109. Xenicane Diterpenes Revisited: Thermal (*E*)→(*Z*) Isomerization and Conformational Motions. A Unifying Picture

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Kinetic and equilibrium studies show that typical xenicanes such as dictyolactone (**1**) and 4-hydroxydictyolactone (**3**) undergo slow conformation medium-ring flipping between the predominant *trans*-(**1a** or **3a**; Me(20) *trans* to H–C(3)) and the minor *cis*-conformers (**1b** or **3b**; Me(20) *cis* to H–C(3); see *Scheme 1*). The formation of the latter is inhibited in heterocyclic-ring-opened congeners such as 18-acetoxy-4-hydroxydictyo-19-al (**7**). Molecular-mechanics calculations suggest that typical-xenicane *cis*-conformers are disfavoured by mainly C(4)–C(5) torsional strain. This is confirmed by the observation of two sizably populated *cis*- and *trans*-conformers for the unnatural 4-oxoxenicanes **10–12**. Unusually facile thermal (*E*)→(*Z*) isomerization of xenicanes **1**, **3**, **10–12**, and **7** is also observed (→ **13–17** and **9**, resp.; *Scheme 3*), reflecting great strain relief in the transition state. Conflicting results in the literature now fit into this scheme which provides a basis for unravelling recognition phenomena with these biologically active systems.

1. Introduction. – Xenicane diterpenes are widespread constituents of tropical alcyonarians and gorgonians, other than of brown seaweeds in the order Dictyotales from temperate waters and sea hares that feed on them. Central examples are dictyolactone (**1**) [1], isodictyohemiacetal (**2**) [2a], and 18-acetoxy-4-hydroxydictyo-19-al[2]) (= 'hydroxyacetyldictyolal'; **7**) [2] [3].

In agreement with the X-ray structures [1a], both **1** and 4-hydroxydictyolactone (**3**) were described as single conformers **1a** and **3a** (as deduced from NMR spectra in solution) that have H–C(3) and Me–C(6) orthogonally to the mean plane of the cyclononadiene ring. These results have largely satisfied the scientific community, except for marginal notes concerning the dynamic NMR for the structurally related dictyotalide A (**4**) [4a] and the xeniaphyllane antheliolide A [4b,c][3])[4]). This is quite surprising in view of

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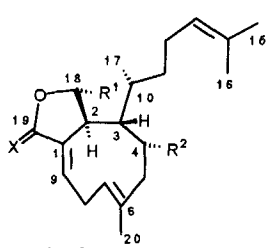
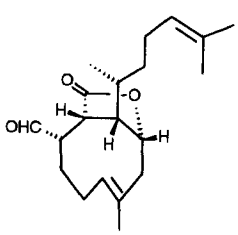
[2]) For convenience, compounds **1–21** are numbered arbitrarily; for systematic names, see *Exper. Part.*

[3]) Reportedly, the 500-MHz ^{1}H-NMR spectrum of dictyotalide A (**4**) showed in $CDCl_3$ at room temperature three aldehyde *s*'s in 5:1:1 integral ratios for three conformers in equilibrium, and in $(CD_3)_2$ SO at 105° only one aldehyde *s* [4a]. Unfortunately, no evidence was provided [4a] as to the reversibility of this phenomenon on cooling. In another report, it was described that antheliolide A, isolated from an alcyonacean coral, was eluted by HPLC as a 1:4 mixture of two components; these were judged to be conformers from chemical exchange in NOE experiments [4b]. Subsequently, the structure of antheliolide A was revised by X-ray diffraction analysis [4c].

[4]) Knowledge concerning the conformations of molecules containing the (*E*)-cyclononene unit of xenicanes, such as caryophyllene [5a] and (*E*)-cyclononene itself [5b], is far from being complete. The first study suggested a low kinetic barrier [5a], lacking any structural deduction; the second, classical study was concerned with racemization kinetics of (*E*)-cyclononenes [5b].



1 $R^1=R^2=H$, X=O[2])
2 $R^1=OH$, $R^2=H$, $X=H_2$
3 $R^1=H$, $R^2=OH$, X=O



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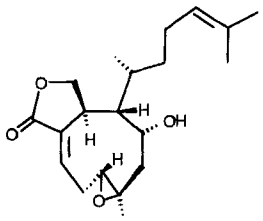

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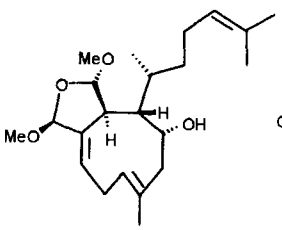

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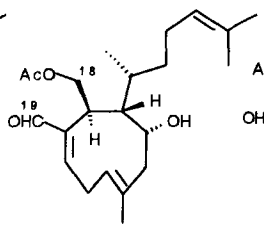

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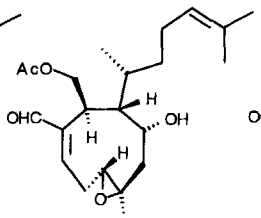

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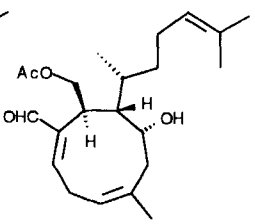

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the antibacterial [1a], antifungal [1a,c], cytotoxic [1c] [4a,f], and feeding deterrent [4e] activities of many xenicanes which suggest that recognition phenomena are closely related to certain conformations. The study of these phenomena requires, as a prerequisite, a detailed knowledge of all structural details of the xenicanes, most importantly their conformational motions.

However, since the conformational equilibria of the cyclononenes as detectable by ^{1}H-NMR were mostly overlooked or not identified unambiguously, we decided to investigate in depth the xenicanes isolated from the brown seaweed *Dictyota* sp. from the Senegal coasts [6], having noticed dynamic NMR phenomena. This study includes compounds **1**–**3**, **7** [2] [3], and **8** [7], the new expoxide **5** of 4-hydroxydictyolactone, acetal **6**, and the (6*Z*)-isomer **9** of 'hydroxyacetyldictyolal' (**7**).

2. Results and Discussion. – 2.1. *Structures of New Natural Xenicanes.* Spectral data for xenicanes **1** [1a], **2** [2a], **3** [3], **7** [2] [3], and **8** [7], isolated from our *Dictyota* sp., matched those reported in the literature.

For the new xenicane **5**, the molecular formula $C_{20}H_{30}O_4$ was determined from both HR-MS and ^{13}C-NMR data. That **5** is the 6,7-epoxide of **3** was judged from the close similarity of NMR signals of **5** and **3** [3], except for the C(7)=C(6)–Me(20) region. The relative configuration of **5** was supported by NOE enhancements (Me(20)/H–C(2), H–C(7)/H–C(3), and Me(17)/H_β–C(18)), as well as by weak H,H couplings between protons H–C(2)/H–C(3), H–C(3)/H_β–C(4), and H–C(10)/H–C(3).

The NMR data for acetal **6** were quite similar to those of its 4-acetyl derivative [2a] whose configuration at C(19) had not been defined [2a], however. For **6**, a NOE enhancement (3%) between H–C(19) and H–C(9) allowed us to establish the β-pseudoaxial orientation for MeO–C(19).

Compound **9** gave the same MS as **7** (*Exper. Part* and [1c]), but the NMR spectra of the two compounds were notably different. Thus, at room temperature, **7** showed only sharp NMR signals, while **9** exhibited several broad ^{1}H-NMR signals. Some of these were splitted, as expected for a couple of conformers in a 85:15 ratio. NOE Enhancement between H–C(7) and Me(20) left no doubt that **9** is the (6*Z*)-isomer of 'hydroxyacetyldictyolal' (**7**) [2a].

2.2. *A Predominating Conformer for Xenicanes* **1** *and* **3**. ^{1}H-NMR Spectra ($CDCl_3$, room temperature) for both dictyolactone (**1**; *Table 1*) and 4-hydroxydictyolactone (**3**) showed signals for two slowly equilibrating conformers in a 95:5 population ratio. The presence of two conformers in equilibrium was proven by cross-saturation experiments [8]: irradiation at H–C(2) of the presumed minor conformer in $CDCl_3$ at 50° led to 25% cross-saturation transfer to the corresponding proton of the major conformer[5]).

Table 1. *^{1}H-NMR Data* ($CDCl_3$) *for Dictyolactone* (**1**) *in the Preferred Conformations* **1a** *and* **1b**

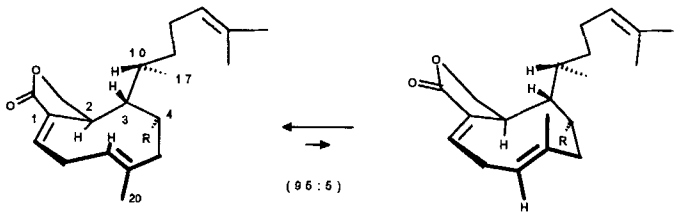
H-Atom[2])	**1a**	**1b**
H–C(2)	2.70 (*ddd*, J(2,18α) = 7.3, J(2,9) = 2.4, J(2,18β) = 1.1)	3.54 (*dtd*, J = 7.5, 2.0, 1.1)
H–C(3)	1.67 (*dd*, J(3,4α) = 9.4, J(3,4β) = 1.7)	1.50 (*m*)
H_β–C(4)	1.48 (*m*)	1.45–1.55 (*m*)
H_α–C(4)	1.75 (*m*)	1.45–1.55 (*m*)
H_β–C(5)	1.98 (*ddd*, J_{gem} = 12.9, J(5β,4α) = 12.4, J(5β,4β) = 5.4)	2.42 (*dt*, J = 12.7, 8.9)
H_α–C(5)	2.23 (*ddd*, J_{gem} = 12.9, J(5α,4β) = 2.3, J(5α,4α) = 4.7)	2.24 (*m*)
H–C(7)	5.36 (br. *dd*, J(7,8α) = 11.4, J(7,8β) = 3.7)	5.54 (*dd*, J = 12.9, 4.5)
H_α–C(8)	3.11 (*ddd*, J_{gem} = 17.0, J(8α,7) = 11.4, J(8α,9) = 2.4)	3.23 (*m*)
H_β–C(8)	2.90 (*ddd*, J_{gem} = 17.0, J(8β,9) = 7.7, J(8β,7) = 3.7)	2.98 (*m*)
H–C(9)	6.94 (*dt*, J(9,8β) = 7.7, J(9,8α) = 2.4)	6.86 (*dt*, J = 4.0, 2.0)
H–C(10)	1.61 (*m*)	1.55 (*m*)
CH_2(11)	1.17–1.22 (*m*)	1.17–1.22 (*m*)
CH_2(12)	1.92 (*m*)	1.92 (*m*)
H–C(13)	5.03 (*sept. t*, J = 1.5, J(13,12) = 7.2)	5.03 (*sept. t*, J = 1.5, 7.2)
Me(15)	1.66 (*d*, J = 1.5)	1.66 (*d*, J = 1.5)
Me(16)	1.56 (br. *s*)	1.56 (br. *s*)
Me(17)	0.93 (*d*, J(17,10) = 6.6)	0.89 (*d*, J = 6.7)
H_β–C(18)	4.52 (*dd*, J_{gem} = 9.6, J(18β,2) = 1.1)	4.44 (*dd*, J = 9.6, 1.1)
H_α–C(18)	4.02 (*dd*, J_{gem} = 9.6, J(18α,2) = 7.3)	4.09 (*dd*, J = 9.6, 7.5)
Me(20)	1.71 (*d*, J = 1.5)	1.59 (*d*, J = 1.5)

A detailed NMR analysis involving differential decoupling irradiations [9], ^{1}H,H COSY [10], HMQC [11], and, most relevantly, 1D and 2D low-temperature NOE allowed us to define the conformational equilibria in terms of flipping of the (*E*)-configurated C(7)=C(6)–Me(20) unit from Me(20) *trans* to H–C(3) in the major conformer **1a** or **3a** to *cis* in the minor conformer **1b** or **3b** (*Scheme 1*). Consistently, marked downfield shifts were observed for signals of the minor *cis*-conformer with respect to the corresponding signals of the major *trans*-conformer, *i.e.*, 0.8 ppm for H–C(2) and 5.5 ppm for C(20) in **3**.

The results of molecular-mechanics (MM) calculations [12] were in full accordance with J values, H,H distances, and conformer population ratios derived from

[5]) At room temperature, the effect was too weak to be measured due to proton relaxation being faster than conformational motions.

Scheme 1[2])



trans
1a R = H
3a R = OH

cis
1b R = H
3b R = OH

NMR spectra. These calculations also suggested that *a*) the C(3) side chain takes a preferred conformation with the dihedral angle H–C(3)–C(10)–H *ca.* 90°, like in the crystal [1a][6]), and *b*) adjacent dihedral angles along the nine-membered ring in the major conformer **1a** take opposite signs, in contrast with the same sign for the two couples of adjacent dihedral angles C(3)–C(4)–C(5)–C(6)/C(4)–C(5)–C(6)–C(7) and C(5)–C(6)–C(7)–C(8)/C(6)–C(7)–C(8)–C(9) in the minor conformer **1b**[7]). This implies staggering along the whole medium-sized ring in the major conformer **1a**, while in the minor conformer **1b** eclipsing must occur to a large extent between the methylene protons at C(4) and C(5) and to a lesser, but significant, extent in the C(8) region. Such a relief of torsional strain in the *trans*-type conformer is partially counterbalanced by both bending factors, particularly for the (6*E*)-double bond[8]), and transannular repulsive interactions, which are larger in the major than in the minor conformer[9]). Similar conclusions hold for **3**.

2.3. *A Single Conformer for the Natural Xenicane* **7**. The above analysis shows that the population ratio of xenicane conformers is regulated by a fine balance of divergent factors. Any structural change that alters this balance is reflected in a shift of the conformational equilibrium towards either the *trans*- or *cis*-type conformer (*Scheme 1*), depending on the nature of the prevailing interactions. Thus, MM calculations suggested that opening of the lactone ring, such as in **7**, should lead to an eclipsed conformation for both H_β–C(5)/OH–C(4) (30°) and H_β–C(4)/H_β–C(5) (36°) in the *cis*-type conformer. In contrast, repulsive transannular interactions are absent in the *trans*-type conformer. Accordingly, only the *trans*-type conformer of **7** was detected by NMR, and no signal broadening was observed.

2.4. *Two Sizably Populated Conformers for 4-Oxoxenicanes* **10–12**. If the above interpretation is correct, oxidation at C(4) to a keto group should shift the conforma-

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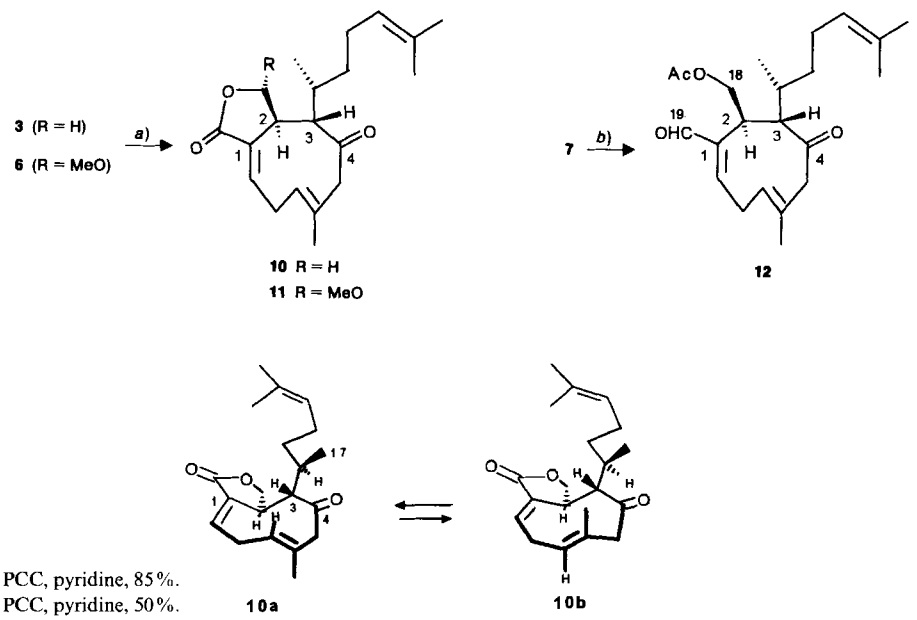
[6]) According to our calculations, there is no steric restriction to free rotation for the C(3) side chain in the range from –90 to–180° of the dihedral angle H–C(3)–C(10)–H; this contradicts recent views for these systems [2a].

[7]) Starting from the dihedral angle C(5)–C(6)–C(7)–C(8) and moving clockwise, dihedral angles were calculated to be 162, –110, 40, 2, –89, 132, –79, 50, and –85° for **1a** and –164, 60, 33, 3, –98, 110, –91°, 43, and 56° for **1b**.

[8]) Thus, the mean twisting angle (defined as the arithmetic mean of the torsional angles C(5)–C(6)–C(7)–H and C(8)–C(7)–C(6)–Me(20)) was calcualted to be 10 and 9° for **1a** and **1b**, respectively. Out-of-plane distortion of the (6*E*)-double bond turned out to be only *ca.* 2° in both cases.

[9]) H,H Distances were calculated to be 2.18 Å for H–C(3) and H–C(7) in **1a**, 2.32 Å for H–C(2) and H–C(7) in **1b**, 2.62 Å for H–C(2) and Me(20) in **1a**, and 2.96 Å for H–C(3) and Me(20) in **1b**.

Scheme 2[2])



a) PCC, pyridine, 85%.
b) PCC, pyridine, 50%.

tional equilibrium towards the *cis*-type conformer, providing direct spectroscopic access to the elusive *cis*-conformers. MM Calculations were in accordance, suggesting a small strain-energy difference of 0.5 kcal/mol between the favored *trans*-type and the disfavoured *cis*-type conformers of 4-oxoxenicanes. Although no natural xenicane of this type has yet been described, semisynthetic 4-oxoxenicanes **10**–**12** could be prepared by oxidation of **3**, **6**, and **7**, respectively (*Scheme 2*). It was rewarding to observe experimentally a 3:1 mixture of the *trans*- (**10a**) and *cis*-type (**10b**) conformers (*Scheme 2*). Strikingly larger $J(3,10)$ values were observed for conformers **10a** (11.0 Hz) and **10b** (8.8 Hz) than for xenicanes **1**, **3**, and **7** ($J \approx 0$ Hz) with sp^3-hybridization at C(4). Moreover, $J(2,3)$ of **10a** (1.6 Hz) and **10b** (3.7 Hz) were different. MM Simulations suggested that **10a** is in fast equilibrium (6:1) with a minor conformer that differs with respect to the conformation of the C(3) side chain. The H–C(3)–C(10)–H dihedral angle is *ca.* 180° in the former (corresponding to $J(3,10) = 12.5$ Hz, calculated by the equations given by *Haasnoot et al.* [13]) and 90° in the latter (corresponding to a calculated $J(3,10) \approx 0$ Hz). The average value, accounting for fast exchange at room temperature, was calculated to be $J(3,10) = 10.7$ Hz, in good agreement with the experimental value of 11.0 Hz. A similar analysis of **10b** revealed a 7:3 preference for a C(3) side-chain conformation with a H–C(3)–C(10)–H dihedral angle of *ca.* 180° over that with an angle of 90°, corresponding to an average $J(3,10) = 8.6$ Hz (experimental value $J(3,10) = 8.8$ Hz). Moreover, the calculated dihedral angle H–C(2)–C(3)–H turned out to be in accordance with NMR data (−103° for **10a**, corresponding to a negligibly small $J(2,3)$, and −123° for **10b**, corresponding to $J(2,3) = 3.5$ Hz). NOE Experiments further supported these conclusions, in particular by showing enhancement at H_β–C(18) on irradiation at H–C(10).

Similar observations were made for the *trans*- and *cis*-type conformers of 4-oxoxenicane **11**, indicating that substituents at C(18) play a secondary role.

Due to the absence of the lactone substructure, the minimum-energy conformations of **12** are now dependent on the conformations of the side chains at both C(2) and C(3). The difference in strain energy between the *trans*- and *cis*-type conformers of **12** was calculated to be 0.65 kcal/mol, in good agreement with the experimental 4:1 population of conformers (see below, *Table 2*).

2.5. *Kinetic Parameters.* Kinetic parameters for the conformational processes involved with compounds **1–3** and **10–12** were obtained from dynamic ^{1}H-NMR experiments in $(CD_3)_2SO$ in the temperature range 20–140°. Though the polarity of $(CD_3)_2SO$ and $CDCl_3$ are quite distinct, coupling patterns and conformer populations were much the same in both solvents. Moreover, $(CD_3)_2SO$ allowed the observation of dynamic NMR changes in the whole range from slow to fast exchange, through coalescence.

Several NMR signals were simulated employing the program DNMR5 [14], yielding directly rate constants for the exchange processes. In *Fig. 1*, experimental and calculated ^{1}H-NMR line shapes for the H–C(9) signal of 4-oxoxenicane **11** are given; kinetic

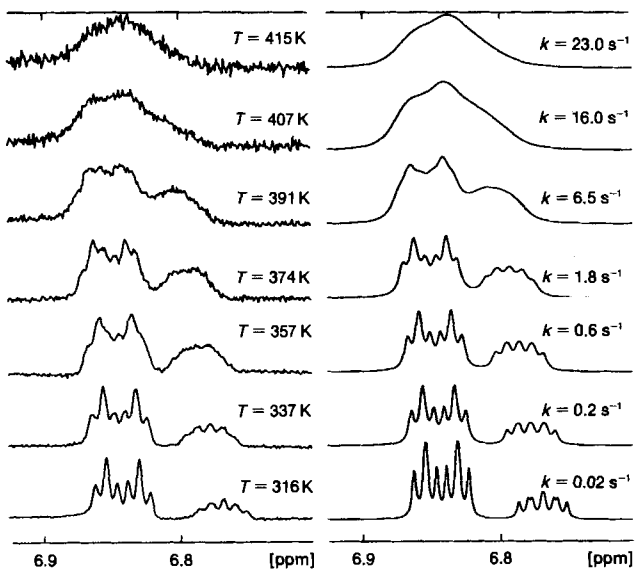


Fig. 1. *Experimental* (in $(CD_3)_2SO$; left) *and DNMR5-calculated* (right) *^{1}H-NMR line shape for the H–C(9) signal of conformers* **11a** *and* **11b** *in equilibrium*

parameters were calculated from the *Eyring* plot. Accordingly, a $\Delta G^{\neq}$ of 20.7 kcal/mol resulted from mainly enthalpic contributions. Similar results were obtained for the other xenicanes (*Table 2*). This activation energy is mainly due to both torsional strain and transannular repulsive interactions in the transition state, where the (6*E*)-double bond is forced from its low-energy, orthogonal orientation into the mean plane of the nine-mem-

Table 2. *^{1}H-NMR-Derived Thermodynamic and Kinetic Parameters for Conformational Interconversion of Various Xenicane-Type Compounds*[a])

	x_a/x_b[b])	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [cal/mol K]	$\Delta G^{\neq}$[c]) [kcal/mol]
1	93:7	16.9 ± 0.7	−11.2 ± 2	20.3 ± 0.2
3	94:6	–	–	20.3 ± 0.5
10	65:35	16.1 ± 0.2	−13.5 ± 0.6	20.1 ± 0.2
11	65:35	17.5 ± 0.1	−10.7 ± 0.5	20.7 ± 0.2
12	80:20	–	–	20.9 ± 0.5[d])
19	79:21	18.9 ± 0.1	− 5.3 ± 1.1	20.5 ± 0.5
21	89:11	–	–	20.8 ± 0.5[d])
22	75:25	14.7 ± 0.2	− 4.5 ± 0.6	16.1 ± 0.3[e])
23	50:50	19.4 ± 2	≈ 0	19.2 ± 0.2[f])
24	45:55	–	–	18.9[g])
25	78:22	–	–	25.5[g])

[a]) Statistical relative errors are given for $\Delta H^{\neq}$ and $\Delta S^{\neq}$, whereas errors in the temperature and rate constants are reflected in the errors indicated for $\Delta G^{\neq}$.

[b]) Determined by NMR-signal integration at r.t.

[c]) Determined by least-square analysis of the DNMR5-derived kinetic data based on the *Eyring* equation with transmission coefficient $k = 1$ and $T = 298$ K.

[d]) Calculated from the *Eyring* equation $\Delta G^{\neq} = 1.982T_c(23.760 + \ln T_c/k_{exch})$ where $k_{exch} \approx (\Pi/\sqrt{2})\,\Delta\nu$.

[e]) Evaluated to be 16.25 ± 0.11 kcal/mol from ^{13}C-NMR data in [5a].

[f]) See [5b].

[g]) Evaluated as above in *Footnote d* from the data reported in [21].

bered ring. Consequently, in the transition state, H–C(7) is forced to be in close proximity of H–C(3), resulting in significant angular strain of the ring system.

Relative energy barriers were also obtained from MM calculations by simulating conformer interconversion through the simultaneous change of two dihedral angles. The algebraic values of torsional angles for conformers of the *trans*- and *cis*-type suggest no 'simple' reaction coordinate that allows the interconversion of conformers. Thus, skeletal movements operated through a single dihedral driver, *e.g.*, C(4)–C(5)–C(6)–C(20), starting from the *trans*-type conformer, failed to arrive at the *cis*-type conformer but led to a distorted *trans*-conformer through a hypothetical transition state of quite high energy. However, conformer interconversion could be obtained through the simultaneous change of two dihedral angles, C(6)–C(7)–C(8)–C(9) (*e.g.*, from −110° in **1a** to +60° in **1b**, using steps of 10°) and C(5)–C(6)–C(7)–C(8) (*e.g.*, from +160° in **1a** to −160° in **1b**, using steps of 5°). Scanning through the latter dihedral (limited range 40°) allowed us to investigate its positive and negative values for energy value of the former dihedral, leading to a tridimensional diagram where changes of the two dihedral angles are reported in the plane, while strain energies, calculated for every couple of values for the two dihedral angles, are reported in the third dimension. A simpler and more reliable procedure was to drive preliminary to minimization through the two above torsional angles on H-deprived skeletons and then to insert the H-atoms. Thus, it proved possible through MM calculations to convert the *trans*-type into the *cis*-type conformers, searching for the lowest path along the reaction coordinate. This approach, applied to all above xenicanes, gave $\Delta E^{\neq}$ strain values in the range 19.4–21.7 kcal/mol (*Table 3*), in good agreement with the experimental values listed in *Table 2*.

Table 3. *Molecular-Mechanics Calculations of Thermodynamic and Kinetic Paramaters* [kcal/mol] *for Nine-Membered-Ring Flipping of Various Xenicanes*

	ΔE[a])	x_a/x_b[b])	$\Delta E_{ab}^{\neq}$[c])	$\Delta E_{ba}^{\neq}$[d])	ΔE[e])
1	1.30	90:10	20.7	19.3	19.4
3	1.71	95:5	21.3	19.6	19.7
10	0.50[f])	70:30	21.6	21.4	21.5
11	0.50[f])	70:30	21.6	21.4	21.5
12	0.65[g])	75:25	22.1	21.6	21.7
19	0.23	60:40	19.9	19.7	19.8
21	1.42	92:8	20.0	20.3	20.1
22	−0.33	36:64	18.2	18.5	18.3
23	0.00	50:50	19.8	19.8	19.8
24	−0.26	39:61	18.2	18.4	18.3
25	0.24	60:40	26.9	26.6	26.7

[a]) Difference of strain energies between the *cis*- (**b**) and *trans*-type (**a**) conformers.
[b]) Population ratio for the *trans*- and *cis*-type conformers (x = molar fraction) calculated at $T = 298$K from the equation $x_a = (1 + \exp(-\Delta E/RT))^{-1}$.
[c]) Difference of strain energies between the transition state and the *trans*-type conformer.
[d]) Difference of strain energies between the transition state and the *cis*-type conformer.
[e]) Calculated from the relationship $\Delta E^{\neq} = [\Delta E_{ab}^{\neq} + \Delta E_{ba}^{\neq} - (x_a - x_b)\Delta E]/2$.
[f]) This value represents the difference between the weighted mean strain energy for *trans*-type conformers and *cis*-type conformers resulting from rotation around the C(3)–C(10) bond.
[g]) This value has the same meaning as in *Footnote f*, account being also given to the contributions resulting from rotation around the C(2)–C(18) bond.

2.6. *(6E)→(6Z) Isomerization of Xenicanes.* During the above NMR studies on xenicanes **1** and **3** and 4-oxoxenicanes **10–12** in $(CD_3)_2SO$ at relatively high temperatures, irreversible (6*E*)→(6*Z*) isomermerization was noticed. The (6*Z*)-isomers **13–17** were obtained on pure form (*Scheme 3*). The (6*Z*)-configuration of **13–17** was supported by NMR data and unequivocally established by a similar isomerization of **7** to **9**, the latter being identical with the sample obtained here from the *Dictyota* sp.

On raising the temperature of the $(CD_3)_2SO$ solutions of **1**, **3**, or **10–12**, the ^{1}H-NMR signal of H–C(7) changed from a classical *dd*(J = 11.4, 4.2) to a '*t*'(= *dd* with similar couplings, J = 8.8, 7.4), accompanied by *ca.* 0.2 ppm upfield shift. The (6*Z*)-isomers **13–17** showed a marked NOE enhancement at Me(20) on irradiation at H–C(7), and in the ^{13}C-NMR spectra, a downfield shift of *ca.* 8 ppm with respect to the (6*E*)-isomers was observed for the Me(20) *q* (removal of the γ-effect) and an upfield shift of *ca.* 8 ppm for the C(3) *d* (removal of the strong transannular δ-effect).

Scheme 3[2])

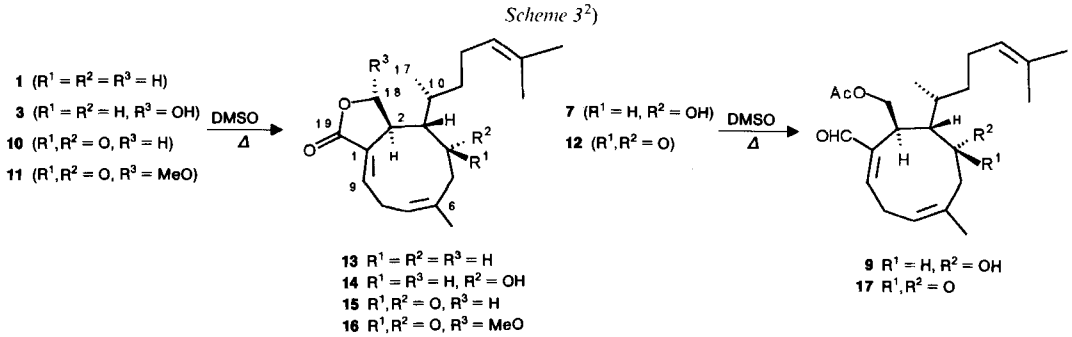


Table 4. *Kinetic Parameters for (E)→(Z) Isomerization of Various Xenicanes*

Isomerization	Temp. [°C]	$10^4 \cdot k$ [a]) [s^{-1}]	$t_{1/2}$ [min]	$\Delta G^{\neq}$ [b]) [kcal/mol]
1→**13**	134	2.9	39	30.6 ± 0.5
3→**14**	175	0.8	145	35.0 ± 0.5
7→ **9**	152	4.3	27	31.7 ± 0.5
10→**15**	134	0.35	330	32.3 ± 0.5
11→**16**	148	7.7	15	30.9 ± 0.5
12→**17**	148	14.0	8	30.4 ± 0.5

[a]) Calculated from the equation $k = [\ln(x_E^0/x_E^t)]/t$, where x_E^0 and x_E^t are the molar fraction of the (*E*)-isomer at times 0 and *t*, resp.

[b]) Calculated from the *Eyring* equation $\Delta G^{\neq} = 1.9872T(23.76 + \ln T/k)$.

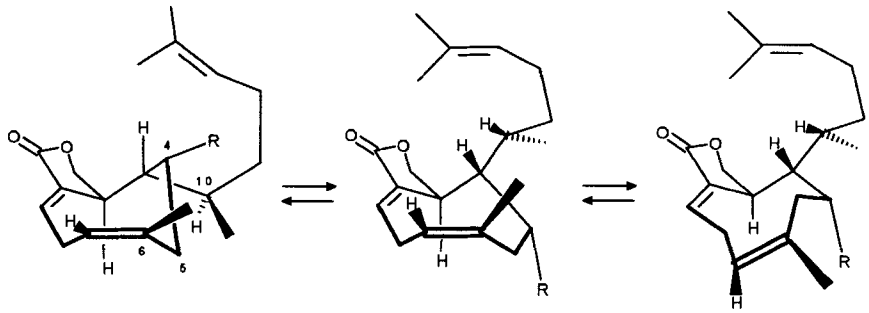
The kinetic data for the (6*E*)→(6*Z*) isomerizations (see *Table 4*) were calculated assuming irreversible first-order processes for the observed decrease of the H–C(7) signal (*dd*) intensity and show that these are unusually facile isomerizations, comparable to those of *p*-substituted tetraphenylethylenes [15]. Energy barriers for (*E*)→(*Z*) isomerizations of typical olefins such as but-2-ene [16] are *ca.* 30 kcal/mol higher. MM Calculations suggested that in the preferred conformations of the xenicanes **9** and **13**–**17**, the H–C(7) bond bisects the H_α–C(8)–H_β bond angle in the (6*Z*)-isomers, while the H–C(7)–C(8)–H_α dihedral angle takes a value of *ca.* 170° in the (6*E*)-isomers. These calculations suggested also that relief of distortion from planarity of the highly strained (*E*)–H–C(7)=C(6)–Me unit heavily contributes to the irreversibility of these isomerizations.

2.7. *(6Z)-Isomers of Xenicanes.* The (6*Z*)-isomers of natural xenicanes and their semisynthetic 4-oxo-derivatives can be classified into two groups as far as the dynamic NMR behaviour is concerned. Thus, compounds **13** and **15**–**17** showed only sharp ^{1}H-NMR signals, suggesting either that there is a prevailing conformer or that the conformers are in fast exchange. In contrast, compounds **9** and **14** showed broad ^{1}H-NMR signals at room temperature, which sharpened on either raising or lowering the temperature. This suggested that sizably populated conformers in slow equilibrium are involved.

According to NMR data, the preferred conformation of the (6*Z*)-isomers differs markedly from that of the corresponding (6*E*)-isomers. Thus, besides changes in the H–C(7) pattern (*Sect. 2.6*), the (6*Z*)→(6*E*) isomerization was accompanied by marked δ(C) values for C(5) and C(20) ($\Delta\delta$ (**10**–**15**) 20 and −10 ppm, resp., for **15** *vs.* **16**) and an increase in the *J*(2,3) values (*J* = 11.2 Hz for **15**). In line with this, MM calculations suggested 90% weight for conformer **13a**, in fast exchange ($\Delta E^{\neq}$ = 8 kcal/mol) with the minor conformers **13b** and **13c** (*Scheme 4*). In contrast, similar calculations for **15** and **16** suggested that *a*) the most populated (> 90%) conformer belongs to the **c**-type, in fast exchange ($\Delta E^{\neq} \approx$ 8 kcal/mol) with minor **a**- and **b**-type conformers, and *b*) the C(3) side chain takes a pseudoequatorial position with such an orientation as to allow a H–C(3)–C(10)–H dihedral angle of *ca.* 140°. This is in line with the experimentally observed *J*(3,10) of 5–6 Hz for both **15** and **16**.

Compound **14**, examined by ^{1}H-NMR in the temperature range −80 to +50°, *i.e.* from slow to fast-exchange conditions, showed a different behaviour. At low temperature, signal integration revealed a 7:3 population ratio for conformers **14a** and **14b** (*Scheme 4*).

Scheme 4[2])



13a (R=H) **13b** (R=H) **13c** (R=H)

14a (R=OH) **14b** (R=OH) **14c** (R=OH)

The energy barrier, $\Delta G^{\neq} = 13.1$ kcal/mol, was evaluated using the DNMR5 computer program and is represented in *Fig. 2* (where the sequence of conformers, from left to right, is drawn for convenience), together with that for the **3** → **14** isomerization. The conformational interconversion of **3a** and **3b** and the irreversible isomerization of **3** into **14** occur on sufficiently different time scales to allow the separate investigation of the kinetics for the two processes.

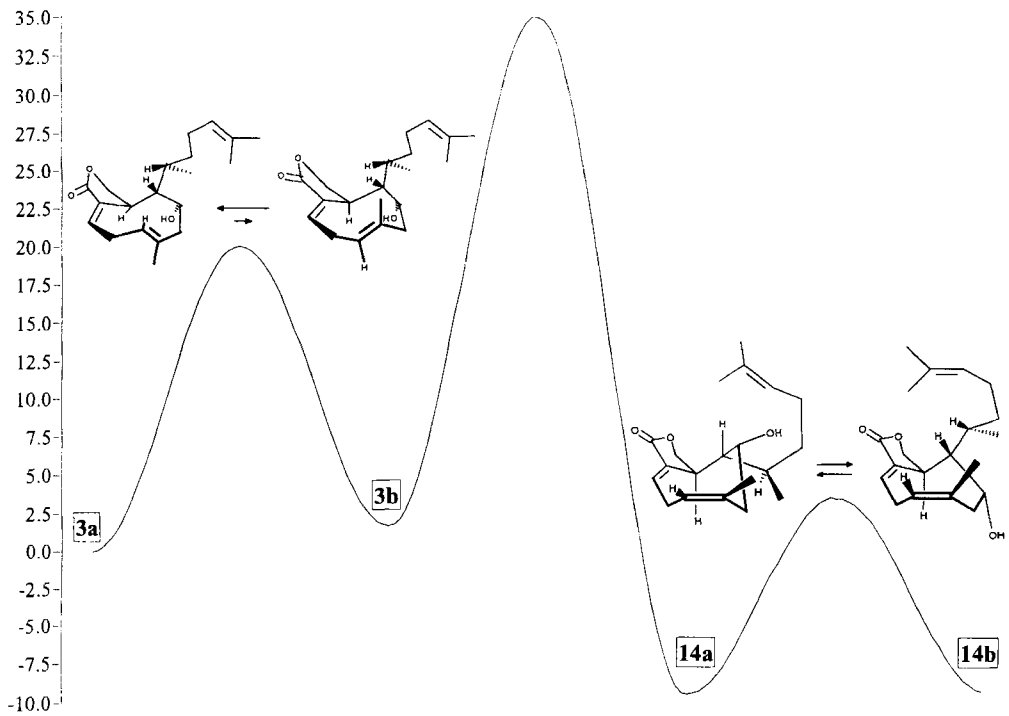


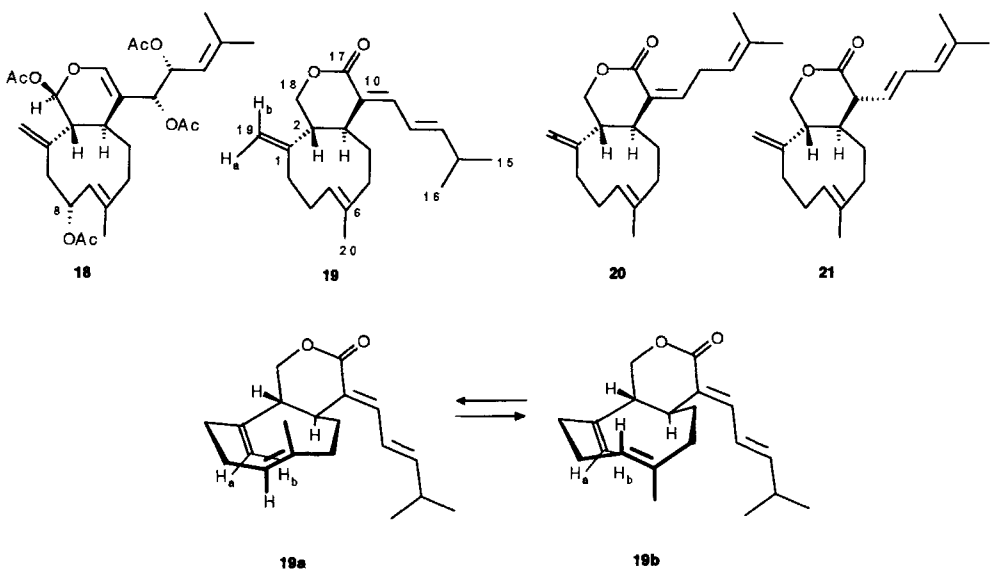
Fig. 2. *Relative energy profile* [kcal/mol] *for the* (E) → (Z) *isomerization* **3** → **14** *and of their conformational equilibria* (exper. values, except for the energy difference between the minimum-energy conformers of **3** and **14**, derived from MM calculations)

According to MM calculations, which were in excellent agreement with NMR data, conformer interconversion involves rotation around the C(4)–C(5) bond, by which the OH group changes from pseudoequatorial (in the major conformer **14a**) to pseudoaxial orientation (in the minor conformer **14b**; *Fig. 2* and *Scheme 4*). In both conformers, the C(3) side chain takes a pseudoequatorial orientation, allowing a H–C(3)–C(10)–H dihedral angle of 110–120°. This is reflected in small $J(3,10)$ values (0.6–0.8 Hz). These calculations suggested also that on fast exchange, conformer **14c** (which derives from **14b** *via* rotation around the C(5)–C(6) bond, *Scheme 4*), though scarcely populated, takes part in the conformation equilibria ($\Delta E^{\neq} = 9.5$ kcal/mol).

2.8. *The Xeniolides.* Aimed at extending the above observations to xenicane-type compounds of invertebrate origin, we examined a series of xeniolides (**19–21**) isolated from the gorgonian *Paragorgia arborea* collected in the South Indian Ocean at 280 m depth [17], and thus presumably free of photosynthetic symbionts. These xeniolides are structurally related to the long known xenicin (**18**), isolated from coral [18], which, in comparison to **1–8** of algal origin, has opposite configuration at both C(2) and C(3).

Our MM calculations suggested that *a*) xenicin (**18**) in solution exists in a single conformation, corresponding to the shape in the crystal [18], as the result of the preferred equatorial position of AcO–C(8), and *b*) xeniolides **19–21** exist in two equilibrium conformations in solution. Thus, the ^{1}H-NMR spectra of coraxeniolide B (**19**) demonstrated sizable presence of a minor conformer (1:4) that had escaped previous attention [17] [19]. Both conformers **19a** and **19b** (*Scheme 5*) could be fully characterized using differential spin decoupling [9], COSY [10], HMQC [11], and NOE; the prevailing conformer **19a** turned out to have Me(20) *trans* to both H–C(3) and the exocyclic methylidene group. The $\Delta\delta$(H), but not the $\Delta\delta$(C), were less marked than for typical xenicanes (**1**, **3**, **10**, and **11**, *Sect. 2.2*). Variable-temperature NMR spectra in $(CD_3)_2SO$

Scheme 5[2])



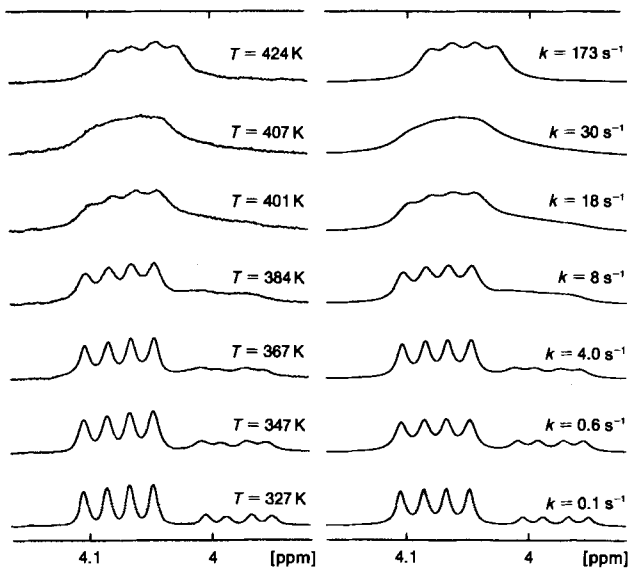


Fig. 3. *Experimental* (in $(CD_3)_2SO$; left) *and DNMR5-calculated* (right) *^{1}H-NMR line shape for the H_β–C(18) signal of conformers* **19a** *and* **19b** *in equilibrium*

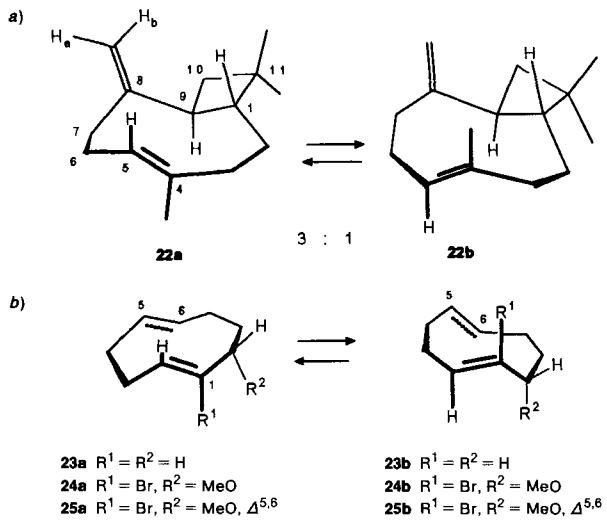
were correctly simulated by the DNMR5 program (*Fig. 3*), allowing the calculation of the conformational barriers. These turned out to be much the same as for xenicanes (*Table 2*), pointing to similar transannular repulsive interactions in the transition state for nine-membered-ring flipping. Similar results were obtained for **20** and **21**, showing that the side chain at C(10) has minor importance.

All the xeniolides examined here proved to resist to (6*E*)→(6*Z*) isomerization. *E.g.*, **19**, heated at reflux in $(CD_3)_2SO$ for 1 h, failed to give the (*Z*)-isomer in HPLC (UV)-detectable amount. The strikingly facile (6*E*)→(6*Z*) isomerization of xenicanes may tentatively be explained by a homoallylic stabilization of xenicane radical intermediates generated on rotation of the C(6)=C(7) bond. In accordance, xeniolides **18**–**21**, lacking this possibility, resist (*E*)→(*Z*) isomerization. Photoisomerization of 4-hydroxydictyolactone (**3**) to the corresponding crenulatane [20] may be explained accordingly.

2.9. *Caryophyllene.* It was reported from dynamic ^{13}C-NMR experiments that caryophyllene (**22**) exists as two equilibrating conformers in a 3:1 population ratio. This conclusion was confirmed here, and the attribution of the major conformer to **22a** was unequivocally secured by low-temperature NOE experiments (*Scheme 6a*). We also studied the mechanism of these processes by carrying out MM and DNMR5 calculations, suggesting that the unusually low kinetic barrier for conformational inversion of caryophyllene [5a] (*Table 2*) reflects a transition state that is unusually devoid of transannular interactions between H–C(5) and H–C(9). Accordingly, caryophyllene turns out to be an unsuitable model for xeniaphyllanes, which warrant direct investigation by dynamic NMR. The antheliolides offer this possibility[10]).

[10]) *Smith et al.* [4c] in their structural revision of antheliolide A (see *Footnote 3*) concluded that this xeniaphyllane has in the crystal a markedly different nine-membered-ring conformation than caryophyllene in solution [5a].

Scheme 6



3. Conclusions. – We have shown here that typical xenicanes (**1** and **3**) undergo slow ring inversion between the predominant *trans*-conformer (Me(20) *trans* to H–C(3)), such as **1a**, and the minor *cis*-conformer (Me(20) *cis* to H–C(3)), such as **1b**. The formation of the *cis*-conformer is inhibited for corresponding compounds with cleaved heterocyclic ring, *e.g.* **7**. The H–C(4)–C(5)–H's torsional strain in *cis*-conformers is the main reason for this inhibition, suggesting to place a keto group at C(4) to control molecular motion. According to expectation, this leads to a 1:3 equilibrium of *cis*- and *trans*-conformers in the case of **10**–**12**, allowing also the direct structural investigation of the elusive *cis*-conformers.

These observations suggest that the change from (6*E*)- to (6*Z*)-configuration in xenicane-type compounds involves such a dramatic relief of strain that isomerization should occur under relatively mild conditions. This is the case (formation of **9** and **13**–**17**), while xeniolides **18**–**21** – though behaving conformationally like the xenicanes with equally high kinetic barriers – are resistant to isomerization. This may be due to the absence of homoallylic stabilization of free-radical species arising from rotation around the C(6)=C(7) bond of the xeniolides. Kinetic barriers are too high, however, to account for the presence of **9** in nature in sizable amounts (1/7 of the major xenicane **7**). A photochemical (6*E*)→(6*Z*) conversion is also unlikely to occur in nature, notwithstanding the large exposure of the alga at low tide to tropical solar irradiation. In fact, formation of either crenulatanes (from **3** [20]) or 6,7-epoxides (from **1**, unpublished) was observed. Thus, it is likely that **5** and **8** derive from epoxidation of **3** and **7**, respectively, in the alga at low tide under the strong solar irradiation of the tropics.

The data in *Table 2* add to the scanty list of kinetic data available for conformational motions in (*E*)-cyclononene-type compounds, which only comprise caryophyllene [5a] (**22**), (*E*)-cyclononene [5b] (**23**), and its derivatives **24**–**25**[11]) (*Scheme 6b*). *Table 2* shows

[11]) We evaluated the kinetic barriers for conformational inversion of both **24** and **25** from their published ^{1}H-NMR data [21].

that the kinetic energy barrier decreases in the order **25** > xenicanes ≈ xeniolides > **24** ≈ **23** > **22**, confirmed by MM simulations (*Table 3*).

Conflicting results in the literature now fit into the scheme presented here, thus allowing a more thorough understanding of thermal motions in (*E*)-cyclononenes which is a prerequisite for the study of recognition phenomena with these systems.

We thank Dr. *M. D'Ambrosio* for a generous gift of raw xeniolides **19**–**21**, Mr. *M. Rossi* and Mr. *A. Sterni* for skilled technical assistance, and *MURST*(Progetti 40%) and *CNR*, Roma, for financial support.

Experimental Part

1. *General.* Evaporations were carried out at reduced pressure. Yields are given for natural products rel. to dry seaweed after extraction and for semisynthetic compounds rel. to reacted substrates. Xeniolides **19**–**21** [17] were freed from accompanying analogues by reversed-phase HPLC. Caryophyllene from *Fluka* was used as such. Flash chromatography (FC): *Merck* silica gel *Si-60* 15–25 μm. HPLC: *Merck LiChrosorb Si60* and *LiChrosorb CN* (7 μm) columns. NMR: *Varian XL-300* (^{1}H at 299.94 MHz, ^{13}C at 75.43 MHz); δ in ppm rel. to internal Me_4Si (= 0 ppm) and J in Hz (derived from differential spin decoupling [9]); $CDCl_3$ solns. at 20°, unless otherwise stated; $(CD_3)_2SO$ solns. for variable-temp. experiments; calibration of the ^{1}H-NMR probe for high-temp. measurements at ±1°; COSY 120 experiments [10] for all compounds; ^{13}C,^{1}H NMR inverse-detection shift-correlation experiments [11] for **1**, **10**, **11**, and **19**. Differential NOE data: 5 s pre-irradiation (1D-NOE); indication of δ (irradiated H)→δ (observed H's) (% NOE); 2D-NOE with mixing time 1 s, saturation-transfer effects were obtained with the same pulse sequence as used for 1D-NOE experiments. EI-MS (*m*/*z* (%)): *Kratos MS80*, with home-built computerized acquisition system. Calculations: for ΔH in *Table 3*, default dielectric constant $\varepsilon = 1.5$; for NMR line-shape simulation (*Figs. 1* and *3*), computer program DNMR5 [14]; for molecular mechanics (MM), 'PCMODEL 4.0' computer program based on the MMX force field, by *Serena Software*, Bloomington, Indiana.

2. *Collection and Isolation.* The seaweed *Dictyota* sp., probably *Dictyota ciliolata* [6] (Phaeophyta, Dictyotales, Dictyotaceae), collected at low tide in September 1991 at the Pointe de Senti à Joal, 100 km south of Dakar, was immediately soaked in MeOH and homogenized. The solvent was evaporated and the residue extracted with first hexane and then AcOEt. The oily residue (1.2 g) from the hexane extract was subjected to FC (hexane/AcOEt gradient, 40-ml fractions). *Fractions 17–26* were combined and evaporated, and the residue was subjected to *CN*-HPLC (hexane/i-PrOH 98:2): *dictyolactone* (**1**; t_R 12.0 min; 8 mg, 0.04%). Similarly, *Fr. 27–32* gave *isodictyohemiacetal* (**2**; hexane/i-PrOH 97:3, t_R 5.5 min; 3.5 mg, 0.013%) and *'hydroxyacetyldictyolal'* (**7**; hexane/i-PrOH 97:3, t_R 10.2 min; 7 mg, 0.035%). *Fr. 33–36*, on *CN*-HPLC (hexane/i-PrOH 95:5), gave eluates at t_R 7.2 and 11.5 min. The t_R 7.2 min eluate was evaporated and subjected to HPLC (hexane/i-PrOH 97:3): **6** (t_R 11.8 min; 6 mg, 0.03%). The t_R 11.5 min eluate was evaporated and subjected to HPLC (hexane/i-PrOH 95:5): **9** (t_R 10.0 min; 2 mg, 0.01%). *Fr. 37–44* were evaporated, and the residue was subject to *CN*-HPLC (hexane/i-PrOH 95:5), giving eluates at t_R 13.8 and 16.0 min. The latter eluate was evaporated: *4-hydroxydictyolactone* (**3**; 15 mg, 0.07%). The t_R 13.8 min eluate was evaporated and subjected to HPLC (hexane/i-PrOH 95.5): **8** (t_R 18.0 min; 4 mg, 0.02%). *Fr. 45–50*, on HPLC (hexane/i-PrOH 9:1), gave **5** (t_R 15.5 min; 3 mg, 0.015%).

3. *Dictyolactone* (= *(3aS,4S,7E,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-7-methyl-1H-cyclonona[c]furan-1-one*; **1**). $[\alpha]_D^{25} = -122$ ($c = 0.15$, CCl_4). MS: 302 (9, M^+), 287 (3, $[M - Me]^+$), 259 (4, $[M - MeCO]^+$), 233 (11, $[M - C_5H_9]^+$), 222 (11), 137 (40), 82 (96), 41 (100).

Conformer **1a**: NOE: 5.36→1.67 (7%), 1.98 (6%), 2.90 (4%); 1.71→2.70, 2.23; 0.93→4.52. ^{13}C-NMR: 136.48 (*s*, C(1)); 43.93 (*d*, C(2)); 47.38 (*d*, C(3)); 30.55 (*t*, C(4)); 40.19 (*t*, C(5)); 135.34 (*s*, C(6)); 122.96 (*d*, C(7)); 28.78 (*t*, C(8)); 140.35 (*d*, C(9)); 32.65 (*d*, C(10)); 37.41 (*t*, C(11)); 25.94 (*t*, C(12)); 124.13 (*d*, C(13)); 131.66 (*s*, C(14)); 25.64 (*q*, C(15)); 17.36 (*q*, C(16)); 17.58 (*q*, C(17)); 68.22 (*t*, C(18)); 173.27 (*s*, C(19)); 17.68 (*q*, C(20)).

4. *Isodictyohemiacetal* (= *(1S,10S,10aS,3aE,6E)-10-[(R)-1,5-Dimethylhex-4-enyl]-3,5,8,9,10,10a-hexahydro-7-methyl-1H-cyclonona[c]furan-1-ol*; **2**). $[\alpha]_D^{25} = -45.0$ ($c = 0.25$, CCl_4). ^{13}C-NMR: 145.48 (*s*, C(1)); 45.84 (*d*, C(2)); 54.00 (*d*, C(3)); 40.63 (*t*, C(4)); 45.84 (*t*, C(5)); 134.73 (*s*, C(6)); 125.90 (*d*, C(7)); 29.92 (*t*, C(8)); 120.23 (*d*, C(9)); 31.70 (*d*, C(10)); 37.79 (*t*, C(11)); 26.23 (*t*, C(12)); 124.68 (*d*, C(13)); 131.43 (*s*, C(14)); 25.70 (*q*, C(15)); 17.68 (*q*, C(16)); 17.68 (*q*, C(17)); 100.73 (*d*, C(18)); 71.46 (*t*, C(19)); 17.14 (*q*, C(20)). MS: 304 (6, M^+), 286 (3, $M - H_2O]^+$), 215 (9), 203 (16), 147 (28), 133 (27), 119 (27), 105 (33), 91 (30), 69 (98), 41 (100).

5. *4-Hydroxydictyolactone* (= *(3aS,4S,5R,7E,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-5-hydroxy-7-methyl-1H-cyclonona[c]furan-1-one*; **3**). $[\alpha]_D^{25} = -247$ ($c = 0.17$, CCl_4). MS: 318 (3, M^+), 303 (2,

$[M - Me]^+$), 300 (2, $[M - H_2O]^+$), 287 (10), 249 (16, $[M - C_5H_9]^+$), 165 (29), 136 (21), 109 (31), 81 (41), 69 (97), 41 (100).

Conformer **3a**: ^{1}H-NMR: 3.39 (br. *d*, *J* = 7.8, H–C(2)); 2.02 (br. *s*, H–C(3)); 4.28 (*m*, H–C(4)); 2.32 (*dd*, *J* = 12.8, 4.3, H_β–C(5)); 2.17 (*dd*, *J* = 12.8, 2.0, H_α–C(5)); 5.30 (br. *dd*, *J* = 11.4, 4.2, H–C(7)); 3.19 (*ddt*, *J* = 17.6, 11.4, 2.3, H_α–C(8)); 2.94 (*ddd*, *J* = 17.6, 7.5, 4.2, H_β–C(8)); 6.92 (*dt*, *J* = 7.5, 2.3, H–C(9)); 1.61 (*m*, H–C(10)); 1.17–1.22 (*m*, 2 H–C(11)); 1.92 (*m*, 2 H–C(12)); 5.02 (*sept. t*, *J* = 7.2, 1.5, H–C(13)); 1.66 (br. *s*, 3 H–C(15)); 1.56 (br. *s*, 3 H–C(16)); 1.06 (*d*, *J* = 6.7, 3 H–C(17)); 4.44 (*dd*, *J* = 9.5, 1.2, H_β–C(18)); 4.09 (*dd*, *J* = 9.5, 7.8, H_α–C(18)); 1.89 (*d*, *J* = 1.3, 3 H–C(20)). NOE: 5.30→2.02; 1.89→3.39. ^{13}C-NMR: 136.08 (*s*, C(1)); 35.74 (*d*, C(2)); 50.97 (*d*, C(3)); 72.71 (*d*, C(4)); 49.05 (*t*, C(5)); 135.36 (*s*, C(6)); 125.28 (*d*, C(7)); 29.42 (*t*, C(8)); 139.39 (*d*, C(9)); 32.25 (*d*, C(10)); 37.86 (*t*, C(11)); 25.87 (*t*, C(12)); 123.90 (*d*, C(13)); 131.87 (*s*, C(14)); 25.64 (*q*, C(15)); 17.69 (*q*, C(16)); 18.13 (*q*, C(17)); 68.73 (*t*, C(18)); 173.39 (*s*, C(19)); 20.00 (*q*, C(20)).

Conformer **3b**: ^{1}H-NMR: 3.84 (*m*, H–C(2)); 1.80 (br. *s*, H–C(3)); 4.28 (*m*, H–C(4)); 2.24 (*m*, H_β–C(5)); 2.75 (*m*, H_α–C(5)); 5.60 (*m*, H–C(7)); 3.23 (*m*, H_α–C(8)); 2.94 (*m*, H_β–C(8)); 6.87 (*dt*, *J* = 7.5, 2.4, H–C(9)); 1.02 (*d*, *J* = 6.7, 3 H–C(17)); 4.38 (*dd*, *J* = 9.7, 1.3, H_β–C(18)); 4.19 (*dd*, *J* = 9.7, 8.3, H_α–C(18)); 1.53 (*d*, *J* = 1.3, 3 H–C(20)). ^{13}C-NMR: 50.23 (*d*, C(3)); 67.49 (*d*, C(4)); 46.21 (*t*, C(5)); 130.80 (*d*, C(7)); 29.42 (*t*, C(8)); 140.24 (*d*, C(9)); 25.87 (*t*, C(12)); 123.68 (*d*, C(13)); 131.87 (*s*, C(14)); 25.64 (*q*, C(15)); 17.69 (*q*, C(16)); 18.13 (*q*, C(17)); 68.73 (*t*, C(18)); 172.78 (*s*, C(19)); 25.51 (*q*, C(20)); signals for C(1), C(2), C(6), C(10), C(11) not detected.

6. *4-Hydroxydictyolactone (6*R*,7*R*)-Epoxide (= (3a*S*,4*S*,5*R*,6*R*,7*R*,10*E*)-4-[(*R*)-1,5-Dimethylhex-4-enyl]-6,7-epoxy-3,3a,4,5,6,7,8,9-octahydro-5-hydroxy-7-methyl-1*H*-cyclonona[*c*]furan-1-one*; **5**). $[\alpha]_D^{25} = -34$ (*c* = 0.16, CCl_4). ^{1}H-NMR: 3.64 (br. *d*, *J* = 7.4, H–C(2)); 1.96 (br. *s*, H–C(3)); 4.26 (br. *dd*, *J* = 4.5, 2.6, H–C(4)); 2.39 (*dd*, 14.1, 2.6, H_β–C(5)); 1.22 (*dd*, *J* = 14.1, 4.5, H_α–C(5)); 3.07 (*dd*, *J* = 11.0, 2.5, H–C(7)); 2.29 (*ddt*, *J* = 17.6, 11.0, 2.1, H_α–C(8)); 2.98 (*ddd*, *J* = 17.6, 8.2, 2.5, H_β–C(8)); 6.90 (*dt*, *J* = 8.2, 2.1, H–C(9)); 1.75 (*m*, H–C(10)); 1.15 (*m*, 2 H–C(11)); 1.90 (*m*, 2 H–C(12)); 4.99 (*sept. t*, *J* = 7.1, 1.3, H–C(13)); 1.65 (*d*, *J* = 1.3, 3 H–C(15)); 1.55 (*d*, *J* = 1.3, 3 H–C(16)); 1.09 (*d*, *J* = 6.6, 3 H–C(17)); 4.52 (*dd*, *J* = 9.7, 1.3, H_β–C(18)); 4,16 (*dd*, *J* = 9.7, 7.4, H_α–C(18)); 1.57 (*s*, 3 H–C(20)). NOE: 4.99→1.65 (7%); 4.52→1.09; 3.64→1.57 (9%); 3.07→1.96 (15%); 1.09→4.52, 4.26, 3.07. ^{13}C-NMR: 136.52 (*s*, C(1)); 36.57 (*d*, C(2)); 50.38 (*d*, C(3)); 68.12 (*d*, C(4)); 48.13 (*t*, C(5)); 59.46 (*s*, C(6)); 62.36 (*d*, C(7)); 27.92 (*t*, C(8)); 134.47 (*d*, C(9)); 32.26 (*d*, C(10)); 37.05 (*t*, C(11)); 25.79 (*t*, C(12)); 123.62 (*d*, C(13)); 132.12 (*s*, C(14)); 25.63 (*q*, C(15)); 17.72 (*q*, C(16)); 17.97 (*q*, C(17)); 68.40 (*t*, C(18)); 173.29 (*s*, C(19)); 20.18 (*q*, C(20)). MS: 334 (2, M^+), 319 (1, $[M - Me]^+$), 316 (2, $[M - H_2O]^+$), 265 (1, $[M - C_5H_9]^+$), 109 (59), 69 (100), 41 (100).

7. *(18*S*,19*S*)-19-Deoxo-4-hydroxy-18,19-dimethoxydictyolactone (= (1*S*,3*S*,3a*S*,4*S*,5*R*,7*R*,10*E*)-4-[(*R*)-1,5-Dimethylhex-4-onyl]-3,3a,4,5,6,9-hexahydro-1,3-dimethoxy-7-methyl-1*H*-cyclonona[*c*]furan-5-ol*; **6**). $[\alpha]_D^{25} = -96$ (*c* = 0.28, CCl_4). ^{1}H-NMR: 3.02 (br. *s*, H–C(2)); 1.96 (br. *s*, H–C(3)); 4.26 (br. *dd*, *J* = 4.2, 2.3, H–C(4)); 2.31 (*dd*, *J* = 13.1, 2.3, H_α–C(5)); 2.13 (*dd*, *J* = 13.1, 4.2, H_β–C(5)); 5.32 (br. *dd*, *J* = 11.4, 3.9, H–C(7)); 3.16 (*ddt*, *J* = 16.1, 11.4, 1.9, H_α–C(8)); 2.72 (*ddd*, *J* = 16.1, 7.8, 3.9, H_β–C(8)); 5.87 (*dq*, *J* = 7.8, 1.9, H–C(9)); 1.60 (*m*, H–C(10)); 1.20 (*m*, 2 H–C(11)); 1.90 (*m*, 2 H–C(12)); 5.06 (*sept. t*, *J* = 7.2, 1.4, H–C(13)); 1.67 (*d*, *J* = 1.4, 3 H–C(15)); 1.58 (br. *s*, 3 H–C(16)); 1.07 (*d*, *J* = 6.7, 3 H–C(17)); 5.29 (br. *s*, H–C(19)); 5.09 (*s*, H–C(18)); 1.88 (br. *s*, 3 H–C(20)); 3.47 (*s*, MeO–C(19)); 3.33 (*s*, MeO–C(18)); 1.32 (*d*, *J* = 4.2, OH). NOE: 5.32→1.96; 5.29→3.47 and 5.87; 5.08→3.33; 3.02→1.88; 2.72→5.87. ^{13}C-NMR: 146.04 (*s*, C(1)); 46.23 (*d*, C(2)); 49.20 (*d*, C(3)); 73.07 (*d*, C(4)); 49.00 (*t*, C(5)); 134.79 (*s*, C(6)); 125.34 (*d*, C(7)); 29.04 (*t*, C(8)); 127.34 (*d*, C(9)); 31.18 (*d*, C(10)); 38.38 (*t*, C(11)); 26.03 (*t*, C(12)); 124.47 (*d*, C(13)); 131.51 (*s*, C(14)); 25.71 (*q*, C(15)); 17.78 (*q*, C(16)); 18.68 (*q*, C(17)); 106.63 (*d*, C(18)); 107.08 (*d*, C(19)); 20.01 (*q*, C(20)); 54.61, 55.52 (2*q*, 2 MeO). MS: 364 (1, M^+), 332 (4, $[M - MeOH]^+$), 314 (2, $[M - H_2O - MeOH]^+$), 300 (12), 285 (3, $[M - C_5H_9]^+$), 271 (12), 69 (95), 41 (100).

8. *18-Acetoxy-4-hydroxydictyo-19-al (= (7*R*,8*S*,9*S*,1*E*,4*E*)-9-(Acetoxymethyl)-8-[(*R*)-1,5-dimethylhex-4-enyl]-7-hydroxy-5-methylcyclonona-1,4-diene-1-carbaldehyde*; **7**). $[\alpha]_D^{25} = -190.0$ (*c* = 0.29, CCl_4). MS: 362 (1, M^+), 344 (1.5, $[M - H_2O]^+$), 302 (4, $[M - AcOH]^+$), 284 (5), 109 (33), 81 (66), 69 (100), 43 (98).

9. *18-Acetoxy-4-hydroxydictyo-19-al (6*R*,7*R*)-Epoxide (= (4*R*,5*R*,7*R*,8*S*,9*S*,1*E*)-9-(Acetoxymethyl)-8-[(*R*)-1,5-dimethylhex-4-enyl]-4,5-epoxy-7-hydroxy-5-methylcyclonon-1-ene-1-carbaldehyde*; **8**). $[\alpha]_D^{25} = -98$ (*c* = 0.16, CCl_4). MS: 378 (1, M^+), 360 (1, $[M - H_2O]^+$), 318 (1, $[M - AcOH]^+$), 300 (3), 109 (47), 69 (81), 43 (100).

10. *(6*Z*)-18-Acetoxy-4-hydroxydictyo-19-al (= (7*R*,8*S*,9*S*,1*E*,4*Z*)-9-(Acetoxymethyl)-8-[(*R*)-1,5-dimethylhex-4-enyl]-7-hydroxy-5-methylcyclonona-1,4-diene-1-carbaldehyde*; **9**). $[\alpha]_D^{25} = -26.0$ (*c* = 0.17, CCl_4). ^{1}H-

NMR: 3.50 (br. *m*, H–C(2)); 2.00 (*m*, H–C(3)); 4.11 (br. *m*, H–C(4)); 2.96 (*dd*, J = 13.4, 9.4, H_β–C(5)); 2.10 (*dd*, J = 13.4, 6.4, H_α–C(5)); 5.27 (*dd*, J = 10.1, 6.9, H–C(7)); 3.50 (br. *m*, H_β–C(8)); 2.73 (*dt*, J = 13.8, 6.9, H_α–C(8)); 6.54 (*dd*, J = 9.2, 6.9, H–C(9)); 1.80 (*m*, H–C(10)); 1.20–1.30 (*m*, 2 H–C(11)); 1.90 (*m*, 2 H–C(12)); 5.00 (br. *t*, J = 7.2, H–C(13)); 1.65 (br. *s*, 3 H–C(15)); 1.55 (br. *s*, 3 H–C(16)); 1.02 (*d*, J = 7.0, 3 H–C(17)); 4.67 (*m*, 2 H–C(18)); 9.31 (br. *s*, H–C(19)); 1.69 (br. *s*, 3 H–C(20)); 2.00 (br. *s*, Ac). NOE: 1.69→5.27. MS: 362 (4, $M^{+\cdot}$), 344 (2, $[M - H_2O]^{+\cdot}$), 302 (5, $[M - AcOH]^{+\cdot}$), 293 (2, $[M - C_5H_9]^{+\cdot}$), 284 (8), 109 (45), 69 (100), 43 (84).

11. *Pyridinium-Chlorochromate (PCC) Oxidations.* To a soln. of **3** (5 mg, 0.016 mmol) in dry pyridine (0.8 ml) were added 3 mol-equiv. of PCC. The mixture was stirred for 2 h. Then H_2O (1 ml) and hexane (2 ml) were added, and the mixture was stirred and percolated through a phase-separation filter. The org. phase was evaporated and the residue subjected to *CN*-HPLC (hexane/i-PrOH 95:5): **10** (t_R 12 min; 4 mg, 85%) and **3** (t_R 21.8 min).

Similar treatment of **6** (4 mg, 0.011 mmol), followed by *CN*-HPLC (hexane/i-PrOH 97.5:2.5) gave **11** (t_R 9.6 min; 3 mg, 85%) besides traces of **6** (t_R 11.5 min).

Similarly **7** (4 mg, 0.011 mmol) gave, after *CN*-HPLC (hexane/i-PrOH 98:2), **12** (t_R 13.5 min; 2 mg, 50%).

4-Oxodictyolactone (= *(3aS,4S,7E,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-7-methyl-1H-cyclonona[c]furan-1,5-dione*; **10**): $[\alpha]_D^{25} = -370$ (c = 0.29, CCl_4). MS: 316 (11, $M^{+\cdot}$), 301 (2, $[M - Me]^+$), 285 (20), 260 (9), 69 (82), 41 (100).

Conformer **10a**: ^{1}H-NMR: 2.43 (*ddt*, J = 8.8, 2.9, 1.6, H–C(2)); 3.00 (*dd*, J = 11.0, 1.6, H–C(3)); 3.22 (*dd*, J = 10.6, 0.9, H_β–C(5)); 2.99 (*d*, J = 10.6, H_α–C(5)); 5.56 (br. *dd*, J = 10.6, 5.9, H–C(7)); 3.14 (*m*, H_β–C(8)); 3.21 (*m*, H_α–C(8)); 6.91 (*dt*, J = 6.7, 2.9, H–C(9)); 1.94 (*m*, H–C(10)); 0.95–1.25 (*m*, 2 H–C(11)); 1.96 (*m*, 2 H–C(12)); 5.06 (br. *t*, J = 7.0, H–C(13)); 1.67 (br. *s*, 3 H–C(15)); 1.58 (br. *s*, 3 H–C(16)); 0.84 (*d*, J = 6.7, 3 H–C(17)); 4.45 (*dd*, J = 10.2, 1.6, H_β–C(18)); 4.13 (*dd*, J = 10.2, 8.8, H_α–C(18)); 1.61 (*d*, J = 1.3, 3 H–C(20)). NOE: 5.56→3.00, 3.22; 1.94→4.13. ^{13}C-NMR: 133.94 (*s*, C(1)); 36.71 (*d*, C(2)); 60.44 (*d*, C(3)); 209.42 (*s*, C(4)); 58.82 (*t*, C(5)); 131.07 (*s*, C(6)); 125.74 (*d*, C(7)); 29.21 (*t*, C(8)); 138.58 (*d*, C(9)); 31.34 (*d*, C(10)); 33.42 (*t*, C(11)); 24.76 (*t*, C(12)); 123.36 (*d*, C(13)); 132.43 (*s*, C(14)); 25.70 (*q*, C(15)); 17.65 (*q*, C(16)); 18.28 (*q*, C(17)); 66.45 (*t*, C(18)); 171.91 (*s*, C(19)); 16.91 (*q*, C(20)).

Conformer **10b**: ^{1}H-NMR: 3.26 (br. *ddd*, J = 8.0, 3.7, 2.4, H–C(2)); 2.38 (*dd*, J = 8.8, 3.7, H–C(3)); 2.75 (*dd*, J = 16.1, 0.5, H_β–C(5)); 3.45 (*d*, J = 16.1, H_α–C(5)); 5.47 (*dd quint.*, J = 11.0, 6.2, 1.6, H–C(7)); 3.04 (*m*, H_β–C(8)); 3.33 (*m*, H_α–C(8)); 6.85 (*dt*, J = 5.8, 2.4, H–C(9)); 1.78 (*m*, H–C(10)); 0.95–1.25 (*m*, 2 H–C(11)); 1.96 (*m*, 2 H–C(12)); 5.06 (*sept. t*, J = 7.0, 1.5, H–C(13)); 1.67 (br. *s*, 3 H–C(15)); 1.58 (br. *s*, 3 H–C(16)); 0.88 (*d*, J = 6.7, 3 H–C(17)); 4.44 (*dd*, J = 10.2, 1.6, H_β–C(18)); 4.15 (*dd*, J = 10.2, 8.0, H_α–C(18)); 1.81 (*d*, J = 1.3, 3 H–C(20)). ^{13}C-NMR: 132.54 (*s*, C(1)); 41.73 (*d*, C(2)); 58.85 (*d*, C(3)); 210.46 (*s*, C(4)); 53.91 (*t*, C(5)); 131.72 (*s*, C(6)); 128.85 (*d*, C(7)); 29.26 (*t*, C(8)); 140.43 (*d*, C(9)); 32.38 (*d*, C(10)); 34.97 (*t*, C(11)); 25.13 (*t*, C(12)); 123.26 (*d*, C(13)); 132.43 (*s*, C(14)); 25.70 (*q*, C(15)); 17.65 (*q*, C(16)); 17.70 (*q*, C(17)); 66.91 (*t*, C(18)); 172.15 (*s*, C(19)); 20.35 (*q*, C(20)).

(18S)-18-Methoxy-4-oxodictyolactone (= *(3S,3aS,4S,7E,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-3-methoxy-7-methyl-1H-cyclonona[c]furan-1,5-dione*; **11**): $[\alpha]_D^{25} = -122$ (c = 0.39, CCl_4). MS: 346 (3, $M^{+\cdot}$), 314 (11, $[M - MeOH]^{+\cdot}$), 286 (8), 271 (14), 69 (88), 41 (100).

Conformer **11a**: ^{1}H-NMR: 2.22 (*td*, J = 2.6, 1.9, H–C(2)); 2.98 (*dd*, J = 11.3, 1.9, H–C(3)); 3.19 (*dd*, J = 11.0, 0.8, H_β–C(5)); 3.00 (*d*, J = 11.0, H_α–C(5)); 5.57 (*ddq*, J = 10.7, 5.0, 1.3, H–C(7)); 3.12 (*ddd*, J = 17.7, 7.1, 5.0, H_β–C(8)); 3.25 (*ddt*, J = 17.7, 10.7, 2.6, H_α–C(8)); 6.93 (*dt*, J = 7.1, 2.6, H–C(9)); 1.99 (br. *d sext.*, J = 11.3, 6.5, H–C(10)); 0.95–1.25 (*m*, 2 H–C(11)); 1.97 (*q*, J = 6.5, 2 H–C(12)); 5.03 (br. *t*, J = 7.0, H–C(13)); 1.68 (br. *s*, 3 H–C(15)); 1.60 (br. *s*, 3 H–C(16)); 0.84 (*d*, J = 6.7, 3 H–C(17)); 5.35 (br. *s*, H–C(18)); 1.64 (*d*, J = 1.3, 3 H–C(20)); 3.41 (*s*, MeO–C(18)). NOE: 5.57→2.98, 3.19; 1.64→2.22, 3.00, 3.25; 2.22→5.35, 1.64. ^{13}C-NMR: 132.60 (*s*, C(1)); 44.71 (*d*, C(2)); 59.04 (*d*, C(3)); 208.84 (*s*, C(4)); 58.61 (*t*, C(5)); 131.10 (*s*, C(6)); 125.87 (*d*, C(7)); 29.32 (*t*, C(8)); 139.87 (*d*, C(9)); 31.48 (*d*, C(10)); 33.60 (*t*, C(11)); 24.62 (*t*, C(12)); 123.35 (*d*, C(13)); 132.60 (*s*, C(14)); 25.74 (*q*, C(15)); 17.65 (*q*, C(16)); 18.62 (*q*, C(17)); 103.65 (*d*, C(18)); 56.47 (*q*, *Me*O–C(18)); 170.81 (*s*, C(19)); 17.04 (*q*, C(20)).

Conformer **11b**: ^{1}H-NMR: 3.08 (*dd*, J = 3.9, 1.9, H–C(2)); 2.34 (*dd*, J = 8.9, 3.9, H–C(3)); 2.73 (*d*, J = 16.2, H_β–C(5)); 3.47 (*d*, J = 16.2, H_α–C(5)); 5.48 (*ddq*, J = 11.1, 5.9, 1.6, H–C(7)); 3.05 (*m*, H_β–C(8)); 3.32 (*m*, H_α–C(8)); 6.90 (*dt*, J = 5.6, 1.9, H–C(9)); 1.85 (*d sext.*, J = 8.9, 6.5, H–C(10)); 0.95–1.25 (*m*, 2 H–C(11)); 1.97 (*m*, 2 H–C(12)); 5.03 (br. *t*, J = 7.0, H–C(13)); 1.68 (br. *s*, 3 H–C(15)); 1.60 (br. *s*, 3 H–C(16)); 0.90 (*d*, J = 6.7, 3 H–C(17)); 5.35 (br. *s*, H–C(18)); 1.80 (*d*, J = 1.6, 3 H–C(20)); 3.44 (*s*, MeO–C(18)). NOE: 5.48→3.08; 1.80→2.73, 2.34. ^{13}C-NMR: 132.60 (*s*, C(1)); 49.01 (*d*, C(2)); 57.94 (*d*, C(3)); 209.67 (*s*, C(4)); 53.78 (*t*, C(5)); 131.20 (*s*, C(6)); 129.03 (*d*, C(7)); 29.32 (*t*, C(8)); 141.56 (*d*, C(9)); 32.45 (*d*, C(10)); 35.19 (*t*, C(11)); 25.00 (*t*, C(12)); 123.20 (*d*, C(13)); 132.86 (*s*, C(14)); 25.74 (*q*, C(15)); 17.65 (*q*, C(16)); 17.86 (*q*, C(17)); 103.51 (*d*, C(18)); 56.43 (*q*, *Me*O–C(18)); 171.04 (*s*, C(19)); 20.21 (*q*, C(20)).

18-Acetoxy-4-oxodictyo-19-al (= *(8S,9S,1E,4E)-9-(Acetoxymethyl)-8-[(R)-1,5-dimethylhex-4-enyl]-5-methyl-7-oxocyclonona-1,4-diene-1-carbaldehyde*; **12**): $[\alpha]_D^{25} = -303$ ($c = 0.15$, CCl_4). MS: 360 (1, M^+), 318 (2, $[M - CH_2CO]^+$), 300 (5, $[M - AcOH]^+$), 149 (69), 69 (79), 43 (100).

Conformer **12a**: ^{1}H-NMR: 2.44 (*ddd*, $J = 10.2, 6.8, 2.9$, H–C(2)); 2.89 (*d*, $J = 9.5$, H–C(3)); 3.19 (*d*, $J = 10.3$, H_β–C(5)); 2.97 (*d*, $J = 10.3$, H_α–C(5)); 5.45 (br. *d*, $J = 10.3$, H–C(7)); 3.19 (*m*, H_β–C(8)); 3.29 (*m*, H_α–C(8)); 6.71 (*dt*, $J = 8.1, 2.9$, H–C(9)); 1.99 (*m*, H–C(10)); 0.95–1.25 (*m*, 2 H–C(11)); 1.90 (*m*, 2 H–C(12)); 5.06 (br. *t*, $J = 7.0$, H–C(13)); 1.67 (br. *s*, 3 H–C(15)); 1.59 (br. *s*, 3 H–C(16)); 0.88 (*d*, $J = 6.8$, 3 H–C(17)); 4.78 (*t*, $J = 10.2$, H_β–C(18)); 4.45 (*dd*, $J = 10.2, 6.8$, H_α–C(18)); 1.67 (br. *s*, 3 H–C(20)); 1.92 (*s*, AcO). ^{13}C-NMR: 147.40 (*s*, C(1)); 37.92 (*d*, C(2)); 59.79 (*d*, C(3)); 207.98 (*s*, C(4)); 58.66 (*t*, C(5)); 129.52 (*s*, C(6)); 124.09 (*d*, C(7)); 29.34 (*t*, C(8)); 155.36 (*d*, C(9)); 31.01 (*d*, C(10)); 35.02 (*t*, C(11)); 24.99 (*t*, C(12)); 124.09 (*d*, C(13)); 129.02 (*s*, C(14)); 25.71 (*q*, C(15)); 17.71 (*q*, C(16)); 18.47 (*q*, C(17)); 61.56 (*t*, C(18)); 170.65 (*s*, MeCOO–C(18)); 20.91 (*q*, *Me*COO–C(18)); 195.03 (*d*, C(19)); 16.91 (*q*, C(20)).

Conformer **12b**: ^{1}H-NMR: 3.35 (*ddd*, $J = 9.0, 6.8, 3.8$, H–C(2)); 2.47 (*dd*, $J = 8.0, 3.8$, H–C(3)); 2.72 (*d*, $J = 14.5$, H_β–C(5)); 3.49 (*d*, $J = 14.5$, H_α–C(5)); 5.79 (br. *dd*, $J = 9.6, 7.4$, H–C(7)); 3.11 (*ddd*, $J = 19.4, 7.4, 2.6$, H_β–C(8)); 3.41 (*ddd*, $J = 19.4, 9.6, 7.0$, H_α–C(8)); 6.66 (*dd*, $J = 7.0, 2.6$, H–C(9)); 1.90 (*m*, H–C(10)); 0.95 (*d*, $J = 6.8$, 3 H–C(17)); 4.57 (*dd*, $J = 10.7, 9.0$, H_β–C(18)); 4.47 (*dd*, $J = 10.7, 6.8$, H_α–C(18)); 1.70 (br. *s*, 3 H–C(20)); 1.97 (*s*, AcO). ^{13}C-NMR: 42.36 (*d*, C(2)); 58.53 (*d*, C(3)); 54.73 (*t*, C(5)); 124.02 (*d*, C(7)); 29.34 (*t*, C(8)); 157.79 (*d*, C(9)); 31.59 (*d*, C(10)); 35.90 (*t*, C(11)); 25.24 (*t*, C(12)); 123.92 (*d*, C(13)); 25.71 (*q*, C(15)); 17.71 (*q*, C(16)); 17.84 (*q*, C(17)); 63.08 (*t*, C(18)); 170.80 (*s*, MeCOO–C(18)); 21.00 (*q*, *Me*COO–C(18)); 195.03 (*d*, C(19)); 20.12 (*q*, C(20)).

12. *Thermal Isomerizations of Xenicanes.* A soln. of **1** (3 mg, 0.01 mmol) in 0.55 ml of dry $(CD_3)_2SO$ was heated in the NMR probe. Above 120°, isomerization to **13** occurred. Kinetic analysis gave $t_{1/2}$ 39 min at 134°. Following complete isomerization, the mixture was percolated through a *Merck LiChrosorb Si60* microcolumn: pure **13**.

In a similiar procedure, isomerization of **3** only became detectable above 170°. Product **14** was isolated as described above for **13**.

The isomerizations **7** → **9**, **10** → **15**, **11** → **16**, and **12** → **17** were carried out similarly. Results: *Table 4*.

(6Z)-Dictyolactone (= *(3aS,4S,7Z,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-7-methyl-1H-cyclonona[c]furan-1-one*; **13**): $[\alpha]_D^{25} = +14$ ($c = 0.015$, CCl_4). ^{1}H-NMR: 3.44 (*ddt*, $J = 9.8, 5.9, 1.0$, H–C(2)); 1.65 (*m*, H–C(3)); 1.40 (*m*, 2 H–C(4)); 2.46 (br. *dd*, $J = 12.1, 10.5$, H_α–C(5)); 1.76 (*dd*, $J = 12.1, 5.1$, H_β–C(5)); 5.26 (*ddq*, $J = 8.8, 7.0, 1.5$, H–C(7)); 3.17 (*ddd*, $J = 13.0, 11.1, 8.8$, H_α–C(8)); 2.70 (*dt*, $J = 13.0, 7.0$, H_β–C(8)); 6.77 (*ddd*, $J = 11.1, 7.0, 1.5$, H–C(9)); 1.65 (*m*, H–C(10)); 1.15–1.25 (*m*, 2 H–C(11)); 1.98 (*m*, 2 H–C(12)); 5.05 (br. *t*, $J = 7.0$, H–C(13)); 1.68 (br. *s*, 3 H–C(15)); 1.59 (br. *s*, 3 H–C(16)); 0.91 (*d*, $J = 6.7$, 3 H–C(17)); 4.25 (*dd*, $J = 9.0, 1.0$, H_β–C(18)); 4.17 (*dd*, $J = 9.0, 5.9$, H_α–C(18)); 1.69 (br. *s*, 3 H–C(20)). ^{13}C-NMR: 44.89 (*d*, C(2)); 39.22 (*d*, C(3)); 25.96 (*t*, C(4)); 27.58 (*t*, C(5)); 116.98 (*d*, C(7)); 28.43 (*t*, C(8)); 138.16 (*d*, C(9)); 33.86 (*d*, C(10)); 36.09 (*t*, C(11)); 25.83 (*t*, C(12)); 124.05 (*d*, C(13)); 25.72 (*q*, C(15)); 17.72 (*q*, C(16)); 16.07 (*q*, C(17)); 70.16 (*t*, C(18)); 25.96 (*q*, C(20)). MS: 302 (8, M^+), 287 (8, $[M - Me]^+$), 259 (5, $[M - MeCO]^+$), 233 (4, $[M - C_5H_9]^+$), 221 (3), 137 (18), 81 (52), 69 (100), 41 (86).

(6Z)-Hydroxydictyolactone (= *(3aS,4S,5R,7Z,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-5-hydroxy-7-methyl-1H-cyclonona[c]furan-1-one*; **14**): $[\alpha]_D^{25} = -46$ ($c = 0.05$, CCl_4). ^{1}H-NMR (+40°, fast-exchange conditions): 3.62 (br. *m*, H–C(2)); 1.85 (*d*, $J = 2.5$, H–C(3)); 4.10 (br. *m*, H–C(4)); 2.97 (*dd*, $J = 13.3, 7.4$, H_β–C(5)); 2.05 (br. *m*, H_α–C(5)); 5.34 (br. *t*, $J = 7.6$, H–C(7)); 3.19 (br. *m*, H_α–C(8)); 2.72 (*dt*, $J = 14.1, 7.6$, H_β–C(8)); 6.79 (*ddd*, $J = 9.3, 7.6, 2.0$, H–C(9)); 1.68 (*m*, H–C(10)); 1.20–1.30 (*m*, 2 H–C(11)); 1.95 (*m*, 2 H–C(12)); 5.03 (br. *t*, $J = 7.2$, H–C(13)); 1.67 (br. *s*, 3 H–C(15)); 1.57 (br. *s*, 3 H–C(16)); 1.07 (*d*, $J = 6.9$, 3 H–C(17)); 4.35 (*dd*, $J = 9.5, 0.8$, H_β–C(18)); 4.21 (*dd*, $J = 9.5, 7.1$, H_α–C(18)); 1.74 (br. *s*, 3 H–C(20)); on lowering the temp. to −70°, 2 conformers could be detected, 7:3 ratio. MS: 318 (4, M^+), 303 (2, $[M - Me]^+$), 300 (3, $[M - H_2O]^+$), 287 (3), 249 (4, $[M - C_5H_9]^+$), 165 (33), 135 (23), 109 (36), 81 (38), 69 (95), 41 (100).

(6Z)-4-Oxodictyolactone (= *(3aS,4S,7Z,10E)-4-[(R)-1,5-Dimethylhex-4-enyl]-3,3a,4,5,6,9-hexahydro-7-methyl-1H-cyclonona[c]furan-1,5-dione*; **15**): $[\alpha]_D^{25} = -12$ ($c = 0.11$, CCl_4). ^{1}H-NMR: 3.60 (*ddt*, $J = 11.2, 6.7, 2.8$, H–C(2)); 2.75 (*dd*, $J = 11.2, 5.2$, H–C(3)); 2.75 (*d*, $J = 15.9$, H_α–C(5)); 3.41 (*d*, $J = 15.9$, H_β–C(5)); 5.45 (br. *t*, $J = 8.2$, H–C(7)); 2.93 (*dddt*, $J = 13.8, 11.2, 8.2, 1.2$, H_α–C(8)); 2.66 (*ddd*, $J = 13.8, 8.2, 6.7$, H_β–C(8)); 6.79 (*ddd*, $J = 11.2, 6.7, 2.0$, H–C(9)); 1.82 (*m*, H–C(10)); 1.15–1.25 (*m*, 2 H–C(11)); 1.98 (*m*, 2 H–C(12)); 5.03 (br. *t*, $J = 7.0$, H–C(13)); 1.68 (br. *s*, 3 H–C(15)); 1.60 (br. *s*, 3 H–C(16)); 1.03 (*d*, $J = 6.9$, 3 H–C(17)); 4.18 (*dd*, $J = 9.5, 2.8$, H_β–C(18)); 4.28 (*dd*, $J = 9.5, 6.7$, H_α–C(18)); 1.85 (br. *s*, 3 H–C(20)). NOE (from 2D-NOE experiments): 1.85→5.45, 2.75; 4.18→3.60. ^{13}C-NMR: 128.18 (*s*, C(1)); 46.67 (*d*, C(2)); 60.16 (*d*, C(3)); 210.13 (*s*, C(4)); 38.52 (*t*, C(5)); 134.77 (*s*, C(6)); 120.63 (*d*, C(7)); 28.42 (*t*, C(8)); 138.33 (*d*, C(9)); 33.08 (*d*, C(10)); 35.47 (*t*, C(11)); 25.70 (*t*, C(12)); 123.29 (*d*, C(13)); 132.57 (*s*, C(14)); 25.74 (*q*, C(15)); 17.76 (*q*, C(16)); 15.52 (*q*, C(17)); 68.58 (*t*, C(18));

170.89 (*s*, C(19)); 26.76 (*q*, C(20)). MS: 316 (20, $M^{+\cdot}$), 301 (4, $[M - Me]^+$), 298 (7, $[M - H_2O]^{+\cdot}$), 285 (22), 260 (12), 164 (47), 152 (45), 109 (53), 69 (100), 41 (90).

(18S,6Z)-18-Methoxy-4-oxodictyolactone (= *(3S,3aS,4S,7Z,10E)-4-[(R)-1,5-Dimethylhexy-4-enyl]-3,3a,4,5,6,9-hexahydro-3-methoxy-7-methyl-1H-cyclonona[c]furan-1,5-dione*; **16**): ^{1}H-NMR: 3.43 (*d*, *J* = 11.8, H–C(2)); 2.52 (*dd*, *J* = 11.8, 6.0, H–C(3)); 2.67 (*d*, *J* = 15.8, H_α–C(5)); 3.47 (*d*, *J* = 15.8, H_β–C(5)); 5.47 (br. *t*, *J* = 7.9, H–C(7)); 2.94 (br. *ddd*, *J* = 13.8, 11.7, 7.9, H_α–C(8)); 2.70 (*ddd*, *J* = 13.8, 7.9, 6.7, H_β–C(8)); 6.77 (*ddd*, *J* = 11.7, 6.7, 1.7, H–C(9)); 1.92 (*m*, H–C(10)); 1.15–1.25 (*m*, 2 H–C(11)); 1.98 (*m*, 2 H–C(12)); 5.04 (br. *t*, *J* = 7.0, H–C(13)); 1.69 (br. *s*, 3 H–C(15)); 1.61 (br. *s*, 3 H–C(16)); 1.10 (*d*, *J* = 6.9, 3 H–C(17)); 5.14 (*s*, H_β–C(18)); 1.86 (br. *s*, 3 H–C(20)); 3.47 (*s*, MeO). NOE: 1.86→5.47, 5.14; 5.14→3.47, 2.52. ^{13}C-NMR: 126.67 (*s*, C(1)); 44.64 (*d*, C(2)); 61.04 (*d*, C(3)); 208.59 (*s*, C(4)); 44.68 (*t*, C(5)); 136.10 (*s*, C(6)); 119.77 (*d*, C(7)); 29.70 (*t*, C(8)); 139.45 (*d*, C(9)); 33.23 (*d*, C(10)); 34.81 (*t*, C(11)); 25.70 (*t*, C(12)); 123.37 (*d*, C(13)); 132.56 (*s*, C(14)); 25.74 (*q*, C(15)); 17.79 (*q*, C(16)); 16.11 (*q*, C(17)); 104.56 (*d*, C(18)); 170.83 (*s*, C(19)); 26.75 (*q*, C(20)); 56.53 (*q*, MeO). MS: 346 (3, $M^{+\cdot}$), 314 (11, $[M - MeOH]^{+\cdot}$), 286 (8), 271 (14), 69 (88), 41 (100).

(6Z)-18-Acetoxy-4-oxodictyo-19-al (= *(8S,9S,1E,4Z)-9-(Acetoxymethyl)-8-[(R)-1,5-dimethylhex-4-enyl]-5-methyl-7-oxocyclonona-1,4-diene-1-carbaldehyde*; **17**): $[\alpha]_D^{25} = +22.0$ (*c* = 0.10, CCl_4). ^{1}H-NMR: 3.70 (br. *m*, H–C(2)); 5.43 (br. *t*, *J* = 7.6, H–C(7)); 6.46 (*dd*, *J* = 9.5, 8.1, H–C(9)); 5.05 (br. *t*, *J* = 7.2, H–C(13)); 1.68 (br. *s*, 3 H–C(15)); 1.61 (br. *s*, 3 H–C(16)); 1.10 (*d*, *J* = 7.2, 3 H–C(17)); 4.40 (*m*, 2 H–C(18)); 9.26 (*d*, *J* = 1.8, H–C(19)); 1.90 (br. *s*, 3 H–C(20)); 1.99 (br. *s*, Ac). MS: 360 (1, $M^{+\cdot}$), 318 (2, $[M - CH_2CO]^{+\cdot}$), 300 (5, $[M - AcOH]^{+\cdot}$), 149 (69), 69 (79), 43 (100).

13. *Coraxeniolide B* (= *(4aS,11aR,4E,7E)-4,4a,5,6,9,10,11,11a-Octahydro-7-methyl-11-methylidene-4-[(2E)-4-methylpent-2-enylidene]cyclonona[c]pyran-3(1H)-one*; **19**). *Conformer* **19a**: ^{1}H-NMR: 2.12 (*ddd*, *J* = 12.3, 10.1, 5.7, H–C(2)); 3.01 (*ddt*, *J* = 10.1, 4.2, 1.2, H–C(3)); 1.62 (*m*, H_β–C(4)); 1.51 (*dtd*, *J* = 14.4, 4.0, 1.2, H_α–C(4)); 2.18 (*m*, H_β–C(5)); 2.21 (*m*, H_α–C(5)); 5.44 (*ddq*, *J* = 9.9, 6.3, 1.3, H–C(7)); 2.46 (*m*, H_β–C(8)); 2.06 (*m*, H_α–C(8)); 2.10 (*m*, H_β–C(9)); 2.28 (*m*, H_α–C(9)); 6.88 (*dd*, *J* = 11.0, 1.0, H–C(11)); 6.24 (*ddd*, *J* = 15.0, 11.0, 1.1, H–C(12)); 6.11 (*dd*, *J* = 15.0, 6.7, H–C(13)); 1.06 (*d*, *J* = 6.7, 3 H–C(15) or 3 H–C(16)); 1.07 (*d*, *J* = 6.7, 3 H–C(16) or 3 H–C(15)); 2.42 (*m*, H–C(14)); 4.06 (*dd*, *J* = 11.4, 5.7, H_β–C(18)); 3.56 (*dd*, *J* = 12.3, 11.4, H_α–C(18)); 4.95 (br. *s*, H_a–C(19)); 4.83 (*s*, H_b–C(19)); 1.71 (*d*, *J* = 1.3, 3 H–C(20)). NOE: 6.88→6.11; 5.44→3.01, 2.21, 2.06; 4.83→3.56, 3.01; 3.01→6.24, 5.44, 4.83. ^{13}C-NMR: 151.97 (*s*, C(1)); 49.52 (*d*, C(2)); 43.33 (*d*, C(3)); 38.04 (*t*, C(4)); 40.40 (*t*, C(5)); 135.45 (*s*, C(6)); 124.53 (*d*, C(7)); 24.96 (*t*, C(8)); 34.41 (*t*, C(9)); 131.13 (*s*, C(10)); 137.01 (*d*, C(11)); 120.92 (*d*, C(12)); 151.75 (*d*, C(13)); 31.92 (*d*, C(14)); 21.99 (*q*, C(15) or C(16)); 21.77 (*q*, C(16) or C(15)); 171.42 (*s*, C(17)); 70.87 (*t*, C(18)); 113.43 (*t*, C(19)); 16.44 (*q*, C(20)).

Conformer **19b**: ^{1}H-NMR (coupling patterns only reported if significantly different from those of **19a**): 2.42 (*ddd*, *J* = 11.6, 10.1, 6.1, H–C(2)); 2.93 (*m*, H–C(3)); 1.89 (*m*, H_β–C(4)); 1.60 (*m*, H_α–C(4)); 2.40 (*m*, H_β–C(5)); 2.60 (*m*, H_α–C(5)); 5.38 (*ddt*, *J* = 10.7, 4.3, 1.6, H–C(7)); 2.48 (*m*, H_β–C(8)); 2.20 (*m*, H_α–C(8)); 2.03 (*m*, H_β–C(9)); 2.40 (*m*, H_α–C(9)); 6.94 (*dd*, *J* = 10.6, 1.4, H–C(11)); 6.24 (H–C(12)); 6.11 (H–C(13)); 2.42 (*m*, H–C(14)); 1.07 (*d*, *J* = 6.9, 3 H–C(15) or 3 H–C(16)); 1.08 (*d*, *J* = 6.9, 3 H–C(16) or 3 H–C(15)); 3.98 (*dd*, *J* = 11.5, 4.9, H_β–C(18)); 3.49 (*dd*, *J* = 12.3, 11.5, H_α–C(18)); 4.97 (br. *s*, H_a–C(19)); 4.76 (*s*, H_b–C(19)); 1.68 (*d*, *J* = 1.6, 3 H–C(20)). NOE: 4.76→3.49, 2.93. ^{13}C-NMR: 151.20 (*s*, C(1)); 52.45 (*d*, C(2)); 41.75 (*d*, C(3)); 38.47 (*t*, C(4)); 41.21 (*t*, C(5)); 134.06 (*s*, C(6)); 125.94 (*d*, C(7)); 29.49 (*t*, C(8)); 35.13 (*t*, C(9)); 131.43 (*s*, C(10)); 138.30 (*d*, C(11)); 121.00 (*d*, C(12)); 151.91 (*d*, C(13)); 31.78 (*d*, C(14)); 21.99 (*q*, C(15) or C(16)); 21.77 (*q*, C(16) or C(15)); 170.80 (*s*, C(17)); 70.50 (*t*, C(18)); 113.22 (*t*, C(19)); 21.77 (*q*, C(20)).

14. *Arboxeniolide 1* (= *(4R,4aS,11aR,7E)-4,4a,5,6,9,10,11,11a-Octahydro-7-methyl-11-methylidene-4-[(1E)-4-methylpenta-1,3-dienyl]cyclonona[c]pyran-3(1H)-one*; **21**). *Conformer* **21a**: ^{1}H-NMR: 1.87 (*dt*, *J* = 4.1, 3.3, H–C(2)); 1.79 (*ddt*, *J* = 11.9, 8.9, 3.3, H–C(3)); 1.56 (*m*, H_β–C(4)); 1.46 (*dt*, *J* = 12.5, 3.2, H_α–C(4)); 2.17 (*dt*, *J* = 13.0, 2.6, H_β–C(5)); 2.04 (*m*, H_α–C(5)); 5.34 (*ddq*, *J* = 9.4, 5.1, 1.5, H–C(7)); 2.46 (*m*, H_β–C(8)); 2.06 (*dt*, *J* = 14.9, 9.4, H_α–C(8)); 2.07 (*dtd*, *J* = 14.3, 9.4, 1.3, H_β–C(9)); 2.37 (*ddd*, *J* = 14.3, 8.1, 2.0, H_α–C(9)); 2.91 (*td*, *J* = 8.9, 1.0, H–C(10)); 5.54 (*dd*, *J* = 15.0, 8.9, H–C(11)); 6.28 (*ddd*, *J* = 15.0, 10.7, 1.0, H–C(12)); 5.89 (*sept. d*, *J* = 10.7, 1.4, H–C(13)); 1.74 (br. *s*, 3 H–C(15)); 1.78 (br. *s*, 3 H–C(16)); 4.17 (*dd*, *J* = 11.3, 4.1, H_β–C(18)); 4.17 (*dd*, *J* = 11.3, 3.3, H_α–C(18)); 4.91 (br. *s*, H_a–C(19)); 4.80 (*s*, H_b–C(19)); 1.68 (*d*, *J* = 1.5, 3 H–C(20)). ^{13}C-NMR: 152.75 (*s*, C(1)); 50.01 (*d*, C(2)); 48.51 (*d*, C(3)); 35.23 (*t*, C(4)); 39.77 (*t*, C(5)); 135.50 (*s*, C(6)); 124.47 (*d*, C(7)); 24.71 (*t*, C(8)); 35.03 (*t*, C(9)); 46.86 (*d*, C(10)); 124.29 (*d*, C(11)); 126.18 (*d*, C(12)); 130.96 (*d*, C(13)); 135.88 (*s*, C(14)); 25.97 (*q*, C(15)); 18.36 (*q*, C(16)); 174.43 (*s*, C(17)); 67.70 (*t*, C(18)); 113.38 (*t*, C(19)); 16.28 (*q*, C(20)).

Conformer **21b**: ^{1}H-NMR: 2.40 ('*q*', *J* = 4.2, H–C(2)); 1.80 (*m*, H–C(3)); 5.35 (*m*, H–C(7)); 2.40 (*m*, H_β–C(8)); 2.04 (*m*, H_α–C(8)); 1.94 (*m*, H_β–C(9)); 2.41 (*m*, H_α–C(9)); 2.96 (*td*, *J* = 8.9, 1.0, H–C(10)); 5.54 (*dd*, *J* = 15.0, 8.9, H–C(11)); 6.30 (*ddd*, *J* = 15.0, 10.7, 1.0, H–C(12)); 5.89 (*sept. d*, *J* = 10.7, 1.4, H–C(13)); 1.74 (br. *s*, 3 H–C(15)); 1.78 (br. *s*, 3 H–C(16)); 4.15 (*dd*, *J* = 11.3, 4.2, H_β–C(18)); 3.94 (*dd*, *J* = 11.3, 4.2, H_α–C(18)); 4.96

(br. *s*, H_a–C(19)); 4.74 (*s*, H_b–C(19)); 1.59 (*d*, J = 1.4, 3 H–C(20)). ^{13}C-NMR: 152.25 (*s*, C(1)); 50.53 (*d*, C(2)); 43.78 (*d*, C(3)); 126.04 (*d*, C(7)); 35.50 (*t*, C(9)); 126.74 (*d*, C(11)); 126.72 (*d*, C(12)); 131.07 (*d*, C(13)); 135.88 (*s*, C(14)); 25.97 (*q*, C(15)); 18.36 (*q*, C(16)); 68.65 (*t*, C(18)); 113.84 (*t*, C(19)); 21.82 (*q*, C(20)).

15. *Caryophyllene* (= *(1R,9S,4E)-4,11,11-Trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene*; **22**). *Conformer* **22a**: ^{1}H-NMR: 1.68 (*td*, J = 10.2, 2.3, H–C(1)); 1.50 (*m*, 2 H–C(2)); 1.91 (*td*, J = 1.18, 5.4, H_β–C(3)); 2.09 (*dt*, J = 11.8, 3.4, H_α–C(3)); 5.31 (*dd*, J = 10.2, 5.8, H–C(5)); 1.99 (*dt*, J = 11.5, 8.2, H_β–C(6)); 2.34 (*m*, H_α–C(6)); 2.18 (*ddd*, J = 14.8, 8.2, 3.4, H_β–C(7)); 2.23 (*ddd*, J = 14.8, 8.2, 3.2, H_α–C(7)); 2.32 (*dt*, J = 10.2, 8.8, H–C(9)); 1.62 (*m*, 2 H–C(10)); 0.97 (*s*, Me_α–C(11)); 1.00 (*s*, Me_β–C(11)); 1.61 (*d*, J = 1.3, Me–C(4)); 4.82 (*d*, J = 2.0, H_a of CH_2=C(8)); 4.94 (*d*, J = 2.0, H_b of CH_2=C(8)). NOE (–40°): 1.68→5.31, 1.00; 1.61→2.09, 2.34; 5.31→1.68, 1.91, 1.99. ^{13}C-NMR: 53.51 (*d*, C(1)); 29.24 (*t*, C(2)); 39.93 (*t*, C(3)); 135.42 (*s*, C(4)); 124.30 (*d*, C(5)); 28.35 (*t*, C(6)); 34.76 (*t*, C(7)); 154.60 (*s*, C(8)); 48.46 (*d*, C(9)); 40.31 (*t*, C(10)); 32.97 (*s*, C(11)); 22.62 (*q*, Me_α–C(11)); 30.05 (*q*, Me_β–C(11)); 16.27 (*q*, *Me*–C(4)); 111.65 (*t*, CH_2=C(8)).

Conformer **22b**: ^{1}H-NMR: 1.50 (*m*, H–C(1)); 1.57 (*m*, 2 H–C(2), 2 H–C(3)); 5.26 (br. *d*, J = 11.5, H–C(5)); 1.87 (*m*, H_β–C(6)); 2.08 (*m*, H_α–C(6)); 2.20 (*m*, 2 H–C(7)); 2.25 (*m*, H–C(9)); 1.62 (*m*, 2 H–C(10)); 0.96 (*s*, Me_α–C(11)); 1.00 (*s*, Me_β–C(11)); 1.59 (br. *s*, Me–C(4)); 4.87 (br. *s*, H_a of CH_2=C(8)); 4.94 (br. *s*, H_b of CH_2=C(8)). ^{13}C-NMR: 55.85 (*d*, C(1)); 31.34 (*t*, C(2)); 42.60 (*t*, C(3)); 134.94 (*s*, C(4)); 124.49 (*d*, C(5)); 29.72 (*t*, C(6)); 34.82 (*t*, C(7)); 154.92 (*s*, C(8)); 49.32 (*d*, C(9)); 40.31 (*t*, C(10)); 32.59 (*s*, C(11)); 21.91 (*q*, Me_α–C(11)); 29.83 (*q*, Me_β–C(11)); 22.00 (*q*, *Me*–C(4)); 110.78 (*t*, CH_2=C(8)).

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