

Conformational Bias in Macrocyclic Ethers and Observation of High Solvolytic Reactivity at a Masked Furfuryl (= 2-Furylmethyl) C-Atom

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New polyhalogenated, twelve-membered, O-bridged cyclic C₁₅-ethers, having in common oxygenation at C(6) and a bromoallene side chain at C(4) (where C(1) is the bromoallene-chain terminus), were isolated from the red seaweed *Laurencia obtusa* from the Turkish Mediterranean Sea, *i.e.*, the 9,12-O-bridged obtusallene VII (**5**), the 6,9:9,12-bis-O-bridged obtusallene V (**3**) and obtusallene VI (**4**), as well as the 6,9-O-bridged obtusallene VIII (**8**) and obtusallene IX (**9**). The behavior of portions of the macrocycle involved in fast motions and their equilibrium position depend on the particular compound, revealing a subtle conformational behavior of these macrocycles, while **8** and **9** show an unprecedented solvolytic reactivity at the masked furfuryl (= 2-furylmethyl) C-atom.

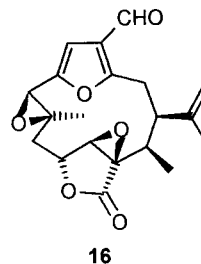
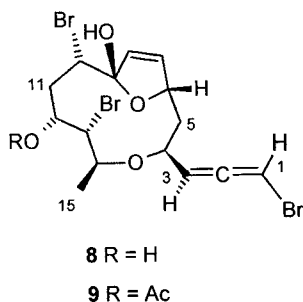
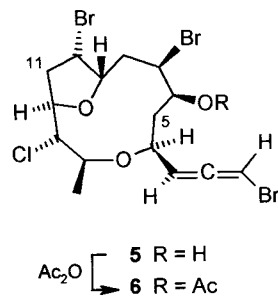
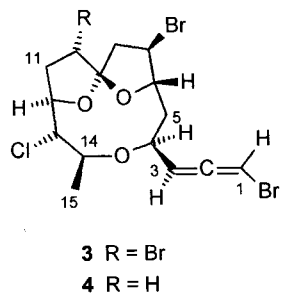
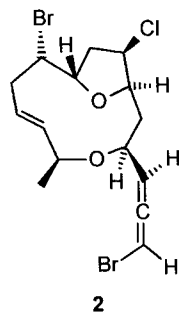
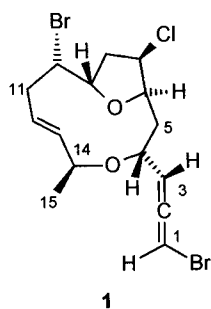
1. Introduction. – We recently described obtusallene IV (**1**), isolated from a red seaweed, *Laurencia obtusa*, from the Turkish Mediterranean Sea [1]. This compound belongs to a rare family of macrocyclic C₁₅-ethers, the first of which, obtusallene I (**2**), was isolated from the same nominal species from the Turkish Aegean Sea [2]. Actually, the species name *L. obtusa* is taxonomically poorly defined, standing for different ecads, varieties, or biological species.

Obtusallenes bearing a *trans* olefinic unit in the macrocycle are characterized by slow conformational motions on the NMR time scale, resulting from 180° flipping of the olefinic bond [1]. This phenomenon, first noticed for obtusallene IV (**1**) [1], was missed – probably by relying mostly on X-ray diffraction analysis for the structural elucidation – for the same compound independently isolated from a marine herbivorous mollusk and called dactylallene [3], in disregard of it belonging to the obtusallene family.

We report here that our Turkish-Mediterranean *L. obtusa* contains other macrocyclic C₁₅-ethers that are characterized by a peculiar solvolytic behavior and/or subtle fast motions involving the macrocycle.

2. Results and Discussion. – 2.1. *Spirocyclic Obtusallenes V (3) and VI (4)*. The bromoallene moiety of obtusallene V (**3**) shows diagnostic ¹³C-NMR resonances (75.34 (*d*), 200.96 (*s*), 101.87 (*d*); *Table I*) and is lost in the EI-MS to give a prominent fragment ion [1] at *m/z* 403 of composition C₁₂H₁₆Br₂ClO₃ (HR-EI-MS) (*Exper. Part*). This establishes the composition C₁₅H₁₈Br₃ClO₃ for compound **3**, implying five

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unsaturations, of which three must be cycles once the allene moiety is subtracted. COSY and differential decoupling experiments support the C(4)–O–C(14) moiety, thus pointing to a 12-membered macrocycle that bears both a Me group at C(14) (characterized by a distinctive *d* at $\delta(\text{C})$ 76.95) and a bromoallene chain at C(4). Oxygenation at C(6), C(9) and C(12), bromination at C(7) and C(10), and chlorination at C(13) are supported by ^{13}C -NMR and HMQC data. The latter revealed also long-range couplings of C(9) with H–C(6), 2 H–C(8), H–C(10), and H–C(12), which support the spiro-ketal structure, observed for the first time in this class of compounds.

The assignment of the relative configurations in **3** proved more troublesome because of the superimposition of ^1H -NMR signals and fast conformational motions in

Table 1. NMR Data (C₆D₆) for Obtusallene V (**3**). δ in ppm, J in Hz.

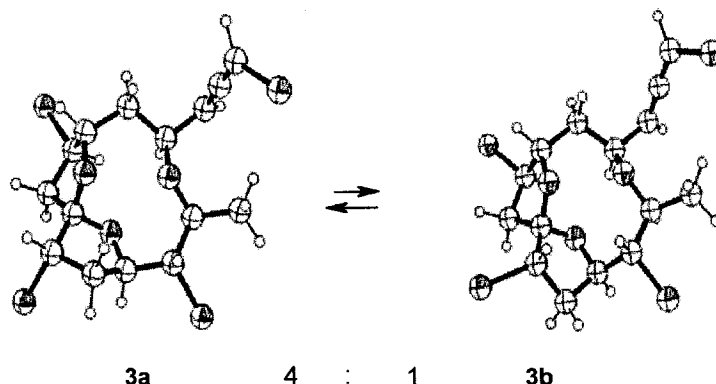
	¹ H	¹³ C
H–C(1)	5.58 (<i>dd</i> , $J(1,3) = 5.6$, $J(1,4) = 1.2$)	73.54 (<i>d</i>)
C(2)	–	200.96 (<i>s</i>)
H–C(3)	4.88 (<i>dd</i> , $J(3,1) = 5.6$, $J(3,4) = 7.7$)	101.87 (<i>d</i>)
H–C(4)	4.02 (<i>ddd</i> , $J(4,1) = 1.2$, $J(4,3) = 7.7$, $J(4,5\beta) = 8.7$, $J(4,5\alpha) = 1.0$)	74.28 (<i>d</i>)
CH ₂ (5)	1.39 (<i>ddd</i> , $J(5\alpha,6) = 3.6$, $J(5\alpha,4) = 1.0$, $J_{\text{gem}} = 15.3$); 1.68 (<i>ddd</i> , $J(5\beta,6) = 4.6$, $J(5\beta,4) = 8.7$, $J_{\text{gem}} = 15.3$)	36.96 (<i>t</i>)
H–C(6)	4.26 (<i>ddd</i> , $J(6,5\beta) = 4.6$, $J(6,5\alpha) = 3.6$, $J(6,7) = 6.8$)	86.48 (<i>d</i>)
H–C(7)	4.00 (<i>ddd</i> , $J(7,8\alpha) = 7.1$, $J(7,8\beta) = 9.8$, $J(7,6) = 6.8$)	57.44 (<i>d</i>)
CH ₂ (8)	2.53 (<i>dd</i> , $J(8\alpha,7) = 7.1$, $J_{\text{gem}} = 13.0$); 2.31 (<i>dd</i> , $J(8\beta,7) = 9.8$, $J_{\text{gem}} = 13.0$)	46.45 (<i>t</i>)
C(9)	–	116.32 (<i>s</i>)
H–C(10)	3.88 (<i>dd</i> , $J(10,11\alpha) = 2.4$, $J(10,11\beta) = 5.6$)	51.28 (<i>d</i>)
CH ₂ (11)	2.26 (<i>ddd</i> , $J(11\alpha,10) = 2.4$, $J(11\alpha,12) = 7.2$, $J_{\text{gem}} = 14.2$); 2.22 (<i>ddd</i> , $J(11\beta,10) = 5.6$, $J(11\beta,12) = 7.5$, $J_{\text{gem}} = 14.2$)	42.73 (<i>t</i>)
H–C(12)	4.61 (<i>br.q</i> , $J(12,11\alpha) \approx J(12,11\beta) \approx J(12,13) = 7.5$)	83.62 (<i>d</i>)
H–C(13)	3.59 (<i>dd</i> , $J(13,12) = 7.7$, $J(13,14) = 8.3$)	60.66 (<i>d</i>)
H–C(14)	3.62 (<i>qd</i> , $J(14,15) = 6.0$, $J(14,13) = 8.3$)	76.95 (<i>d</i>)
H–C(15)	1.39 (<i>d</i> , $J(15,14) = 6.0$)	22.45 (<i>q</i>)

the C(10) to C(14) portion of the macrocycle. The problem of signal superimposition was solved by running ¹H-NMR spectra in both CDCl₃ (*Exper. Part*) and C₆D₆ (*Table 1*), relying on their different shift-inducing power. The fast motions allowed us to obtain only averaged J couplings and NOEs.

Thus, assuming arbitrarily the (*S*^{*})-configuration at C(4) of **3**, a strong NOE between H–C(4) and H–C(14) points to (*S*^{*})-configuration at C(14). Support to the spatial dispositions H _{β} –C(6) and H _{α} –C(7) is based on a positive NOE between H–C(6) and both H _{β} –C(5) (defined by *trans*-diaxial coupling with H–C(4)) and H _{β} –C(8). These conclusions agree with the observed coupling constants $J(6,7)$ and $J(7,8\beta)$. Similar values $J(14,13) = 8.5$ and $J(13,12) = 7.7$ Hz suggest fast conformational motions, thus being of no help in defining the configuration. However, the spatial positions H _{α} –C(12) and H _{α} –C(14) are supported by a NOE between these two protons, while H _{β} –C(13) is defined by a NOE with 3 H–C(15).

The assignment of the configuration at the spirocenter of **3** was not straightforward because the configuration at C(10) was not uniquely defined by a weak NOE between H _{β} –C(8) and H–C(10). However, a coupling $J(10,11\beta)$ of 5.6 Hz favors H _{β} –C(10): for H _{α} –C(10) a coupling of at least 12 Hz would be expected.

The configurational conclusions leading to formula **3** are in accordance with molecular-mechanics (MM) calculations for obtusallene V, which suggest two lowest-strain-energy conformers **3a** (pseudoaxial Br _{α} –C(10)) and **3b** (pseudoequatorial Br _{α} –C(10)) in a 4:1 population ratio, respectively, resulting from fast flipping of the C(10) to C(12) portion of the tetrahydrofuran ring (*Scheme 1*). The population of the minor conformer **3b** is sufficient to affect J coupling constants of the C(10) to C(14) segment. Good agreement with the experimental ³ J values is observed (see *Table 2*), in particular as to the average coupling constants (calculated by *Altona's* equation [4]) for the C(10) to C(14) segment. For a hypothetical H _{α} –C(10) epimer, the calculated J coupling constants are in sharp disagreement with the experimental values. It should be noticed that these MM calculations were carried out by replacing the bromoallene with the allene group, for the latter only is implemented in the computer program used (MM3(96)). There is no reason to expect a different trend for the real case of bromoallene **3**.

Scheme 1. *Predominant and Minor Conformers, 3a and 3b, Respectively, of Obtusallene V (3), According to MM Calculations and in Agreement with NMR Data*

The structure of obtusallene VI (**4**) rests on similar evidence. In particular, H–C(10) in place of Br–C(10) is reflected in the NMR spectra (C_6D_6) by a high-field shift and multiplicity change of $\delta(C(10))$ (from 51.28 (*d*) to 32.68 (*t*)) and of $\delta(H-C(10))$ (from 3.88 (*dd*) to 1.90 (*m*, non-first-order coupling pattern for 2H–C(10) and 2H–C(11)). COSY, HMQC, and HMBC maps are in accordance with these conclusions.

Table 2. *Experimental and Calculated $^3J^a$) Coupling Constants for Obtusallene V (3) and Obtusallene VI (4)*

Vicinal protons	Calculated 3J [Hz]		Experimental 3J [Hz] of 3 in C_6D_6	Calculated 3J [Hz]		Experimental 3J [Hz] of 4 in C_6D_6
	3a ^b)	3b ^b)		3a -type ^c)	3b -type ^c)	
H–C(4), H α –C(5)	1.7	1.4	1.0	1.4	1.4	1.5
H–C(4), H β –C(5)	11.4	11.3	8.7	11.2	11.2	10.4
H α –C(5), H–C(6)	1.3	0.9	3.6	1.5	1.1	1.5
H β –C(5), H–C(6)	5.7	6.7	4.6	5.3	6.3	4.8
H–C(6), H–C(7)	8.6	8.3	6.8	7.7	7.5	7.0
H–C(7), H α –C(8)	6.7	6.7	7.1	6.9	6.7	7.0
H–C(7), H β –C(8)	11.0	10.9	9.8	10.6	10.8	10.3
H α –C(10), H α –C(11)	–	–	–	6.6	9.7	^d)
H α –C(10), H β –C(11)	–	–	–	13.2	0.1	^d)
H β –C(10), H α –C(11)	1.4	10.4	2.4	5.9	10.5	^d)
H β –C(10), H β –C(11)	5.5	7.2	5.6	10.8	9.8	^d)
H α –C(11), H–C(12)	5.1	7.7	7.2	5.9	8.0	6.3
H β –C(11), H–C(12)	11.2	1.1	7.5	10.8	1.1	2.6
H–C(12), H–C(13)	4.2	9.2	7.2	4.5	9.1	10.0
H–C(13), H–C(14)	9.6	9.2	8.3	9.6	8.6	7.9

^a) A minimized-conformation input file obtained from the computer program MM3(96) served as input to the computer program PCWIN, where a subroutine based on *Altona's* equation [4] was used. ^b) Calculations by the computer program MM3(96) gave $\Delta E = 0.91$ kcal mol⁻¹ as the strain energy between the hypothetical conformers **3b** and **3a**. ^c) Strain energy $\Delta E = 0.55$ kcal mol⁻¹ for the **3a**-type minus the **3b**-type conformers of **4**, *i.e.*, a reverse situation with respect to the data of **3** in *Footnote b*; see text. ^d) No 3J value could be determined from the coupling-pattern analysis (see text).

The conformational behavior of **4** differs from that of **3**, however. A different coupling pattern of H–C(12) of **4** ($J(12,11\beta) = 2.6$ and $J(12,13) = 10.0$ Hz vs. 7.5 and 7.7 Hz, resp. in the case of **3**), suggest that the different behavior arises from segment C(10) to C(13). Following the same MM procedure as used for **3**, two least-strain conformers of type **3a** and **3b** resulted for compound **4**, differing by only 0.55 kcal mol⁻¹ in strain energy; contrary to the case of **3**, the **3b**-type conformer is the most populated conformer of **4**. There is a good agreement of the calculated experimental ³*J* values of **4** (see Table 2), in particular as to the mean vicinal *J* coupling values.

2.2. *Natural Obtusallene VII (5) and Semisynthetic Obtusallene VII Acetate (6)*. Obtusallene VII (**5**) differs from both **3** and **4** for bearing a single tetrahydrofuran ring, characterized by $\delta(\text{C})$ of 76.14 (*d*) for C(9). Oxygenation at C(6) is still present, however, in the form of a free OH group, which accounts for a higher polarity than either **3** or **4** and for monoacetylation to give obtusallene VII acetate (**6**). The ¹³C-NMR spectrum of **5** at ordinary probe temperature was observed at near coalescence of signals, in particular as to those from the C(4) to C(8) segment. This found analogy in the ¹H-NMR spectrum.

These phenomena were less marked with obtusallene VII acetate (**6**), with a ¹³C-NMR spectrum that showed some broadening only of the signals, while the ¹H-NMR signals were sharp. This may be attributed to the bulk of the AcO–C(6) substituent. Correspondingly, 1D and 2D NMR analysis of **6** proved simpler, in particular revealing C(6) oxygenation, the C(9)–O–C(12) bridge, bromination at C(1), C(7), and C(10), and chlorination at C(13). According to the MM procedure used for **3** and **4**, the relative configurations for both **5** and **6** were established by comparing calculated and experimental *J* coupling patterns. The position of the conformational equilibrium is opposite for **6** and **5**: MM calculations suggest a large predominance of conformer **6a** for compound **6** (Table 3 and Scheme 2), while it is a **6b**-type conformer that dominates in the case of **5**.

Scheme 2. *Largely Predominant Conformer 6a and Very Minor Conformer 6b of Obtusallene VII Acetate (6), According to MM Calculations and in Agreement with NMR Data*

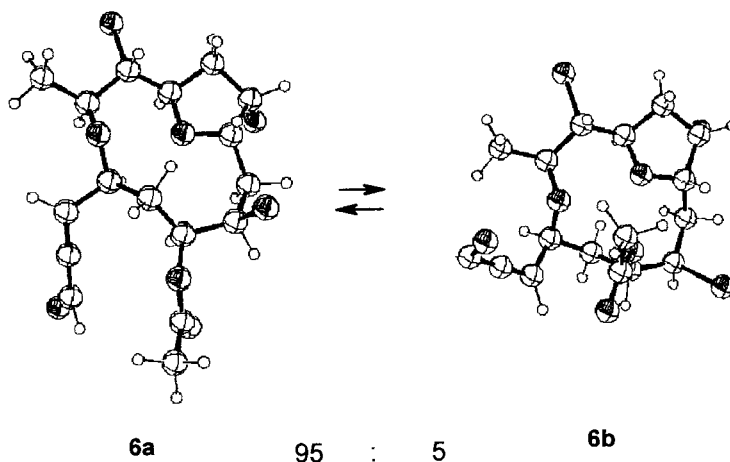


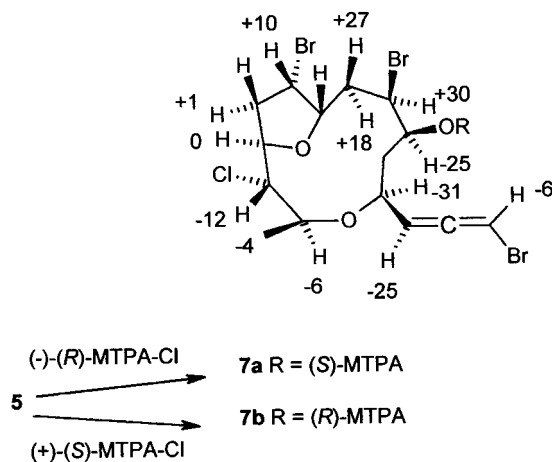
Table 3. Experimental and Calculated 3J Coupling Constants [Hz] for Obtusallene VII Acetate (**6**) and Obtusallene IX (**9**)

Vicinal protons	3J of 6a		3J of 9	
	calc.	exper.	calc.	exper.
H–C(4), H _α –C(5)	10.2	7.9	1.2	1.2
H–C(4), H _β –C(5)	1.1	1.0	11.0	8.6
H _α –C(5), H–C(6)	3.9	3.6	2.5	3.5
H _β –C(5), H–C(6)	4.9	4.1	3.8	3.2
H–C(6), H–C(7)	1.6	1.3	2.7	2.7
H–C(7), H _α –C(8)	2.7	2.6	–	–
H–C(7), H _β –C(8)	4.2	5.3	–	–
H _α –C(8), H–C(9)	11.0	9.6	–	–
H _β –C(8), H–C(9)	1.1	1.3	–	–
H–C(9), H–C(10)	3.2	2.8	–	–
H–C(10), H _α –C(11)	1.5	0.6	10.4	10.7
H–C(10), H _β –C(11)	5.1	5.1	1.2	1.2
H _α –C(11), H–C(12)	5.0	6.1	1.1	1.0
H _β –C(11), H–C(12)	11.0	9.0	9.5	10.8
H–C(12), H–C(13)	9.6	10.3	2.9	2.9
H–C(13), H–C(14)	9.4	8.4	9.3	10.0

The configurations AcO_β–C(6) and Br_β–C(7) of **6** rest on small J coupling constants of H–C(6) with both 2H–C(5) and H–C(7), and of the latter with 2H–C(8). This agrees with a NOE between H–C(6) and both H–C(4) and H–C(7). β-Positions of both the allene group and Me(15) rest on similar evidence as for **3**. The coupling patterns for all other protons in both **5** and **6** are in accordance with these conclusions.

The free secondary-alcohol group of **5** allowed us to prepare Mosher's MTPA esters **7a** and **7b** (MTPA = α-methoxy-α-(trifluoromethyl)benzeneacetic acid; see *Exper. Part*). A homogeneous trend of $\Delta\delta$ ($\delta_S - \delta_R$) values for these esters (*Scheme 3*) is only compatible with the absolute configuration (*S*) at C(6) of **5**. The absolute configuration (*aR*) of the bromoallene moiety for all these new obtusallenes rests on negative Cotton effects (*Exper. Part*).

Scheme 3. (*S*)-MTPA Ester **7a** and (*R*)-MTPA Ester **7b** of **5**. $\Delta\delta$ (H) (**7a**–**7b**) values are given in the formula.



A marked broadening of the $^1\text{H-NMR}$ signals for both the bromoallene and $\text{C}(14)\text{--O--C}(4)\text{--C}(5)$ moieties of **7a** and **7b** is difficult to rationalize. From *Dreiding* models, the bulky MTPA group appears to exert steric compression against the bromoallene side chain, resulting in a large distortion of the dihedral angle $\text{C}(14)\text{--O--C}(4)\text{--C}(5)$. Whether this is borne out by MM calculations, and may explain broadening of the signals, was not investigated because of the tremendous burdening of the so many additional degrees of freedom introduced by the MTPA substituent.

2.3. *Obtusallenes VIII and IX (8 and 9, resp.)*. Obtusallenes VIII (**8**) and IX (**9**) undergo easy degradation, thus requiring a mild workup under N_2 of the polar fractions containing them. Obtusallene IX (**9**), having composition $\text{C}_{17}\text{H}_{21}\text{Br}_3\text{O}_5$ (MS and NMR data in the *Exper. Part*), a bromoallene group (established as for the other compounds above), an acetyl group, and a (*Z*)-disubstituted $\text{C}=\text{C}$ bond, must be bicyclic. A 12-membered cycle is suggested by a characteristic $\delta(\text{H})$ for Me(15) (*d*). HMQC and HMBC experiments support the hemiketal group, with a $\text{C}(6)\text{--O--C}(9)$ bridge, thus locating the five-membered ring. MM Calculations for obtusallene IX (**9**) point to a single conformer (*Fig.*), in accordance with NMR data (*Table 3*).

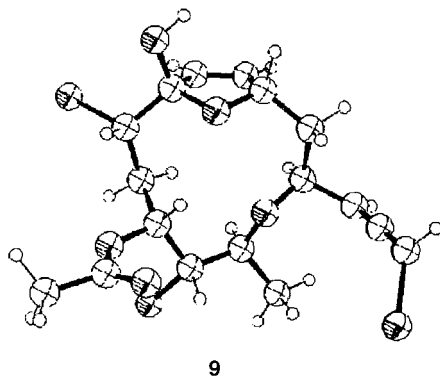
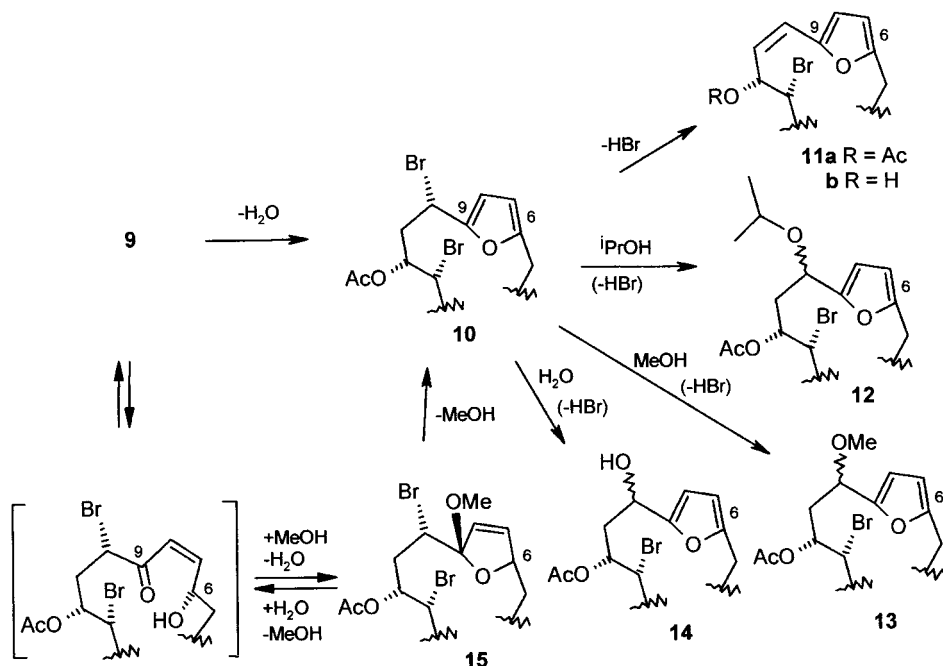


Fig. 1. *Lowest-energy conformation of obtusallene IX (9), according to MM calculations and in agreement with NMR data*

Typical $\delta(\text{C})$ values of **9** support a Br-substituent at both C(10) and C(13). The relative configurations at C(4), C(10), C(12), and C(13) rest on strong NOEs between $\text{H--C}(14)$ and pseudoaxial $\text{H--C}(4)$, as well as between pseudoaxial $\text{H}_\beta\text{--C}(12)$ and both pseudoaxial $\text{H}_\beta\text{--C}(10)$ and pseudoequatorial $\text{H}_\beta\text{--C}(13)$.

The degradation of compounds **8** and **9** was examined in some detail. On warming a solution of compound **9** in CDCl_3 to 40° , signals for the dehydration product **10** (*Scheme 4*) emerged within a few minutes. These signals persisted long enough for NMR observation, and also MS measurements could be taken from the residue obtained on evaporation of an aliquot of the solution. All attempts at HPLC purification of **10** failed, however; either the solvents ($i\text{PrOH}$, MeOH , and H_2O) were incorporated into **10** to give a variety of products, or elimination of HBr occurred, yielding products **11–14** which could be either isolated or identified in mixture.

Scheme 4. Suggested Mechanism for the Spontaneous Transformation of **9** into **11–15** in the Given Solvents

Decay of obtusallene IX (**9**) along two parallel pathways may be envisaged (Scheme 4) arriving at pivotal **10** either directly by irreversible dehydration or by MeOH addition to an elusive intermediate, followed by MeOH loss from the subsequently formed **15**. Pivotal **10** may then undergo S_N1 or S_N2 substitution of the Br-atom by the solvent, or **11** is first formed by β -elimination, followed by *Markovnikov* addition of the solvent (not shown).

Benzyl-like electrophilicity arising from masked functionalities, as in compounds **8** and **9**, finds no precedents. What is well known is the benzyl-like furfuryl (=2-furylmethyl) C-atom reactivity, resulting from conjugation to the C-atom remote from the O-atom of the furan moiety, discovered in furanosesquiterpenes from terrestrial plants [5]. In this case solvolysis was suggested to occur *via* an S_N2 reaction to account for the observed stereochemistry [5]. Compound **10** also recalls the hypothesized reactivity of lophotoxin (**16**) at the epoxy-substituted furfuryl position accounting for the irreversible inactivation of the nicotinic acetylcholine receptor [6]. It can also be imagined that selective cytotoxicity displayed by other marine-cembrane diterpenes, bipinnatins [7], results from conjugate addition reactions by nucleophilic centers. Still other marine cembranoids contain a nucleofuge in a benzyl-like position similar to that of **10** [8], or with an interposed further C=C bond [9]; however, neither the reactivity nor structure/bioactivity correlations have been described for these compounds.

3. Perspective. – The subtle fast motions described here for macrocyclic obtusallenes that lack flipping olefinic bonds extend our knowledge as to the conformational behavior of macrocyclic ethers [1]. Probably, these conformational

changes serve to adapt these bioactive [10] compounds into the active cavity of the receptor. The strong competition of marine life, in particular for edible seaweeds like the one at issue, may also suggest that phenomena of the type described here are at the basis of an ecological role for these compounds.

These observations urge investigations in model systems, in particular as to a putative activation of cellular signals at the cell membrane by reactive compounds such as **8** and **9**. This might add to our knowledge of cellular signaling and gene activation/deactivation regulation by a small molecule/receptor interaction, which are largely open problems at the textbook level [11].

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Experimental Part

General. See [1]. Moreover, all evaporations were carried out at r.t. at reduced pressure, and yields are given on reacted reagents. HPLC: t_R in min. UV: λ_{max} in nm (ϵ in $\text{mol}^{-1} \text{l cm}^{-1}$). CD: λ ($\Delta\epsilon$) in nm. NMR Multiplicities are from DEPT, while assignments are from ^1H , ^1H -COSY, ^{13}C , ^1H -COSY, and differential NOE (with 4 s preirradiation). EI-MS and HR-EI-MS (70 eV): *Kratos-MS80* mass spectrometer equipped with a home-built computerized data-acquisition system. MM Calculations were carried out by the programs MM3(96) from *QCPE*, University of Indiana.

Isolations of Compounds. Obtusallenes V–IX (**3**–**9**) were isolated from both an air-dried sample (400 g) of *Laurencia obtusa* collected in October 1987 near Kaş, Antalya, in the Turkish Mediterranean Sea [12] and from another sample of the same seaweed (752M, 250 g) collected during the summer 1994 in the same location. The latter sample, according to the previous procedure [1], was extracted with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 2:1 to give 7 g of evaporated extract that was subjected to FC (gradient hexane/AcOEt): 21 fractions of 40 ml each. The residue of *Fr. 2* was subjected to sequential FC (gradient hexane/toluene), reversed-phase HPLC (*RP18*, MeCN/ H_2O 85:15), and HPLC (*Si-60*, hexane/ PrOH 99.9:0.1): *obtusallene V* (**3**; t_R 5.0; 8 mg) and *obtusallene VI* (**4**; t_R 6.2; 6.5 mg). The residue of *Fr. 8* was subjected first to HPLC (*Si-60*, hexane/ PrOH 98:2), collecting material at t_R 7–8; this was then subjected to reversed-phase HPLC (*RP18*, MeCN/ H_2O 7:3): *obtusallene VII* (**5**; t_R 13.3; 6 mg). The residue of the combined, more polar *Fr. 14–17* was subjected to sequential FC (hexane/AcOEt 1:1) and prep. TLC ($\text{CHCl}_3/\text{MeOH}$ 55:1), to give pure, albeit unstable *obtusallene IX* (**9**; R_f 0.5; 13.4 mg) and *obtusallene VIII* (**8**; R_f 0.2).

Obtusallene V (= (*1R**,*2S**,*4R**,*5S**,*6S**,*8S**,*10S**,*11R**)-2,11-Dibromo-8-[(*aR*)-3-bromopropa-1,2-dienyl]-5-chloro-6-methyl-7,13,14-trioxatricyclo[8.2.1.1^{1,4}]tetradecane; **3**). UV (EtOH): 203 (14700). CD (EtOH): 223 (–7.1). $[\alpha]_D^{20} = -76$ ($c = 0.40$, EtOH). $^1\text{H-NMR}$ (CDCl_3): 6.04 (*dd*, $J(1,3) = 5.6$, $J(1,4) = 0.9$, H–C(1)); 5.33 (*dd*, $J(3,1) = 5.6$, $J(3,4) = 8.3$, H–C(3)); 4.41 (*dddd*, $J(4,1) = 0.9$, $J(4,5\alpha) = 1.2$, $J(4,3) = 8.3$, $J(4,5\beta) = 9.5$, H–C(4)); 1.78 (*ddd*, $J(5\alpha,6) = 2.8$, $J(5\alpha,4) = 1.2$, $J_{gem} = 15.3$, H $_{\alpha}$ –C(5)); 2.11 (*ddd*, $J(5\beta,6) = 4.8$, $J(5\beta,4) = 9.5$, $J_{gem} = 15.3$, H $_{\beta}$ –C(5)); 4.49 (*ddd*, $J(6,5\beta) = 4.8$, $J(6,5\alpha) = 2.8$, $J(6,7) = 6.4$, H–C(6)); 4.42 (*ddd*, $J(7,8\alpha) = 7.3$, $J(7,8\beta) = 10.0$, $J(7,6) = 6.4$, H–C(7)); 2.79 (*dd*, $J(8\alpha,7) = 7.3$, $J_{gem} = 13.2$, H $_{\alpha}$ –C(8)); 2.52 (*dd*, $J(8\beta,7) = 10.0$, $J_{gem} = 13.2$, H $_{\beta}$ –C(8)); 4.39 (*dd*, $J(10,11\alpha) = 3.0$, $J(10,11\beta) = 5.8$, H–C(10)); 2.76 (*ddd*, $J(11\alpha,10) = 3.0$, $J(11\alpha,12) = 7.5$, $J_{gem} = 14.5$, H $_{\alpha}$ –C(11)); 2.68 (*ddd*, $J(11\beta,10) = 5.8$, $J(11\beta,12) = 7.0$, $J_{gem} = 14.5$, H $_{\beta}$ –C(11)); 4.76 (*br. q*, $J(12,11\alpha) \approx J(12,11\beta) \approx J(12,13) = 7.0$, H–C(12)); 3.77 (*dd*, $J(13,12) = 7.5$, $J(13,14) = 8.5$, H–C(13)); 3.87 (*qd*, $J(14,15) = 6.2$, $J(14,13) = 8.5$, H–C(14)); 1.42 (*d*, $J(15,14) = 6.2$, Me(15)). $^{13}\text{C-NMR}$ (CDCl_3): 73.02 (*d*, C(1)); 201.04 (*s*, C(2)); 101.38 (*d*, C(3)); 74.73 (*d*, C(4)); 37.06 (*t*, C(5)); 86.45 (*d*, C(6)); 56.97 (*d*, C(7)); 46.40 (*t*, C(8)); 116.43 (*s*, C(9)); 49.72 (*d*, C(10)); 42.92 (*t*, C(11)); 83.52 (*d*, C(12)); 60.31 (*d*, C(13)); 77.43 (*d*, C(14)); 22.50 (*q*, C(15)). MS: 439, 441, 443, 445 (0.8, 2.1, 1.5, 0.5, $[M - \text{Br}]^+$); 401, 403, 405, 407 (38, 84, 61, 13, $[M - \text{C}_3\text{H}_2\text{Br}]^+$); 383, 385, 387 (3, 6, 4, $[M - \text{C}_3\text{H}_2\text{Br} - \text{H}_2\text{O}]^+$); 365, 367, 369 (6, 12, 6, $[M - \text{C}_3\text{H}_2\text{Br} - \text{HBr}]^+$); 285, 287 (35, 31, $[M - \text{C}_3\text{H}_2\text{Br} - \text{HBr} - \text{HCl}]^+$); 251, 253 (11, 13), 149, 151 (41, 38); 55 (100). HR-EI-MS: 400.9150 \pm 0.001 ($\text{C}_{12}\text{H}_{16}\text{Br}_2\text{ClO}_3$, $[M - \text{C}_3\text{H}_2\text{Br}]^+$; calc. 400.9154).

Obtusallene VI (= (*1S**,*3R**,*4S**,*6S**,*8S**,*9S**,*10R**)-3-Bromo-6-[(*aR*)-3-bromopropa-1,2-dienyl]-9-chloro-6-methyl-7,13,14-trioxatricyclo[8.2.1.1^{1,4}]tetradecane; **4**). UV (EtOH): 203 (15100). CD (EtOH): 223 (–7.3). $[\alpha]_D^{20} = -80$ ($c = 0.42$, EtOH). $^1\text{H-NMR}$ (C_6D_6): 5.58 (*dd*, $J(1,3) = 5.2$, $J(1,4) = 0.9$, H–C(1)); 4.92 (*dd*, $J(3,1) =$

5.2, $J(3,4) = 7.9$, H–C(3)); 4.28 (dddd, $J(4,1) = 0.9$, $J(4,5\alpha) = 1.5$, $J(4,3) = 7.9$, $J(4,5\beta) = 10.4$, H–C(4)); 1.42 (ddd, $J(5\alpha,6) \approx J(5\alpha,4) = 1.5$, $J_{\text{gem}} = 15.2$, H_{α} –C(5)); 1.94 (ddd, $J(5\beta,6) = 4.8$, $J(5\beta,4) = 10.4$, $J_{\text{gem}} = 15.2$, H_{β} –C(5)); 4.25 (ddd, $J(6,5\beta) = 4.8$, $J(6,5\alpha) = 1.5$, $J(6,7) = 7.0$, H–C(6)); 4.16 (ddd, $J(7,8\alpha) \approx J(7,6) = 7.0$, $J(7,8\beta) = 10.3$, H–C(7)); 2.06 (dd, $J(8\alpha,7) = 7.0$, $J_{\text{gem}} = 12.3$, H_{α} –C(8)); 1.88 (dd, $J(8\beta,7) = 10.3$, $J_{\text{gem}} = 12.3$, H_{β} –C(8)); 1.81–2.00 (series of *m*, 2H–C(10), 2H–C(11)); 4.16 (dddd, $J(12,11\alpha) = 6.3$, $J(12,11\beta) = 2.6$, $J(12,13) = 10.0$, H–C(12)); 3.89 (dd, $J(13,12) = 10.0$, $J(13,14) = 7.9$, H–C(13)); 3.66 (qd, $J(14,15) = 6.5$, $J(14,13) = 7.9$, H–C(14)); 1.54 (d, $J(15,14) = 6.5$, Me(15)). ^{13}C -NMR (C_6D_6): 73.21 (d, C(1)); 201.05 (s, C(2)); 102.00 (d, C(3)); 74.95 (d, C(4)); 36.86 (t, C(5)); 84.91 (d, C(6)); 57.83 (d, C(7)); 46.26 (t, C(8)); 114.92 (s, C(9)); 32.68 (t, C(10)); 30.52 (t, C(11)); 84.39 (d, C(12)); 62.47 (d, C(13)); 78.51 (d, C(14)); 24.04 (q, C(15)). MS: 361, 363, 365 (2.0, 2.4, 0.8, $[M - \text{Br}]^+$); 323, 325, 327 (62, 81, 21, $[M - \text{C}_3\text{H}_2\text{Br}]^+$); 287, 289 (8, 8, $[M - \text{C}_3\text{H}_2\text{Br} - \text{HCl}]^+$); 173 (28); 123 (84); 41 (100). HR-EI-MS: 323.0044 ± 0.001 ($\text{C}_{12}\text{H}_{17}\text{BrClO}_3^+$, $[M - \text{C}_3\text{H}_2\text{Br}]^+$; calc. 323.0049).

Obtusallene VII (= (IR*,2S*,3S*,5S*,7S*,8R*,10S*,11S*)-8,11-Dibromo-5-[(aR)-bromopropa-1,2-dienyl]-2-chloro-3-methyl-4,13-dioxabicyclo[8.2.1]tridecan-7-ol; **5**). $[\alpha]_D^{20} = -119$ ($c = 0.68$, CHCl_3). ^1H -NMR (CDCl_3): 6.07 (dd, $J(1,3) = 5.6$, $J(1,4) = 1.2$, H–C(1)); 5.32 (dd, $J(3,1) = 5.6$, $J(3,4) = 6.8$, H–C(3)); 4.62 (br. *m*, H–C(4)); 1.89 (br. *d*, $J_{\text{gem}} = 15.8$, H_{α} –C(5)); 2.34 (br. *d*, $J_{\text{gem}} = 15.8$, H_{β} –C(5)); 4.06 (*m*, H–C(6)); 4.53 (br. *m*, H–C(7)); 2.38 (*m*, 2H–C(8)); 4.27 (td, $J(9,8\alpha) = J(9,10) = 2.7$, $J(9,8\beta) = 7.0$, H–C(9)); 4.49 (ddd, $J(10,9) = 2.7$, $J(10,11\alpha) = J(10,12) = 0.6$, $J(10,11\beta) = 5.5$, H–C(10)); 2.90 (ddd, $J(11\alpha,10) = 0.6$, $J(11\alpha,12) = 6.8$, $J_{\text{gem}} = 14.9$, H_{α} –C(11)); 2.44 (ddd, $J(11\beta,10) = 5.5$, $J(11\beta,12) = 8.4$, $J_{\text{gem}} = 14.9$, H_{β} –C(11)); 4.52 (dddd, $J(12,10) = 0.6$, $J(12,11\alpha) = 6.8$, $J(12,11\beta) = 8.3$, $J(12,13) = 10.4$, H–C(12)); 3.55 (dd, $J(13,12) = 10.4$, $J(13,14) = 9.0$, H–C(13)); 3.79 (qd, $J(14,15) = 6.3$, $J(14,13) = 9.0$, H–C(14)); 1.47 (d, $J(15,14) = 6.3$, Me(15)). ^{13}C -NMR (CDCl_3): 73.55 (d, C(1)); 202.15 (s, C(2)); 100.33 (br. *d*, C(3)); 37.80 (br. *t*, C(8)); 76.14 (d, C(9)); 54.70 (d, C(10)); 45.60 (t, C(11)); 79.94 (br. *d*, C(12)); 58.01 (br. *d*, C(13)); 80.15 (br. *d*, C(14)); 23.21 (q, C(15)); the resonances of C(4) to C(7) were not detected (see text). MS: 403, 405, 407, 409 (10, 24, 17, 4, $[M - \text{C}_3\text{H}_2\text{Br}]^+$); 385, 387, 389 (2, 4, 2, $[M - \text{C}_3\text{H}_2\text{Br} - \text{H}_2\text{O}]^+$); 367, 369, 371 (4, 8, 4, $[M - \text{C}_3\text{H}_2\text{Br} - \text{HCl}]^+$); 287, 289 (7, 7, $[M - \text{C}_3\text{H}_2\text{Br} - \text{HBr} - \text{HCl}]^+$); 251, 253 (6, 6), 149, 151 (29, 26), 41 (100). HR-EI-MS: 402.9315 ± 0.001 ($\text{C}_{12}\text{H}_{18}\text{Br}_2\text{ClO}_3$, $[M - \text{C}_3\text{H}_2\text{Br}]^+$; calc. 402.9311).

Obtusallene VII (Acetate **6**). To a soln. of **5** (4 mg) in dry pyridine (0.2 ml), Ac_2O (0.2 ml) was added. The mixture was stirred overnight at r.t. Then sat. aq. CuSO_4 (2 ml) and hexane (4 ml) were added successively, and the resulting biphasic system was percolated through a Whatman phase-separation filter. The filtrate was evaporated and the residue was subjected to FC (*Si-60*, hexane/ AcOEt gradient): **6** (4.5 mg, 90%). CD (EtOH): 222 (–8.5). $[\alpha]_D^{20} = -123$ ($c = 0.22$, EtOH). ^1H -NMR (CDCl_3): 6.07 (dd, $J(1,3) = 5.6$, $J(1,4) = 1.4$, H–C(1)); 5.37 (dd, $J(3,1) = 5.6$, $J(3,4) = 6.8$, H–C(3)); 4.31 (dddd, $J(4,1) = 1.4$, $J(4,5\beta) = 1.0$, $J(4,5\alpha) = 7.9$, $J(4,3) = 6.8$, H–C(4)); 1.89 (ddd, $J(5\alpha,6) = 3.6$, $J(5\alpha,4) = 7.9$, $J_{\text{gem}} = 15.8$, H_{α} –C(5)); 2.34 (ddd, $J(5\beta,6) = 4.1$, $J(5\beta,4) = 1.0$, $J_{\text{gem}} = 15.8$, H_{β} –C(5)); 5.15 (ddd, $J(6,5\beta) = 4.1$, $J(6,5\alpha) = 3.6$, $J(6,7) = 1.3$, H–C(6)); 4.38 (ddd, $J(7,8\alpha) = 2.6$, $J(7,8\beta) = 5.3$, $J(7,6) = 1.3$, H–C(7)); 2.09 (ddd, $J(8\alpha,7) = 2.6$, $J(8\alpha,9) = 9.6$, $J_{\text{gem}} = 14.9$, H_{α} –C(8)); 2.31 (ddd, $J(8\beta,7) = 5.3$, $J(8\beta,9) = 1.3$, $J_{\text{gem}} = 14.9$, H_{β} –C(8)); 4.27 (ddd, $J(9,8\alpha) = 9.6$, $J(9,10) = 2.8$, $J(9,8\beta) = 1.4$, H–C(9)); 4.48 (ddd, $J(10,9) = 2.8$, $J(10,11\alpha) = J(10,12) = 0.6$, $J(10,11\beta) = 5.1$, H–C(10)); 2.93 (ddd, $J(11\alpha,10) = 0.6$, $J(11\alpha,12) = 6.1$, $J_{\text{gem}} = 14.9$, H_{α} –C(11)); 2.41 (ddd, $J(11\beta,10) = 5.1$, $J(11\beta,12) = 9.0$, $J_{\text{gem}} = 14.9$, H_{β} –C(11)); 4.60 (dddd, $J(12,10) = 0.6$, $J(12,11\alpha) = 6.1$, $J(12,11\beta) = 9.0$, $J(12,13) = 10.3$, H–C(12)); 3.60 (dd, $J(13,12) = 10.3$, $J(13,14) = 8.4$, H–C(13)); 3.79 (qd, $J(14,15) = 6.1$, $J(14,13) = 8.4$, H–C(14)); 1.47 (d, $J(15,14) = 6.1$, Me(15)); 2.00 (s, MeCO). ^{13}C -NMR (CDCl_3): 73.57 (d, C(1)); 201.24 (s, C(2)); 102.29 (d, C(3)); 81.35 (d, C(4)); 41.23 (t, C(5)); 76.35 (d, C(6)); 62.20 (d, C(7)); 41.04 (t, C(8)); 76.00 (d, C(9)); 54.90 (d, C(10)); 45.71 (t, C(11)); 82.06 (d, C(12)); 59.72 (d, C(13)); 81.30 (d, C(14)); 23.68 (q, C(15)); 170.41 (s, MeCO); 21.32 (q, MeCO).

Obtusallene VII *α*-Methoxy-*α*-(trifluoromethyl)benzeneacetates (**7**). Obtusallene VII (**5**; 1 mg) was treated with 5 equiv. of (+)-(*S*)-*α*-methoxy-*α*-(trifluoromethyl)benzeneacetyl chloride ((+)-(*S*)-MTPA-Cl) and 0.5 mg of 4-(dimethylamino)pyridine in dry pyridine (0.5 ml). The same procedure was followed with (–)-(*R*)-MTPA-Cl. In each case, the mixture was quenched after 3 h by addition of 1 ml of sat. aq. CuSO_4 soln., followed by 4 ml of Et_2O . The mixture was then filtered on a Whatman phase-separator, the org. phase evaporated, and the residue subjected to FC (*Si-60*, hexane/ AcOEt gradient): **7a** (t_R 9.8; 1 mg) from (–)-(*R*)-MTPA-Cl and **7b** (t_R 9.7; 1 mg) from (+)-(*S*)-MTPA-Cl.

Data of 7a: ^1H -NMR (CDCl_3 , 50°): 5.96 (br. *d*, $J(1,3) = 5.7$, H–C(1)); 5.17 (dd, $J(3,1) = 5.7$, $J(3,4) = 7.6$, H–C(3)); 4.27 (br. *t*, $J(4,5\alpha) = J(4,3) = 7.6$, H–C(4)); 1.91 (*m*, H_{α} –C(5)); 2.22 (*m*, H_{β} –C(5)); 5.36 (br. *t*, $J(6,5\beta) = J(6,5\alpha) = 4.5$, H–C(6)); 4.50 (br. *m*, H–C(7)); 2.48 (*m*, H_{α} –C(8)); 2.13 (ddd, $J(8\beta,7) = 6.6$, $J_{\text{gem}} = 14.9$, H_{β} –C(8)); 4.18 (*m*, H–C(9)); 4.44 (br. *dd*, $J(10,9) = 2.8$, $J(10,11\beta) = 4.8$, H–C(10)); 2.93 (*m*,

$H_a-C(11)$); 2.41 (*m*, $H_\beta-C(11)$); 4.60 (*br. q*, $J(12,11\alpha)=J(12,11\beta)=J(12,13)=8.4$, $H-C(12)$); 3.54 (*dd*, $J(13,12)=8.4$, $J(13,14)=10.0$, $H-C(13)$); 3.77 (*qd*, $J(14,15)=6.1$, $J(14,13)=10.0$, $H-C(14)$); 1.45 (*d*, $J(15,14)=6.1$, $Me(15)$); 7.53 (*m*, *arom.* 2H); 7.40 (*m*, *arom.* 3H); 3.55 (*s*, MeO).

Data of 7b: ^1H-NMR ($CDCl_3$, 50°): 5.98 (*br. d*, $J(1,3)=5.7$, $H-C(1)$); 5.27 (*dd*, $J(3,1)=5.7$, $J(3,4)=8.1$, $H-C(3)$); 4.37 (*m*, $H-C(4)$); 1.95 (*m*, $H_a-C(5)$); 2.38 (*m*, $H_\beta-C(5)$); 5.45 (*br. t*, $J(6,5\beta)=J(6,5\alpha)=4.9$, $H-C(6)$); 4.41 (*br. m*, $H-C(7)$); 2.43 (*m*, $H_a-C(8)$); 2.04 (*m*, $H_\beta-C(8)$); 4.14 (*m*, $H-C(9)$); 4.39 (*m*, $H-C(10)$); 2.91 (*m*, $H_a-C(11)$); 2.41 (*m*, $H_\beta-C(11)$); 4.60 (*br. q*, $J(12,11\alpha)=J(12,11\beta)=J(12,13)=8.4$, $H-C(12)$); 3.58 (*m*, $H-C(13)$); 3.79 (*qd*, $J(14,15)=6.1$, $J(14,13)=10.0$, $H-C(14)$); 1.46 (*d*, $J(15,14)=6.1$, $Me(15)$); 7.52 (*m*, 2 *arom.* H); 7.40 (*m*, 3 *arom.* H); 3.53 (*s*, MeO).

Obtusallene VIII (= $(1S^*,3S^*,5S^*,6R^*,7R^*,9S^*,10S^*)-6,9-Dibromo-3-[(aR)-3-bromopropa-1,2-dienyl]-5-methyl-4,13-dioxabicyclo[8.2.1]tridec-11-ene-7,10-diol$; **8**). $[\alpha]_D^{20} = -11.3$ ($c=0.33$, $CHCl_3$). ^1H-NMR ($CDCl_3$): 6.02 (*d*, $J(1,3)=5.6$, $H-C(1)$); 5.37 (*dd*, $J(3,1)=5.6$, $J(3,4)=8.6$, $H-C(3)$); 3.88 (*br. t*, $J(4,3)=J(4,5\beta)=8.6$, $H-C(4)$); 1.83 (*br. dd*, $J(5\alpha,6)=3.3$, $J_{gem}=16.1$, $H_a-C(5)$); 2.37 (*ddd*, $J(5\beta,6)=3.5$, $J(5\beta,4)=8.3$, $J_{gem}=15.9$, $H_\beta-C(5)$); 5.27 (*q*, $J(6,5\beta)\approx J(6,5\alpha)\approx J(6,7)=3.3$, $H-C(6)$); 6.42 (*dd*, $J(7,8)=6.0$, $J(7,6)=3.0$, $H-C(7)$); 6.12 (*br. d*, $J(8,7)=6.0$, $H-C(8)$); 4.63 (*dd*, $J(10,11\alpha)=10.6$, $J(10,11\beta)=1.5$, $H-C(10)$); 2.04 (*m*, 2 $H-C(11)$); 4.39 (*m*, $H-C(12)$); 4.02 (*dd*, $J(13,12)=3.0$, $J(13,14)=10.1$, $H-C(13)$); 3.55 (*qd*, $J(14,15)=5.9$, $J(14,13)=10.1$, $H-C(14)$); 1.46 (*d*, $J(15,14)=5.9$, $Me(15)$). $^{13}C-NMR$ ($CDCl_3$): 73.51 (*d*, C(1)); 200.29 (*s*, C(2)); 102.81 (*d*, C(3)); 76.28 (*d*, C(4)); 38.96 (*t*, C(5)); 84.04 (*d*, C(6)); 130.92 (*d*, C(7)); 134.94 (*d*, C(8)); 112.68 (*s*, C(9)); 51.59 (*d*, C(10)); 41.05 (*t*, C(11)); 69.47 (*d*, C(12)); 66.72 (*d*, C(13)); 79.08 (*d*, C(14)); 20.87 (*q*, C(15)).

Obtusallene IX (= *Obtusallene VIII 12-Acetate*; **9**). UV (MeCN): 205 (13100). CD (MeCN): 222 (-7.6). $[\alpha]_D^{20} = -24$ ($c=0.12$, $CHCl_3$). ^1H-NMR ($CDCl_3$): 6.02 (*d*, $J(1,3)=5.6$, $J(1,4)=0.9$, $H-C(1)$); 5.37 (*dd*, $J(3,1)=5.6$, $J(3,4)=8.6$, $H-C(3)$); 3.88 (*tt*, $J(4,1)\approx J(4,5\alpha)=1.0$, $J(4,3)=J(4,5\beta)=8.6$, $H-C(4)$); 1.82 (*ddd*, $J(5\alpha,4)=1.2$, $J(5\alpha,6)=3.5$, $J_{gem}=15.9$, $H_a-C(5)$); 2.42 (*ddd*, $J(5\beta,6)=3.2$, $J(5\beta,4)=8.6$, $J_{gem}=15.9$, $H_\beta-C(5)$); 5.26 (*q*, $J(6,5\beta)\approx J(6,5\alpha)\approx J(6,7)=3.2$, $H-C(6)$); 6.42 (*dd*, $J(7,8)=6.0$, $J(7,6)=2.7$, $H-C(7)$); 6.15 (*br. d*, $J(8,7)=6.0$, $H-C(8)$); 4.20 (*dd*, $J(10,11\beta)=1.2$, $J(10,11\alpha)=10.7$, $H-C(10)$); 1.99 (*ddd*, $J(11\alpha,10)=10.7$, $J(11\alpha,12)=1.0$, $J_{gem}=14.9$, $H_a-C(11)$); 2.42 (*ddd*, $J(11\beta,12)=10.8$, $J(11\beta,10)=1.2$, $J_{gem}=14.9$, $H_\beta-C(11)$); 5.60 (*ddd*, $J(12,11\alpha)=1.0$, $J(12,11\beta)=10.6$, $J(12,13)=2.9$, $H-C(12)$); 4.08 (*dd*, $J(13,12)=2.9$, $J(13,14)=10.0$, $H-C(13)$); 3.51 (*qd*, $J(14,15)=6.0$, $J(14,13)=10.0$, $H-C(14)$); 1.43 (*d*, $J(15,14)=6.0$, $Me(15)$); 2.13 (*s*, MeCO). $^{13}C-NMR$ ($CDCl_3$): 73.91 (*d*, C(1)); 200.60 (*s*, C(2)); 103.36 (*d*, C(3)); 77.78 (*d*, C(4)); 39.31 (*t*, C(5)); 84.43 (*d*, C(6)); 131.17 (*d*, C(7)); 135.59 (*d*, C(8)); 112.82 (*s*, C(9)); 51.04 (*d*, C(10)); 37.73 (*t*, C(11)); 73.06 (*d*, C(12)); 59.58 (*d*, C(13)); 79.66 (*d*, C(14)); 20.88 (*q*, C(15)); 171.19 (*s*, MeCO); 21.64 (*q*, MeCO). MS: 444, 446, 448 (3, 6, 3, $[M-HBr-H_2O]^+$); 402, 404, 406 (0.4, 0.8, 0.4, $[M-HOAc-HBr]^+$); 385, 387, 389 (0.4, 0.8, 0.4, $[M-HOAc-HBr-OH]^+$); 365, 367 (2.2, 2.2, $[M-BrOH-HBr]^+$); 323, 325 (7, 7, $[M-HOAc-BrOH-HBr]^+$); 305, 307 (20, 20); 225 (10); 177 (24); 159 (20); 107 (20); 43 (100).

Degradation of Obtusallene IX (9). A soln. of **9** (10 mg) in $CDCl_3$ (0.5 ml) was monitored directly in the ^1H-NMR probe heated at 40° . Within a few min, signals emerged for **10** and persisted long enough for observation. The mixture was evaporated, hexane/ i PrOH 9:1 (0.5 ml) added, and the mixture finally subjected to HPLC (*RPI8*, MeOH/ H_2O 4:1): **14** (t_R 6.3), **13** (t_R 7.0), **12** (t_R 8.3), **11b** (t_R 8.5), **11a** (t_R 9.4).

Data of (3S,5S,6R,7R,9S)-6,9-Dibromo-3-[(aR)-3-bromopropa-1,2-dienyl]-5-methyl-4,13-dioxabicyclo[8.2.1]trideca-10,12-dien-7-ol Acetate (10): ^1H-NMR ($CDCl_3$): 6.02 (*br. d*, $J(1,3)=6.6$, $H-C(1)$); 5.37 (*br. t*, $J(3,1)=J(3,4)=6.6$, $H-C(3)$); 4.58 (*br. q*, $J(4,5\alpha)=J(4,3)=J(4,5\beta)=6.6$, $H-C(4)$); 2.98 (*m*, $J_{gem}=15.9$, $CH_2(5)$); 6.36 (*d*, $J(7,8)=3.2$, $H-C(7)$); 6.08 (*br. d*, $J(8,7)=3.2$, $H-C(8)$); 5.18 (*dd*, $J(10,11\beta)=4.4$, $J(10,11\alpha)=12.0$, $H-C(10)$); 2.47, 2.90 (2 *m*, 2 $H-C(11)$); 4.29 (*br. d*, $J(12,11\beta)=7.3$, $H-C(12)$); 4.08 (*br. d*, $J(13,14)=9.6$, $H-C(13)$); 4.03 (*qd*, $J(14,15)=6.5$, $J(14,13)=9.6$, $H-C(14)$); 1.51 (*d*, $J(15,14)=6.6$, $Me(15)$); 2.13 (*s*, MeCO). $^{13}C-NMR$ ($CDCl_3$): 74.25 (*d*, C(1)); 207.79 (*s*, C(2)); 102.37 (*d*, C(3)); 74.31 (*d*, C(4)); 42.68 (*t*, C(5)); 151.40 (*s*, C(6)); 111.96 (*d*, C(7)); 108.52 (*d*, C(8)); 151.20 (*s*, C(9)); 40.71 (*d*, C(10)); 32.83 (*t*, C(11)); 71.31 (*d*, C(12)); 60.48 (*d*, C(13)); 76.41 (*d*, C(14)); 19.40 (*q*, C(15)); 170.18 (*s*, MeCO); 21.05 (*q*, MeCO). MS: 444, 446, 448 (2.4, 4.6, 2.4, $[M-HBr]^+$); 385, 387, 389 (1.1, 2.2, 1.1, $[M-HOAc-Br]^+$); 365, 367 (2, 2, $[M-BrOH-HBr]^+$); 323, 325 (5, 5); 305, 307 (16, 16); 225 (7); 177 (18); 159 (16); 107 (18); 43 (100).

Data of (3S,5S*,6R*,7R*)-6-Bromo-3-[(aR)-3-bromopropa-1,2-dienyl]-5-methyl-4,13-dioxabicyclo[8.2.1]trideca-8,10,12-trien-7-ol Acetate (11a)*: ^1H-NMR ($CDCl_3$): 6.09 (*d*, $J(1,3)=5.8$, $J(1,4)=1.0$, $H-C(1)$); 5.49 (*t*, $J(3,1)=J(3,4)=5.8$, $H-C(3)$); 3.94 (*tdd*, $J(4,1)\approx J(4,5\alpha)=1.0$, $J(4,3)=5.8$, $J(4,5\beta)=10.7$, $H-C(4)$); 2.75 (*dd*,

2) The numbering of **9** is retained.

$J(5\alpha,4) = 1.0$, $J_{\text{gem}} = 14.9$, $H_{\alpha}-C(5)$; 2.95 (*ddd*, $J(5\beta,7) = 1.2$, $J(5\beta,4) = 10.7$, $J_{\text{gem}} = 14.9$, $H_{\beta}-C(5)$); 6.05 (*dd*, $J(7,8) = 3.2$, $J(7,5\beta) = 1.2$, $H-C(7)$); 6.18 (*br. d.*, $J(8,7) = 3.2$, $H-C(8)$); 6.28 (*dd*, $J(10,11) = 11.8$, $J(10,12) = 1.5$, $H-C(10)$); 5.32 (*dd*, $J(11,10) = 11.8$, $J(11,12) = 6.7$, $H-C(11)$); 6.99 (*td*, $J(12,11) = 6.7$, $J(12,10) = J(12,13) = 1.5$, $H-C(12)$); 4.01 (*dd*, $J(13,12) = 1.5$, $J(13,14) = 10.3$, $H-C(13)$); 3.23 (*qd*, $J(14,15) = 6.0$, $J(14,13) = 10.3$, $H-C(14)$); 1.36 (*d.*, $J(15,14) = 6.0$, $\text{Me}(15)$); 2.10 (*s.*, MeCO). $^{13}\text{C-NMR}$ (CDCl_3): 74.19 (*d.*, $\text{C}(1)$); 202.56 (*s.*, $\text{C}(2)$); 102.08 (*d.*, $\text{C}(3)$); 75.37 (*d.*, $\text{C}(4)$); 33.32 (*t.*, $\text{C}(5)$); 152.00 (*s.*, $\text{C}(6)$); 107.24 (*d.*, $\text{C}(7)$); 109.82 (*d.*, $\text{C}(8)$); 150.32 (*s.*, $\text{C}(9)$); 126.57 (*d.*, $\text{C}(10)$); 118.34 (*d.*, $\text{C}(11)$); 71.91 (*d.*, $\text{C}(12)$); 61.60 (*d.*, $\text{C}(13)$); 76.57 (*d.*, $\text{C}(14)$); 19.86 (*q.*, $\text{C}(15)$); 170.37 (*s.*, MeCO); 21.32 (*q.*, MeCO). MS: 444, 446, 448 (1.1, 2.2, 1.1, M^{+}); 401, 403, 405 (0.4, 0.8, 0.4, $[M - \text{MeCO}]^{+}$); 365, 367 (1.5, 1.5, $[M - \text{Br}]^{+}$); 323, 325 (4, 4); 305, 307 (9, 9); 225 (4); 177 (17); 159 (10); 107 (16); 43 (100).

Data of (3S*,5S*,6R*,7R*)-6-Bromo-3-[(aR)-3-bromopropa-1,2-dienyl]-5-methyl-4,13-dioxabicyclo[8.2.1]-trideca-8,10,12-trien-7-ol (**11b**): $^1\text{H-NMR}$ (CDCl_3): 6.08 (*d.*, $J(1,3) = 5.8$, $J(1,4) = 2.0$, $H-C(1)$); 5.49 (*t.*, $J(3,1) = J(3,4) = 5.8$, $H-C(3)$); 3.95 (*td*, $J(4,1) \approx J(4,5\alpha) = 2.0$, $J(4,3) = 5.8$, $J(4,5\beta) = 10.6$, $H-C(4)$); 2.75 (*dd*, $J(5\alpha,4) = 2.0$, $J_{\text{gem}} = 15.3$, $H_{\alpha}-C(5)$); 2.89 (*br. dd.*, $J(5\beta,4) = 10.7$, $J_{\text{gem}} = 15.3$, $H_{\beta}-C(5)$); 6.05 (*dd.*, $J(7,8) = 3.0$, $J(7,5\beta) = 1.2$, $H-C(7)$); 6.15 (*br. d.*, $J(8,7) = 3.0$, $H-C(8)$); 6.23 (*dd.*, $J(10,11) = 11.7$, $J(10,12) = 1.4$, $H-C(10)$); 5.35 (*dd.*, $J(11,10) = 11.7$, $J(11,12) = 6.6$, $H-C(11)$); 5.91 (*br. d.*, $J(12,11) = 6.6$, $H-C(12)$); 4.10 (*dd.*, $J(13,12) = 1.8$, $J(13,14) = 10.2$, $H-C(13)$); 3.23 (*qd.*, $J(14,15) = 5.8$, $J(14,13) = 10.3$, $H-C(14)$); 1.36 (*d.*, $J(15,14) = 5.8$, $\text{Me}(15)$); 2.11 (*s.*, MeCO). $^{13}\text{C-NMR}$ (CDCl_3): 74.11 (*d.*, $\text{C}(1)$); 102.21 (*d.*, $\text{C}(3)$); 75.24 (*d.*, $\text{C}(4)$); 33.28 (*t.*, $\text{C}(5)$); 107.18 (*d.*, $\text{C}(7)$); 109.45 (*d.*, $\text{C}(8)$); 130.80 (*d.*, $\text{C}(10)$); 117.31 (*d.*, $\text{C}(11)$); 69.12 (*d.*, $\text{C}(12)$); 67.02 (*d.*, $\text{C}(13)$); 20.18 (*q.*, $\text{C}(15)$); quaternary C could not be detected because of the too-small sample size. MS: 402, 404, 406 (5.5, 11.0, 5.5, M^{+}); 323, 325 (13, 13); 305, 307 (7, 7); 243 (19); 177 (54); 159 (11); 107 (88).

Data of ((3S,5S,6R,7R,9S)-6-Bromo-3-[(aR)-3-bromopropa-1,2-dienyl]-9-isopropoxy-5-methyl-4,13-dioxabicyclo[8.2.1]trideca-10,12-dien-7-ol Acetate; **12**): $^1\text{H-NMR}$ (CDCl_3 ; relevant signals only): 6.06 (*dd.*, $J(1,3) = 5.7$, $J(1,4) = 1.3$, $H-C(1)$); 5.41 (*br. t.*, $J(3,1) = J(3,4) = 5.7$, $H-C(3)$); 4.49 (*m.*, $H-C(4)$); 2.91 (*m.*, $2H-C(5)$); 6.00 (*m.*, $H-C(7)$); 6.25 (*m.*, $H-C(8)$); 4.53 (*m.*, $H-C(10)$); 2.14, 2.28 (2 *m.*, $2H-C(11)$); 4.37 (*m.*, $H-C(12)$); 3.88 (*m.*, $H-C(13)$); 3.85 (*m.*, $H-C(14)$); 1.46 (*m.*, $\text{Me}(15)$); 3.78 (*m.*, Me_2CHO); 1.15 (*m.*, Me_2CHO); 2.03 (*s.*, MeCO). $^{13}\text{C-NMR}$ (CDCl_3): 73.93 (*d.*, $\text{C}(1)$); 102.65 (*d.*, $\text{C}(3)$); 70.43 (*d.*, $\text{C}(4)$); 33.68 (*t.*, $\text{C}(5)$); 153.01 (*s.*, $\text{C}(6)$); 107.43 (*d.*, $\text{C}(7)$); 111.47 (*d.*, $\text{C}(8)$); 151.54 (*s.*, $\text{C}(9)$); 76.00 (*d.*, $\text{C}(10)$); 38.75 (*t.*, $\text{C}(11)$); 74.31 (*d.*, $\text{C}(12)$); 61.18 (*d.*, $\text{C}(13)$); 77.80 (*d.*, $\text{C}(14)$); 19.99 (*q.*, $\text{C}(15)$); 69.72 (*d.*, Me_2CHO); 23.16 (2*q.*, Me_2CHO); 21.68 (*q.*, MeCO). MS: 504, 506, 508 (0.3, 0.6, 0.3, M^{+}); 461, 463, 465 (0.7, 1.4, 0.7); 425, 427 (0.6, 0.6, $[M - \text{Br}]^{+}$); 401, 403, 405 (1.2, 2.4, 1.2, $[M - \text{Me}_2\text{CHO} - \text{MeCO}]^{+}$); 365, 367 (2.5, 2.5); 323, 325 (4.4, 4.4); 305, 307 (3, 3); 243 (4); 177 (27); 159 (5); 107 (21); 43 (100).

Data of **13** and **14**: $^1\text{H-NMR}$ (CDCl_3): very broad and almost superimposable to the signals of **12**.

Ketalization of Obtusallene IX (**9**). On storage in MeOH at 0° for many weeks, **9** underwent partial ketalization (ca. 60%) to give (3S,5S,6R,7R,9S,10S)-6,9-bromo-3-[(aR)-bromopropa-1,2-dienyl]-10-methoxy-5-methyl-4,13-dioxabicyclo[8.2.1]trideca-11-en-7-ol acetate (**15**): $^1\text{H-NMR}$ (CDCl_3 ; on quick recording, otherwise a rapid transformation into **10** occurred; relevant signals only): 5.19 (*dq.*, $J(6,5\beta) \approx J(6,5\alpha) \approx J(6,7) = 3.2$, $H-C(6)$); 6.23 (*m.*, $H-C(7)$, $H-C(8)$); 4.22 (*dd.*, $J(10,11\beta) = 1.2$, $J(10,11\alpha) = 10.7$, $H-C(10)$); 5.51 (*ddd.*, $J(12,11\alpha) = 1.0$, $J(12,11\beta) = 10.6$, $J(12,13) = 2.9$, $H-C(12)$); 1.42 (*d.*, $J(15,14) = 6.0$, $\text{Me}(15)$); 2.13 (*s.*, MeCO), 3.24 (*s.*, MeO).

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