availability (which limited the amount usable) and instability of (−)-**6** (which limited the acquisition time; see *Exper. Part*). Therefore, only the more prominent $^{13}C,^{13}C$ correlation peaks could be revealed.

Table 1. *^{13}C-NMR Chemical Shifts* (δ(C)) *and Multiplicities*[a]) *for the Crossed and the Parallel Conformers of Verecynarmin B* ((−)-**4**), *Verecynarmin C* ((−)-**5**), *and Verecynarmin D* ((−)-**6**) *and Long-Range ^{13}C,^{1}H Correlations for the Crossed Conformer of* (−)-**5** *and* (−)-**6**

C-Atom	(−)-**4** (in C_6D_6)		(−)-**5** (in C_6D_6)		
	Crossed conformer δ(C)	Parallel conformer δ(C)	Crossed conformer δ(C)	^{13}C,^{1}H correlation[b])	Parallel conformer δ(C)
C(1)	50.89 (*s*)	50.61	51.30 (*s*)	Me(15)	50.75
C(2)	32.57 (*t*)	32.35	33.29 (*t*)	Me(15)	33.06
C(3)	25.51 (*t*)	23.94	25.63 (*t*)		23.77
C(4)	132.90 (*d*)	129.91	132.54 (*d*)		128.85
C(5)	127.32 (*s*)	128.97	127.55 (*s*)	H_a–C(6), Me(16)	129.89
C(6)	39.84 (*t*)	40.37	39.85 (*t*)	Me(16)	40.48
C(7)	148.07 (*s*)	148.83	148.15 (*s*)	H_a–C(6), H_b–C(6)	148.91
C(8)	120.40 (*s*)	119.94	121.11 (*s*)	H_a–C(9), H_b–C(9), Me(19)	120.61
C(9)	25.21 (*t*)	23.96	19.24 (*t*)	H–C(10)	17.76
C(10)	44.86 (*d*)	52.17	45.12 (*d*)	Me(15), Me(20)	51.80
C(11)	36.77 (*d*)	37.35	69.24 (*s*)	H–C(10), H–C(12), Me(20)	68.97
C(12)	153.10 (*d*)	153.33	152.01 (*d*)	Me(20)	152.01
C(13)	126.18 (*d*)	126.64	125.07 (*d*)		125.50
C(14)	202.57 (*s*)	202.18	204.03 (*s*)	H–C(12), Me(15)	203.61
C(15)	20.72 (*q*)	20.82	23.36 (*q*)	H–C(10)	23.98
C(16)	18.15 (*q*)	16.97	17.84 (*q*)		16.96
C(17)	122.42 (*s*)	121.63	123.35 (*s*)		122.55
C(18)	136.53 (*d*)	137.04	136.77 (*d*)		137.19
C(19)	9.32 (*q*)	9.27	9.35 (*q*)		9.24
C(20)	21.10 (*q*)	21.03	30.89 (*q*)		31.18

C-Atom	(−)-**6** (in C_6D_6)		(−)-**6** (in $(CD_3)_2CO$)		
	Crossed conformer δ(C)	Parallel conformer δ(C)	Crossed conformer δ(C)	^{13}C,^{1}H correlation[b])	Parallel conformer δ(C)
C(1)	53.11 (*s*)	52.42	53.51 (*s*)	H_a–C(2), Me(15)	52.82
C(2)	33.91 (*t*)	33.66	34.24 (*t*)	Me(15)	34.04
C(3)	25.43 (*t*)	23.53	25.70 (*t*)		23.81
C(4)	132.21 (*d*)	128.50	132.70 (*d*)	H_a–C(6), H_b–C(6), Me(16)	129.04
C(5)	[c])	130.08 (*s*)[d])	128.26 (*s*)	H_a–C(6), H_b–C(6), Me(16)	130.63
C(6)	39.80 (*t*)	40.38	39.91 (*t*)	H–C(4), Me(16)	40.47
C(7)	148.11 (*s*)	148.84	148.33 (*s*)	H_a–C(6), H_b–C(6)	149.05
C(8)	120.77 (*s*)	120.28	121.42 (*s*)	H_a–C(6), H_b–C(6), H_a–C(9), H_b–C(9), H–C(10), Me(19)	120.92
C(9)	19.21 (*t*)	17.74	19.42 (*t*)	H–C(10)	17.97
C(10)	45.08 (*d*)	51.65	45.71 (*d*)	H_a–C(9), Me(20)	52.14
C(11)	70.70 (*s*)	70.47	70.78 (*s*)	H_a–C(9), H_b–C(9), H–C(10), Me(20)	70.67
C(12)	148.80 (*d*)	148.90	149.90 (*d*)	Me(20)	150.02
C(13)	130.13 (*s*)[d])	130.56	129.68 (*d*)	H–C(12), Me(20) (^{4}J)	129.96
C(14)	196.83 (*s*)	196.18	196.76 (*s*)	H–C(12), Me(15)	196.26
C(15)	23.33 (*q*)	24.01	23.48 (*q*)	H–C(10)	24.10
C(16)	17.84 (*q*)	16.92	18.14 (*q*)	H–C(4), H_b–C(6)	17.19
C(17)	123.30 (*s*)	122.50	123.90 (*s*)	Me(19)	123.09
C(18)	136.81 (*d*)	137.24	137.14 (*d*)	Me(19)	137.44
C(19)	9.30 (*q*)	9.18	9.21 (*q*)		9.11
C(20)	30.96 (*q*)	31.20	31.06 (*q*)		31.19

[a]) Multiplicities for only the parallel conformer are reported as they are identical to those for the crossed conformer.

[b]) These protons are correlated with the C-atoms indicated in the first column.

[c]) Submerged by the residual solvent signal.

[d]) These resonances can be interchanged.

233 nm. These data indicate also that 2 H–C(6) is correlated with 2 H–C(9) through the furan ring and confirm most of the correlations established above from 1D *(Table 2)* and 2D ^{1}H-NMR experiments. Due to signal superimpositions, we are unable to find correlations for only the 2 H–C(3)[4]).

Elucidation of the gross structure (–)-**6** thus reveals that verecynarmin D is unique among the briaranes for having a halogen atom at the six-membered ring; in all other cases, the halogen atom is at C(6) in the ten-membered ring [2a, c].

Verecynarmin C ((–)-**5**) has NMR data (*Table 1* and *2*) very similar to verecynarmin D ((–)-**6**), except for deshielding of both C(12) and C(14) *(Table 1)* [6], due to the replacement of the Cl-atom at C(13) by a H-atom. Moreover, an *AB* system is observed for coupling of H–C(13) to H–C(12). All other ^{13}C-NMR and the MS data are in accordance with these conclusions supporting the gross structure (–)-**5**.

With verecynarmin B ((–)-**4**), COSY correlation maps between H–C(10) and H–C(11) *(Fig. 2)* and (which is out of the plot) between H–C(11) and H–C(12), reveal 1 proton more at C(11) than with verecynarmin C and D. The COSY plot further shows the correlations H–C(10), 2 H–C(9), 3 H–C(20), H–C(11), and 2 H–C(9), 2 H–C(6), thus supporting the C-backbone C(13)–C(12)–C(11)–C(10)–C(9)–C(8)–C(7)–C(6). The key role of these 2D experiments is shown by the fact that although the ^{1}H-NMR spectrum is less congested than with verecynarmin C and D, the region around C(9), C(10), and C(11) is too buried to allow decoupling experiments. The main contribution of 1D ^{1}H-NMR experiments with (–)-**4** is to indicate *(Table 2)* a large, and thus *trans* diaxial, coupling of H–C(10) to H–C(11), besides revealing the coupling of H–C(11) to H–C(12) which allows us to extend the fragment up to H–C(13). The MS of (–)-**4** is in accordance with these conclusions, showing the molecular ion, as the base peak, at 16 mass units less than with verecynarmin C ((–)-**5**).

2.2. *The Relative Configuration.* The configuration at the western hemisphere of the verecynarmins, as depicted in *Scheme 1*, is proven by four sets of data. Firstly, H_a–C(9) is so weakly coupled to H–C(10) to require a nearly 90° H_a–C(9)–C(10)–H dihedral angle in all cases. Secondly, the resonance of Me(20) at 0.2–0.1 ppm higher field than expected for a Me group at a quaternary C-atom of the C(11)-type can be attributed to the shielding effect of a furan ring lying over Me(20). Thirdly, the data of *Table 2* reveal that with both (–)-**5** and (–)-**6**, the OH group induces a deshielding of Me–C(15), for mutual 1,3-diaxial relationship, and of both Me(19) and H_b–C(9), for proximity. Fourthly and last, *trans* diaxial relationship between H–C(11) and H–C(10) in (–)-**4** is indicated by a large coupling constant.

As regards the eastern hemisphere, the (*E*) configuration at the C(4)=C(5) bond is indicated by typically high δ(C) values for C(16) *(Table 1)* which result from steric compression between Me(16) and 2 H–C(3) with both conformers [7]. Should the C(4)=C(5) bond have the (*Z*) configuration, the 2 H–C(2), 2 H–C(3) and 2 H–C(9), H–C(10) coupling constants would have drastically different values from those in *Table 2*, while no low-energy conformer with Me(20) above the plane of the furan ring

[4]) NOE effects at r.t. can not be obtained as the two conformers have too short lifetime. Lowering of the temperature to slow down the interconversion process is faced with the problem of finding a suitable low-melting solvent. To this end, both $(CD_3)_2CO$ and CD_3OD result in buried spectra which are unsuitable for NOE studies.

Table 2. *^{1}H-NMR Data for the Parallel and the Crossed Conformer of Verecynarmin B* ((−)-**4**), *C* ((−)-**5**), *and D* ((−)-**6**) *in* C_6D_6

H-Atom	(−)-**4**	
	Crossed conformer	Parallel conformer
H_a–C(2)	2.72 (br. *ddd*, J_{gem} = 14.5, *J*(2a,3b) = 7.0, *J*(2a,3a) = 1.8, *J*(2a,15) small)	2.20[a])
H_b–C(2)	1.13 (*ddd*, J_{gem} = 14.5, *J*(2b,3a) = 10.5, *J*(2b,3b) = 2.0)	1.75[a])
2 H–C(3)	2.05–2.20[a])	2.25–2.35[a])
H–C(4)	5.18 (br. *dd*, *J*(4,3a) = 11.0, *J*(4,3b) = 4.5, *J*(4,16) = 1.3)	5.42 (br. *dd*, *J*(4,3a) = *J*(4,3b) = 8.0, *J*(4,16) and *J*(4,6a) small)
H_a–C(6)	3.12 (br. *d*, J_{gem} = 15.3, *J*(6a,9a) and *J*(6a,16) small)	3.22 (br. *d*, J_{gem} = 15.5, *J*(6a,9a), *J*(6a,4), and *J*(6a,16) small)
H_b–C(6)	3.38 (br. *d*, J_{gem} = 15.3, *J*(6b,9a), *J*(6b,18), and *J*(6b,16) small)	3.36 (br. *d*, J_{gem} = 15.5, *J*(6b,9a), *J*(6b,18), and *J*(6b,16) small)
H_a–C(9)	2.66 (br. *d*, J_{gem} = 14.5, *J*(9a,6a), *J*(9a,6b), and *J*(9a,10) small)	2.42 (br. *d*, J_{gem} = 15.0, *J*(9a,6a), *J*(9a,6b), and *J*(9a,10) small)
H_b–C(9)	1.82 (*dd*, J_{gem} = 14.5, *J*(9b,10) = 10.0)	1.81 (*dd*, J_{gem} = 15.0, *J*(9b,10) = 9.5)
H–C(10)	1.92 (*dd*, *J*(10,9b) = 10.0, *J*(10,11) = 9.5, *J*(10,9a) small)	2.22[a])
H–C(11)	2.01 (*m*, *J*(11,10) = 9.5, *J*(11,20) = 6.8, *J*(11,12) small)	1.99[a])
H–C(12) H–C(13)	5.91 5.92 } (*AB*, J_{AB} = 10.5)[b])	5.92 5.93 } (*AB*, J_{AB} = 10.5)[b])
3 H–C(15)	0.86 (*s*, *J*(15,2a) small)	0.85 (*s*)
3 H–C(16)	1.39 (br. *s*, *J*(16,4) = *J*(16,3b) = 1.3, *J*(16,6a) and *J*(16,6b) small)	1.52 (br. *s*, *J*(16,4), *J*(16,3b), and *J*(16,6a) small)
H–C(18)	6.93 (*dq*, *J*(18,19) = 1.1, *J*(18,6b) small)	6.95 (br. *q*, *J*(18,6b) small, *J*(18,19) = 1.4)
3 H–C(19)	1.74 (*d*, *J*(19,18) = 1.1)	1.75 (*d*, *J*(19,18) = 1.4)
3 H–C(20)	0.74 (*d*, *J*(20,11) = 6.8)	0.77 (*d*, *J*(20,11) = 7.0)

H-Atom	(−)-**5**	
	Crossed conformer	Parallel conformer
H_a–C(2)	2.62[a])	2.1[a])
H_b–C(2)	1.20 (*m*)	1.85[a])
2 H–C(3)	2.2–2.0[a])	2.2–2.0[a])
H–C(4)	5.20 (br. *dd*, *J*(4,3a) = 10.5, *J*(4,3b) = 5.0, *J*(4,16) = 1.2)	5.34 (br. *dd*, *J*(4,3a) = *J*(4,3b) = 8.0, *J*(4,16) small)
H_a–C(6)	3.17 (br. *d*, J_{gem} = 15.3, *J*(6a,9a) and *J*(6a,16) small)	3.26 (br. *d*, J_{gem} = 15.5, *J*(6a,9a) and *J*(6a,16) small)
H_b–C(6)	3.43 (br. *d*, J_{gem} = 15.3, *J*(6b,9a) and *J*(6b,18) small)	3.37 (br. *d*, J_{gem} = 15.5, *J*(6b,9a) and *J*(6b,18) small)
H_a–C(9)	2.48 (br. *d*, J_{gem} = 14.4, *J*(9a,10) = 1.5, *J*(9a,6a) and *J*(9a,6b) small)	2.28 (br. *d*, J_{gem} = 14.6, *J*(9a,10), *J*(9a,6a), and *J*(9a,6b) small)
H_b–C(9)	2.66 (*dd*, J_{gem} = 14.4, *J*(9b,10) = 10.8)	2.76 (*dd*, J_{gem} = 14.6, *J*(9b,10) = 10.4)
H–C(10)	2.23 (*dd*, *J*(10,9b) = 10.8, *J*(10,9a) = 1.5)	2.53 (br. *d*, *J*(10,9b) = 10.4, *J*(10,9a) small)
H–C(11)	–	–
H–C(12) H–C(13)	5.82 5.80 } (*AB*, J_{AB} = 10.0)	5.80 5.79 } (*AB*, J_{AB} = 10.0)
3 H–C(15)	1.04 (*s*)	1.07 (*s*)
3 H–C(16)	1.37 (br. *s*, *J*(16,4) = 1.2, *J*(16,6a) small)	1.54 (br. *s*, *J*(16,4) and *J*(16,6a) small)
H–C(18)	6.99[a])	7.00[a])
3 H–C(19)	2.06 (*d*, *J*(19,18) = 1.3)	2.02 (*d*, *J*(19,18) = 1.3)
3 H–C(20)	0.91 (*s*)	

Table 2 (cont.)

H-Atom	(−)-**6**	
	Crossed conformer	Parallel conformer
H_a–C(2)	2.55[a])	2.05[a])
H_b–C(2)	1.15 (*m*)	1.76 (*m*)
2 H–C(3)	1.90–2.05[a])	2.00–2.15[a])
H–C(4)	5.11[a])[c])	5.13[a])[d])
H_a–C(6)	3.11 (br. *d*, J_{gem} = 15.5, *J*(6a, 9a) and *J*(6a, 16) small)	3.22 (br. *d*, J_{gem} = 15.6, *J*(6a, 9a) and *J*(6a, 16) small)
H_b–C(6)	3.37 (br. *d*, J_{gem} = 15.5, *J*(6b, 9a) and *J*(6b, 18) small)	3.31 (br. *d*, J_{gem} = 15.6, *J*(6b, 9a) = 1.6, *J*(6b, 18) small)
H_a–C(9)	2.37 (br. *d*, J_{gem} = 14.4, *J*(9a, 6a) and *J*(9a, 6b) small, *J*(9a, 10) = 1.3)	2.16 (br. *d*, J_{gem} = 14.6, *J*(9a, 6b) = 1.6, *J*(9a, 6a) and *J*(9a, 10) small)
H_b–C(9)	2.57 (*dd*, J_{gem} = 14.4, *J*(9b, 10) = 10.8)	2.67 (*dd*, J_{gem} = 14.6, *J*(9b, 10) = 10.4)
H–C(10)	2.21 (*dd*, *J*(10, 9b) = 10.8, *J*(10, 9a) = 1.3)	2.47 (br. *d*, *J*(10, 9b) = 10.4, *J*(10, 9a) small)
H–C(11)	–	–
H–C(12)	6.19 (*s*)	6.23 (*s*)
H–C(13)	–	–
3 H–C(15)	1.00 (*s*)	1.01 (*s*)
3 H–C(16)	1.25 (br. *s*, *J*(16, 4) and *J*(16, 6a) small)	1.48 (br. *s*, *J*(16, 4) and *J*(16, 6a) small)
H–C(18)	6.95[a])	6.96[a])
3 H–C(19)	1.98 (*d*, *J*(19, 18) = 1.3)	1.95 (*d*, *J*(19, 18) = 1.3)
3 H–C(20)	0.82 (*s*)	0.82 (*s*)

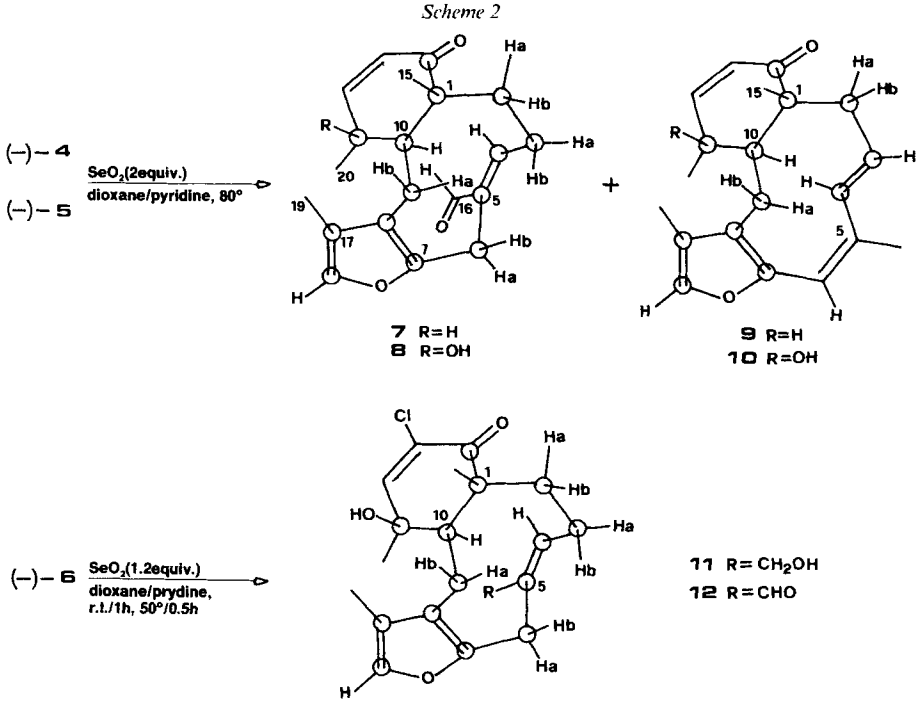
[a]) Superimposed.
[b]) The *B* part of the *AB* system (at 5.91 for the crossed and 5.92 ppm for the parallel conformer) is weakly coupled with H–C(11).
[c]) In $CDCl_3$: 5.48 (br. *dd*, *J*(4, 3a) = 12.0, *J*(4, 3b) = 3.0, *J*(4, 16) small).
[d]) In $CDCl_3$: 5.63 (br. *dd*, *J*(4, 3a) = *J*(4, 3b) = 7.0, *J*(4, 16) small).

(Scheme 1) would be conceivable; Me(20) would be expected to resonate at higher field than observed *(Table 2)*.

2.3. *The Conformations.* From the ^{1}H- and ^{13}C-NMR data in *Tables 1* and *2*, it is seen that the most marked spectral differences between the two conformers are in all cases related to the C(4)H=C(5)(C(16)H$_3$) fragment[5]). With the more abundant conformer, H–C(4) is a *dd* with a large, *trans*-diaxial coupling to H$_a$–C(3) and a small coupling to H$_b$–C(3). With the less abundant conformer, H–C(4) is a *dd* with coupling constants of *ca.* 7 Hz to both H$_a$–C(3) and H$_b$–C(3), indicating a small, *ca.* 35°, H–C(4)–C(3)–H$_a$ dihedral angle and a large, *ca.* 145°, H–C(4)–C(3)–H$_b$ dihedral angle. Therefore, the C(9)–C(10) bond must cross the C(5)=C(4) bond in the more abundant conformer while the two bonds must be parallel to one another in the less abundant conformer; this is the origin of the terms for the two conformers. Two sets of NMR data further support these conclusions. Firstly, C(10) resonates at higher field with the more abundant conformer *(Table 1)* due to steric compression between H–C(10) and Me(16). Secondly, H–C(10) is shielded in the crossed conformer by the C(4)=C(5) bond *(Table 2)*.

The coalescence temperatures and the kinetic parameters for the conformational change of the verecynarmins are derived by ^{1}H-NMR ((CD$_3$)$_2$SO) monitoring the 3

Scheme 2



[5]) That briaranes may exist in slowly changing conformations was already briefly noticed with the non-furanoid briarane diterpenoid stylatulide [2c] where, however, the existence of two conformers was supposed from the mere difference of only two ^{1}H-NMR signals of the ten-membered ring. Though the dynamic phenomenon was not investigated [2c], it is clear that coalescence with stylatulide occurs at much lower temperature than with the verecynarmins.

H–C(16) signal at various temperatures. The data reported in the *Exper. Part,* based on an approximate treatment [8], indicate about 10 conformational inversions per second at r.t. The best proof of the existence of two conformers would be the transformation of a verecynarmin into a compound which shows the NMR spectrum of only one molecular species. To this end, it seems logical to modify a verecynarmin around the centre of the dynamic process, the H–C(4)=C(5)–C(16) fragment. Attempts *via* epoxidation, osmilation, and PhSeCl treatment were unsuccessful[6]). But treatment of verecynarmin B ((–)-**4**) with an excess of SeO_2 at 80° for 1 h led, by oxidation of Me(16) to CH(16)O, to the main product **7** with concomitant isomerization of the C(4)=C(5) bond *(Scheme 2)*. The minor product **9** arose from annular allylic oxidation followed by dehydration. Verecynarmin C ((–)-**5**) behaved the same way, giving mainly compound **8** besides **10**.

Milder conditions, and only a slight molar excess of SeO_2, brought about oxidation of verecynarmin D ((–)-**6**) at Me(16), giving first alcohol **11**, which was then partly oxidized to aldehyde **12** *(Scheme 3)*[7]). Each of the compounds **7**, **8**, **11**, and **12** shows ^{1}H- and ^{13}C-NMR spectra at r.t. for a single molecular species *(Exper. Part)*. In every case, the C(16) group must point towards the six-membered ring from the face opposite to Me(15), since both nuclei of H–C(10) are shielded by the C(4)=C(5) group as in the case of the crossed conformer of the verecynarmins. Moreover, H_a–C(2) (which must lie in the O=C(14)–C(1) plane, pointing towards the O-atom, to account for the deshielding effect of the carbonyl group) is *trans* coupled to H_b–C(3), which is *trans* coupled to H–C(4). The configuration at the C(4)=C(5) bond is unambiguously proven by strong NOE effects *(Exper. Part)* between H–C(4) and either a proton of the CH_2(16) group (with **11**) or the aldehydic proton (with **7**, **8**, and **12**). With **9** and **10**, the (*E*) configuration at the C(3)=C(4) bond rests on a large *J*(3,4) (16 Hz), whereas (*Z*) configuration at the C(5)=C(6) bond is required in order to be able to close the ten-membered ring with *Dreiding* models.

We thank Dr. *G. Chiasera* for devising and setting up the variable-temperature device, Mr. *N. Dematté* for skilled aid in the separation of the verecynarmins, the *Laboratoire Arago* for laboratory facilities, and the *C.N.R.*, and the *M.P.I.* (Progetti di Interesse Nazionale), Roma, for financial support.

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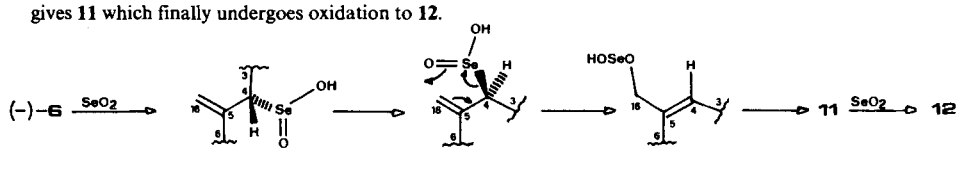
[6]) Both the peracid and the PhSeCl treatment led to non-*Ehrlich*-reactive mixtures showing many TLC spots which were not further investigated. Presumably, the peracid attacks the furan group, too [9]. The osmilation gave a mixture of products of dihydroxylation at the C(4)=C(5) group in too low a yield.

[7]) According to proposed mechanisms for SeO_2 oxidation [10], the first conceivable intermediate in the SeO_2 oxidation of (–)-**6**, **6a**, allows free rotation around the C(5)–C(4) bond with change to the **6b** conformer for release of strain in the ten-membered ring. A 1,3-shift of O=Se(OH) then leads to **6c**, the hydrolysis of which gives **11** which finally undergoes oxidation to **12**.



Experimental Part

1. *General.* All evaporations were carried out at reduced pressure. Silica gel column chromatography and flash chromatography: *Merck Kieselgel 60* (70–230 μm). Reverse-phase flash chromatography: *Merck RP-18 LiChroprep* (40–65 μm). HPLC: *Merck-LiChrosorb Si-60* (7 μm). Reverse-phase HPLC: *Merck-LiChrosorb RP18* (7 μm). All HPLC columns were 25 × 1 cm with solvent flux 5 ml/min; monitoring by UV at 250 nm. Polarimetric data: *JASCO-DP-181* polarimeter; λ(nm) in parentheses. UV (λ_{max} in nm, ε in mol^{-1} 1 cm^{-1}) and IR ($\tilde{\nu}_{max}$ in cm^{-1}): *Perkin-Elmer-Lambda-3* and *Pye-Unicam-SP3-200* spectrometers, respectively. NMR: *Varian-XL-300*; ^{13}C-NMR at 75.43 MHz, ^{1}H-NMR at 300 MHz, probe temperature 22°; δ's (ppm) relative to internal Me_4Si (= 0 ppm) and J in Hz. All ^{1}H-NMR coupling constants were deduced from double irradiations and those greater than 0.5 Hz were confirmed by COSY [3] experiments with compounds (–)-**4**, (–)-**5**, (–)-**6**, **11**, and **12**. The notation 'small' indicates $J < 0.5$ Hz. Multiplicities in ^{13}C-NMR spectra were derived from DEPT experiments [12]. ^{13}C,^{1}H-NMR Shift-correlation experiments [4] were carried out as in previous work for compounds (–)-**4**, (–)-**5**, (–)-**6**, and **11** [1]. The ^{13}C,^{13}C double-quantum coherence experiment [5] with (–)-**6** was carried out during *ca.* 70 h with 2048 points for each FID obtained with 128 time increments and with τ 0.0063 s. The data matrix was zero filled to 4096 × 512, pseudo-echo processed in f_2 dimension, and weighted with an exponential function (10 Hz line broadening) in f_1 dimension. Differential NOE were obtained with preirradiation of 8 s and are reported as irradiated proton(s)→% increment (relaxed proton(s)). With our home-made equipment for dynamic ^{1}H-NMR experiments, the temperature was calibrated on the chemical-shift difference among OH and CH_2 of ethylene glycol [13]. For both conformers of the verecynarmins in $(CD_3)_2SO$, the coalescence temperature (t_c) of the 3 H–C(16) signal was evaluated and the kinetic constant (k) at 30° was calculated *via* approximate treatments [8]. The activation enthalpy ($\Delta H^{\neq}$) was then evaluated. MS (EI; %, m/z): home-built spectrometer based on the *ELFS-4-162-8-Extranuclear* quadrupole [11].

2. *Isolations.* A portion (6.5 g) of the 13.2 g of extract of *A. maculata* of the previous work [1] was subjected to silica-gel flash chromatography (400 g of stationary phase, gradient elution petroleum ether/Et_2O) to achieve partial purification of the 3 new *Ehrlich*-reactive verecynarmins which were eluted in the order of increasing polarity, *i.e.* verecynarmin B ((–)-**4**), D ((–)-**6**), and C ((–)-**5**), while the already known verecynarmin A ((–)-**1**) [1] was eluted between (–)-**4** and (–)-**6**. Thus, the eluate with petroleum ether/Et_2O 3:1 gave, after evaporation and reverse-phase HPLC with MeOH/H_2O 8:2, pure (–)-**4** (t_R 16 min; 0.03% on dry mollusc weight after extraction). Similarly, the eluate with petroleum ether/Et_2O 13:5 yielded (reverse-phase HPLC with CH_3CN/H_2O 7:3) (–)-**6** (t_R 12 min; 0.3%) and the eluate with petroleum ether/Et_2O 1:1 (reverse-phase HPLC with MeOH/H_2O 18:7) (–)-**5** (t_R 16 min; 0.08%).

The yields of the verecynarmins represent a lower limit not only due to the difficulty of dealing with mixtures of largely predominant common fats, in analogy with the case of (–)-**1** [1], but also owing to the limited stability of these compounds which decreases in the order (–)-**6** < (–)-**5** < (–)-**4** ≈ (–)-**1**. Decompositions were particularly fast when the solutions of the verecynarmins were evaporated to dryness without precautions to exclude light. The same verecynarmins were also detected in extracts of *Veretyllum cynomorium* [1].

3. *Verecynarmin B* (= *(–)-(1R*,10S*,11R*,4E,12Z)-Briara-4,7,12,17-tetraen-14-one*[1]); (–)-**4**. Colourless foam on evaporation of MeOH/H_2O solns. to dryness. $[\alpha]^{20}$: –95.6° (589), –99.3° (577), –113.1° (546), –201.3° (435), –258.7 (365; c = 1.75, EtOH). UV (EtOH): 205 (11300), 223 (13700). IR (metastable liquid film): 1690 (C=O). Dynamic ^{1}H-NMR: $t_c = 75 \pm 3°$, $k = 14 \pm 2$ s^{-1}, $\Delta H^{\neq} = 14.5 \pm 0.5$ kcal mol^{-1}. MS: 298 (100, M^+), 283 (6, M^+ – Me), 187 (15), 161 (40), 147 (60), 123 (61), 109 (25), 91 (40).

4. *Reaction of Verecynarmin B* ((–)-**4**) *with* SeO_2. To a soln. of (–)-**4** (7.7 mg, 0.026 mmol) in dry dioxane (2 ml) and 2 drops of pyridine was added SeO_2 (6.0 mg, 0.054 mmol). The mixture was stirred during 1.5 h at 80°, evaporated to 0.5 ml, and then subjected to gradient flash chromatography yielding **9** (1.3 mg, 17%) and **7** (3.8 mg, 47%) with hexane/AcOEt 7:3 or 6:4, resp.

(1R,10S*,11R*,3E,5Z,12Z)-Briara-3,5,7,12,17-pentaen-14-one* (= *(8aR*,12R*,12aS*,4Z,6E,10Z)-8a,12,12a,13-Tetrahydro-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-b]furan-9(8H)-one*; **9**). ^{1}H-NMR (C_6D_6): 3.65 (*dd*, J_{gem} = 12.5, J(2a,3) = 4.3, H_a–C(2)); 1.81 (*dd*, J_{gem} = 12.5, J(2b,3) = 11.2, H_b–C(2)); 5.61 (*ddd*, J(3,4) = 15.8, J(3,2b) = 11.2, J(3,2a) = 4.3, H–C(3)); 6.41 (br. *d*, J(4,3) = 15.8, H–C(4)); 6.18 (br. *s*, J(6,16) = 1.5, J(6,9a) small, H–C(6)); 2.63 (br. *d*, J_{gem} = 15.3, J(9a,6) small, H_a–C(9)); 5.85 (*dd*, J(12,13) = 10.0, J(12,11) = 1.0, H–C(12)); 5.81 (*d*, J(13,12) = 10.0, H–C(13)); 0.81 (*s*, 3 H–C(15)); 1.71 (br. *d*, J(16,6) = 1.5, 3 H–C(16)); 6.95 (br. *q*, J(18,19) = 1.2, H–C(18)); 1.76 (*d*, J(19,18) = 1.2, 3 H–C(19)); 0.60 (*d*, J(20,11) = 7.0, 3 H–C(20)); 1.75–1.95 (series of *m*, H_b–C(9), H–C(10), and H–C(11)). Positive NOE: H_a–C(2)→16 (H_b–C(2)), 8 (H–C(3)); H–C(6)→2 (3 H–C(16)); H_a–C(9)→13 (H–C(4)); 3 H–C(16)→12

(H–C(6)), 5 (H–C(3)). ^{13}C-NMR (C_6D_6): 48.90 (*s*, C(1)); 38.71 (*t*, C(2)); 128.60 (*d*, C(3); only detectable in the DEPT experiment); 136.10 (*d*, C(4)); 136.52 (*s*, C(5)); 116.87 (*d*, C(6)); 122.60 (*s*, C(8)); 25.30 (*t*, C(9)); 47.21 (*d*, C(10)); 37.87 (*d*, C(11)); 153.53 (*d*, C(12)); 126.77 (*d*, C(13)); 201.95 (*s*, C(14)); 18.37 (*q*, C(15)); 19.46 (*q*, C(16)); 121.31 (*s*, C(17)); 137.14 (*d*, C(18)); 9.65 (*q*, C(19)); 20.44 (*q*, C(20)); C(7) was not detected. MS: 296 (40, $M^{+\cdot}$), 281 (20, $M^{+\cdot}$ – Me), 253 (25, 281 – CO), 199 (27), 159 (100), 149 (39), 145 (52), 123 (48), 91 (67).

*(1*R*,*10*S*,*11*R*,*4*E,*12*Z*)-Briara-4,7,12,17-tetraen-14,16-dione* (= *(8a*R*,*12*R*,*12a*S*,*5*E,*10*Z*)-4,7,8,8a,9,12,12a,13-Octahydro-1,8a,12-trimethyl-9-oxobenzo[4,5]cyclodeca[1,2-b]furan-5-carbaldehyde;* **7**). ^{1}H-NMR (C_6D_6): 2.62 (*ddd*, J_{gem} = 14.9, J(2a,3b) = 11.7, J(2a,3a) = 4.5, H_a–C(2)); 0.93 (*ddd*, J_{gem} = 14.9, J(2b,3a) = J(2b,3b) = 4.2, H_b–C(2)); 5.78 (*dd*, J(4,3b) = 11.2, J(4,3a) = 6.5, H–C(4)); 3.70 (*d*, J_{gem} = 15.0, H_a–C(6)); 3.20 (br. *d*, J_{gem} = 15.0, J(6b,16) = 1.1, H_b–C(6)); 2.09 (br. *d*, J_{gem} = 15.4, H_a–C(9)); 5.86 (*s*, H–C(12), H–C(13)); 0.75 (*s*, 3 H–C(15)); 9.09 (*d*, J(16,6b) = 1.1, H–C(16)); 6.88 (br. *q*, J(18,19) = 1.2, H–C(18)); 1.65 (*d*, J(19,18) = 1.2, 3 H–C(19)); 0.66 (*d*, J(20,11) = 6.9, 3 H–C(20)); 1.7–2.1 (series of *m*, 2 H–C(2), H_b–C(9), H–C(10), H–C(11)). Positive NOE: H–C(16)→13 (H–C(4)). ^{13}C-NMR (C_6D_6): 51.60 (*s*, C(1)); 31.40 (*t*, C(2)); 22.95 (*t*, C(3) or C(6) or C(9)); 153.87 (*d*, C(4) or C(12)); 136.74 (*s*, C(5)); 22.80 (*t*, C(6) or C(3) or C(9)); 146.96 (*s*, C(7)); 119.78 (*s*, C(8) or C(17)); 22.52 (*t*, C(9) or C(2) or C(6)); 44.20 (*d*, C(10)); 37.18 (*d*, C(11)); 153.60 (*d*, C(12) or C(4)); 126.71 (*d*, C(13)); 202.04 (*s*, C(14)); 19.91 (*q*, C(15) or C(20)); 193.34 (*d*, C(16)); 120.29 (*s*, C(17) or C(8)); 137.22 (*d*, C(18)); 8.78 (*q*, C(19)); 19.58 (*q*, C(20) or C(15)). MS: 312 (68, $M^{+\cdot}$), 297 (5, $M^{+\cdot}$ – Me), 283 (12, $M^{+\cdot}$ – CHO), 229 (40), 123 (100), 91 (80).

5. *Verecynarmin C* (= *(–)-(1*R*,*10*R*,*11*S*,*4*E,*12*Z*)-11-Hydroxybriara-4,7,12,17-tetraen-14-one*[1]*;* (–)-**5**). Colourless foam on evaporation of MeOH/H_2O solns. to dryness. $[\alpha]^{20}$: –0.9° (589), –1.1° (577), –2.3° (546), – 26.4° (435), –135.4° (365; *c* = 2.19, EtOH). UV (EtOH): 207 (11200), 220 (12000). IR (metastable liquid film): 3350 (OH), 1691 (C=O). Dynamic ^{1}H-NMR: t_c = 83 ± 3°, k = 11 ± 2 s^{-1}, $\Delta H^{\neq}$ = 11.7 ± 0.5 kcal mol^{-1}. MS: 314 (100, $M^{+\cdot}$), 299 (1, $M^{+\cdot}$ – Me), 296 (2, $M^{+\cdot}$ – H_2O), 281 (7, $M^{+\cdot}$ – Me – H_2O), 253 (5, 281 – CO), 213 (11), 201 (11), 161 (45), 159 (42), 147 (40), 145 (32), 84 (65), 43 (100).

6. *Reaction of Verecynarmin C* ((–)-**5**) *with* SeO_2. The reaction was carried out with 8.5 mg (0.027 mmol) of (–)-**5** as described for (–)-**4** in *Exper. 4*, except for a slightly shorter reaction time (1.25 h). Flash chromatography gave **10** (0.4 mg, 5%) and **8** (3.8 mg, 43%) with hexane/AcOEt 13:7 or 11:9, resp.

*(1*R*,*10*R*,*11*S*,*3*E,*5*Z,*12*Z*)-11-Hydroxybriara-3,5,7,12,17-pentaen-14-one* (= *(8a*R*,*12*S*,*12a*R*,*4*Z,*6*E,*10*Z*)-8a,12,12a,13-Tetrahydro-12-hydroxy-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-b]furan-9(8*H*)-one;* **10**). ^{1}H-NMR (C_6D_6): 3.58 (*dd*, J_{gem} = 12.4, J(2a,3) = 4.0, H_a–C(2)); 1.83 (*dd*, J_{gem} = 12.4, J(2b,3) = 11.3, H_b–C(2)); 5.56 (*ddd*, J(3,4) = 16.0, J(3,2b) = 11.3, J(3,2a) = 4.0, H–C(3)); 6.51 (br. *d*, J(4,3) = 16.0, H–C(4)); 6.20 (br. *s*, J(6,16) = 1.3, H–C(6)); 2.49 (br. *d*, J_{gem} = 15.6, H_a–C(9)); 2.93 (*dd*, J_{gem} = 15.6, J(9b,10) = 10.0, H_b–C(9)); 5.67, 5.75 (*AB*, J_{AB} = 10.2, H–C(12), H–C(13)); 1.04 (*s*, 3 H–C(15)); 1.73 (br. *d*, J(16,6) = 1.3, 3 H–C(16)); 6.89 (br. *q*, J(18,19) = 1.3, H–C(18)); 1.97 (*d*, J(19,18) = 1.3, 3 H–C(19)); 0.71 (*s*, 3 H–C(20)).

*(1*R*,*10*R*,*11*S*,*4*E,*12*Z*)-11-Hydroxybriara-4,7,12,17-tetraene-14,16-dione* (= *(8a*R*,*12*S*,*12a*R*,*5*E,*10*Z*)-4,7,8,8a,9,12,12a,13-Octahydro-12-hydroxy-1,8a,12-trimethyl-9-oxobenzo[4,5]cyclodeca[1,2-b]furan-5-carbaldehyde;* **8**). ^{1}H-NMR (C_6D_6): 2.53 (*ddd*, J_{gem} = 15.0, J(2a,3b) = 11.8, J(2a,3a) = 3.4, H_a–C(2)); 0.90 (*ddd*, J_{gem} = 15.0, J(2b,3a) = J(2b,3b) = 3.6, H_b–C(2)); 2.09, 1.84 (2 *m*, 2 H–C(3)); 5.75 (*dd*, J(4,3b) = 12.0, J(4,3a) = 5.8, H–C(4)); 3.79 (*d*, J_{gem} = 14.9, H_a–C(6)); 3.08 (br. *d*, J_{gem} = 14.9, J(6,16) = 0.9, H_b–C(6)); 1.98 (br. *d*, J_{gem} = 14.9, H_a–C(9)); 2.68 (*dd*, J_{gem} = 14.9, J(9b,10) = 9.7, H_b–C(9)); 2.27 (br. *d*, J(10,9b) = 9.7, H–C(10)); 5.72, 5.73 (*AB*, J_{AB} = 10.5, H–C(12), H–C(13)); 1.00 (*s*, 3 H–C(15)); 9.11 (br. *d*, J(16,6b) = 0.9, H–C(16)); 6.90 (br. *q*, J(18,19) = 1.3, H–C(18)); 1.82 (*d*, J(19,18) = 1.3, 3 H–C(19)); 0.72 (*s*, 3 H–C(20)); 1.3 (br. *s*, OH). Positive NOE: H–C(16)→11 (H–C(4)). ^{13}C-NMR (C_6D_6): 51.63 (*s*, C(1)); 32.07 (*t*, C(2)); 23.00 (*t*, C(3) or C(6)); 153.74 (*d*, C(4)); 136.35 (*s*, C(5)); 23.15 (*t*, C(6) or C(3)); 146.73 (*s*, C(7)); 120.51 (*s*, C(8) or C(17)); 17.20 (*t*, C(9)); 43.69 (*d*, C(10)); 69.05 (*s*, C(11)); 151.14 (*d*, C(12)); 125.48 (*d*, C(13)); 202.59 (*s*, C(14)); 22.77 (*q*, C(15)); 193.48 (*d*, C(16)); 121.04 (*s*, C(17) or C(8)); 137.15 (*d*, C(18)); 8.66 (*q*, C(19)); 30.72 (*q*, C(20)). MS: 328 (14, $M^{+\cdot}$), 285 (1), 255 (8), 199 (14), 171 (48), 84 (100).

7. *Verecynarmin D* (= *(–)-(1*R*,*10*R*,*11*R*,*4*E,*12*E*)-13-Chloro-11-hydroxybriara-4,7,12,17-tetraen-14-one*[1]*;* (–)-**6**). Crystalline platelets. M.p. 108–112° (from hexane/AcOEt 96:4). $[\alpha]^{20}$: –27.3° (589), –28.4° (577), – 33.0° (546), –67.4° (435; *c* = 1.26, EtOH). UV (EtOH): 204 (9400), 233 (11100). IR (metastable liquid film): 3400 (OH), 1688 (C=O). Dynamic ^{1}H-NMR: t_c = 82 ± 3°, k = 12 ± 2 s^{-1}, $\Delta H^{\neq}$ = 11.4 ± 0.5 kcal mol^{-1}. MS: 350 (34), 348 (100, $M^{+\cdot}$), 335 (0.5), 333 (1.5, $M^{+\cdot}$ – Me), 317 (1), 315 (3, 333 – H_2O), 313 (1, $M^{+\cdot}$ – Cl), 307 (4), 305 (12, 333 – C=O), 247 (15), 161 (41), 159 (52), 147 (36), 109 (38), 108 (35), 91 (55).

8. *Reaction of Verecynarmin D* ((−)-**6**) *with* SeO_2. The reaction was carried out with 31 mg (0.089 mmol) of (−)-**6**, 2 drops of pyridine, and 12 mg (0.108 mmol) of SeO_2 in dry dioxane as with (−)-**4** in *Exper. 4*, except for stirring the mixture first at r.t. for 1 h and the at 50° for 30 min. The mixture was then evaporated to 0.5 ml and subjected to reverse-phase HPLC with CH_3CN/H_2O 13:7 to give **11** (6.5 mg, 20%) and **2** (9.5 mg, 30%) at t_R 7 and 9 min, resp.

*(1*R*,*10*R*,*11*R*,*4*E,*12*E*)-13-Chloro-11,16-dihydroxybriara-4,7,12,17-tetraen-14-one* (= *(8a*R*,*12*R*,*12a*R*,*5*E,*10*E*)-10-Chloro-7,8,8a,12,12a,13-hexahydro-12-hydroxy-5-(hydroxymethyl)-1,8a,12-trimethylbenzo[4,5]cyclodeca[1,2-*b*]furan-9(4*H*)-one;* **11**). Soft crystalline platelets. M.p. 95–98° (on evaporation to dryness from CH_3CN/H_2O). ^{1}H-NMR (C_6D_6): 2.64 (*ddd*, J_{gem} = 15.0, *J*(2a,3b) = 11.7, *J*(2a,3a) = 3.5, H_a–C(2)); 1.02 (*ddd*, J_{gem} = 15.0, *J*(2b,3a) = *J*(2b,3b) = 3.5, H_b–C(2)); 2.10, 1.80 (2 *m*, 2 H–C(3)); 5.33 (br. *dd*, *J*(4,3b) = 11.9, *J*(4,3a) = 6.1, H–C(4)); 3.37 (br. *d*, J_{gem} = 15.2, *J*(6b,9a) small, H_b–C(6)); 3.22 (*d*, J_{gem} = 15.2, H_a–C(6)); 2.16 (br. *d*, J_{gem} = 15.3, *J*(9a,10) and *J*(9a,6b) small, H_a–C(9)); 2.68 (*dd*, J_{gem} = 15.3, *J*(9b,10) = 10.1, H_b–C(9)); 2.41 (br. *d*, *J*(10,9b) = 10.1, *J*(10,9a) small, H–C(10)); 6.18 (*s*, H–C(12)); 0.96 (*s*, 3 H–C(15)); 3.62, 3.71 (br. *AB*, J_{AB} = 12.8, 2 H–C(16)); 6.87 (br. *q*, *J*(18,19) = 1.3, H–C(18)); 1.85 (*d*, *J*(19,18) = 1.3, 3 H–C(19)); 0.70 (*s*, 3 H–C(20)). Positive NOE: H–C(4)→1 (H_b–C(16)), 6 (H_a–C(16)), 4 (H_a–C(3)); H_b–C(16)→1 (H–C(4)); H_a–C(16)→7 (H–C(4)); 3 H–C(20)→25 (H–C(12)), 2 (2 H–C(16)), 6 (H–C(10)), 2 (3 H–C(19)). ^{13}C-NMR (C_6D_6): 53.17 (*s*, C(1)); 34.45 (*t*, C(2)); 21.88 (*t*, C(3)); 128.10 (*d*, C(4); only detectable in the DEPT experiment); 132.52 (*s*, C(5)); 26.45 (*t*, C(6)); 148.10 (*s*, C(7)); 120.36 (*s*, C(8)); 17.25 (*t*, C(9)); 43.48 (*d*, C(10)); 70.59 (*s*, C(11)); 147.35 (*d*, C(12)); 131.05 (*s*, C(13)); 195.46 (*s*, C(14)); 22.76 (*q*, C(15)); 66.40 (*t*, C(16)); 121.51 (*s*, C(17)); 136.71 (*d*, C(18)); 8.64 (*q*, C(19)); 30.82 (*q*, C(20)). MS: 366 (4), 364 (11, $M^{+\cdot}$), 348 (1), 346 (3, $M^{+\cdot} - H_2O$), 333 (2), 331 (6, 346 − Me), 159 (45), 145 (52), 95 (49), 91 (61), 43 (100).

*(1*R*,*10*R*,*11*R*,*4*E,*12*E*)-13-Chloro-11-hydroxybriara-4,7,12,17-tetraen-14,16-dione* (= *(8a*R,*12*R,*12a*R,*5*E,*10*E*)-10-Chloro-4,7,8,8a,9,12,12a,13-octahydro-12-hydroxy-1,8a,12-trimethyl-9-oxobenzo[4,5]cyclodeca[1,2-*b*]furan-5-carbaldehyde;* **12**). ^{1}H-NMR (C_6D_6): 2.54 (*ddd*, J_{gem} = 15.2, *J*(2a,3b) = 12.0, *J*(2a,3a) = 3.6, H_a–C(2)); 0.86 (*ddd*, J_{gem} = 15.2, *J*(2b,3a) = *J*(2b,3b) = 3.7, H_b–C(2)); 1.72, 1.96 (2 *m*, 2 H–C(3)); 5.72 (br. *dd*, *J*(4,3b) = 11.8, *J*(4,3a) = 6.3, H–C(4)); 3.78 (*d*, J_{gem} = 15.0, H_a–C(6)); 3.01 (br. *d*, J_{gem} = 15.0, *J*(6b,16) = 0.8, *J*(6b,9a) small, H_b–C(6)); 1.86 (br. *d*, J_{gem} = 15.2, *J*(9a,10) and *J*(9a,6b) small, H_a–C(9)); 2.59 (*dd*, J_{gem} = 15.2, *J*(9b,10) = 10.3, H_b–C(9)); 2.16 (br. *d*, *J*(10,9b) = 10.3, *J*(10,9a) small, H–C(10)); 6.10 (*s*, H–C(12)); 0.93 (*s*, 3 H–C(15)); 9.09 (br. *d*, *J*(16,6b) = 0.8, H–C(16)); 6.88 (br. *q*, *J*(18,19) = 1.2, H–C(18)); 1.77 (*d*, *J*(19,18) = 1.2, 3 H–C(19)); 0.64 (*s*, 3 H–C(20)). Positive NOE: H–C(16)→15 (H–C(4)); H–C(4)→20 (H–C(16)); 3 H–C(20)→19 (H–C(12)), 8 (H–C(10)), 3 (3 H–C(19)). ^{13}C-NMR (C_6D_6): 53.05 (*s*, C(1)); 32.63 (*t*, C(2)); 22.74 (*t*, C(3) or C(6)); 153.27 (*d*, C(4)); 136.39 (*s*, C(5)); 23.13 (*t*, C(6) or C(9)); 146.74 (*s*, C(7)); 120.13 (*s*, C(8) or C(17)); 17.13 (*t*, C(9)); 43.52 (*d*, C(10)); 70.44 (*s*, C(11)); 147.43 (*d*, C(12)); 130.72 (*s*, C(13)); 195.16 (*s*, C(14)); 22.64 (*q*, C(15)); 193.38 (*d*, C(16)); 120.88 (*s*, C(17) or C(8)); 137.23 (*d*, C(18)); 8.60 (*q*, C(19)); 30.71 (*q*, C(20)). MS: 364 (4), 362 (12, $M^{+\cdot}$), 349 (0.4), 347 (1.1, $M^{+\cdot}$ − Me), 321 (10), 319 (31, 347 − C=O), 303 (1), 301 (3, 319 − H_2O), 283 (8), 265 (10), 237 (15), 91 (64), 43 (95), 41 (100).

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