# 27. On the Unusual Propensity by the Red Seaweed *Laurencia microcladia* of Il Rogiolo to Form $C_{15}$ Oxepanes: Isolation of Rogioloxepane A, B, C, and Their Likely Biogenetic Acyclic Precursor, Prerogioloxepane

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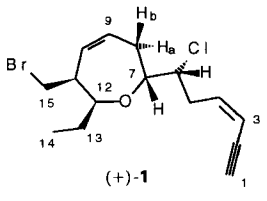
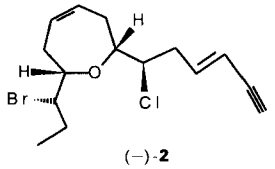
It is shown here that the red seaweed *Laurencia microcladia* KÜTZNING, collected in the Mediterranean off the torrent Il Rogiolo, contains the $C_{15}$ acetogenin rogioloxepane A (= *(+)-(2R,7R)-2-(1-bromopropyl)-7-[(Z)-1-chlorohex-3-en-5-ynyl]-2,3,6,7-tetrahydrooxepin*; (+)-**3**) besides its epoxy derivative rogioloxepane B ((+)-**4**) and the rogioloxepane C ((+)-**5**) derived from (+)-**4** by epoxide opening. Co-occurring is an acyclic $C_{15}$ acetogenin, prerogioloxepane (= (7*R*,3*Z*,9*Z*,12*Z*)-6-chloropentadeca-3,9,12-trien-1-yn-7-ol; **9**), which exists preferentially in a folded conformation as required to give, by intramolecular cyclization, rogioloxepane A (**3TC**) in its favored twist-chair form. Molecular-mechanics calculations support this view and help also to assign the relative configurations at the side chains, whereas the configurations at the seven-membered ring are established *via* NMR spectroscopy and chemical correlations. The absolute configuration is established by *Mosher*'s NMR method applied to the MTPA esters of (+)-**5** or **9**.

**1. Introduction.** – Red seaweeds of the genus *Laurencia* are unique in producing $C_{15}$ acetogenins which end in an enyne or bromoallene group [1]. These compounds may be transferred from these seaweeds to opisthobranch mollusks of the genus *Aplysia* as dietary products [1] [2] and, albeit much less frequently, to sponges, too, possibly *via* spore filtering [3] [4]. Most of these acetogenins have O-heterocyclic structure, while a few are carbocyclic, in both cases based on a linear $C_{15}$ chain [1]. Acyclic $C_{15}$ acetogenins have also been isolated [1].

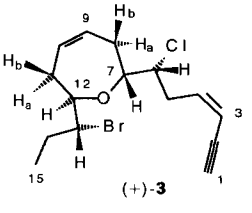
The only known exceptions to this linearity rule are constituted by oxepanes with bromomethyl side chain at C(11)[1]), which are called rogiolenynes [3], such as rogiolenyne D ((+)-**1**) [3a], isolated from *Laurencia microcladia* collected in the Mediterranean off the torrent Il Rogiolo.




(+)-**1**




(–)-**2**




(+)-**3**

[1]) Systematic numbering for the oxepanes is only used here for retrieval purposes (*Exper. Part* and *Abstract*), while all experimental data are discussed in terms of the numbering indicated in formula (+)-**3**.

Excepting the rogiolenynes [3], the only known examples of natural $C_{15}$ oxepanes are the non-branched isolaurepinnacin ((−)-**2**; isolated from *Laurencia pinnata* of Motsuta Point, Hokkaido [5a]), (3*Z*)-isoprelaurefucin (isolated from both *Laurencia nipponica* of Asarai and Hariusu, Hokkaido [5b] and *Laurencia subopposita* of La Jolla, California [5c]), and the isomeric (3*E*)-isoprelaurefucin (isolated from both *L. subopposita* [5c] and *L. nipponica* of Mokeji [5d]).

In contrast with the scarce occurrence of $C_{15}$ oxepanes, natural eight-membered O-heterocyclic $C_{15}$ acetogenins (oxocanes) [1] [6] and five-membered O-heterocycles [1] [7] occur widely, while examples of six- [1] [8], nine- [1] [9], and twelve-membered O-heterocycles [1] [10], or a combination of them [1] [11] [12], are also known.

Due to their wide occurrence, oxocanes have been frequent synthetic targets, although, owing to intrinsic difficulties, only two complete of total syntheses have been reported [13]. In contrast, only a few models for oxepanes have been taken into consideration as synthetic targets [14].

Co-occurring hydroxylated acyclic $C_{15}$ acetogenins have been suggested as the biogenetic precursors of these cyclic ethers [1] [15]. Biosynthetic experiments with bromoperoxidases (which are the implied enzymes of seaweeds of the genus *Laurencia*) failed, however, presumably because of their extreme lability [16]. Lactoperoxidase, which belongs to the same family of enzymes but is more stable, succeeded instead, in the presence of NaBr and $H_2O_2$, in inducing the cyclization of C(6)–C(7) dihydroxy-functionalized acyclic $C_{15}$ acetogenins to oxocanes, albeit in extremely poor yields [16]. This indicates that the high propensity by seaweeds of the genus *Laurencia* to give oxocanes can be imputed not only to the availability in these seaweeds of acyclic $C_{15}$ acetogenins which bear a single OH group at C(6) [1] [15], but also to an intrinsic preference for closure to an eight-membered O-heterocycle, when both OH–C(6) and OH–C(7), or a single OH–C(7) group is available, such as in the presumptive precursor of laurepinnacin [5a] [16].

Following the above reasoning, the rarity of natural $C_{15}$ oxepanes may also reflect scarce availability of acyclic $C_{15}$ acetogenins with a single OH group at C(7), which, to our knowledge, actually have never been isolated. Just because of the unusual abundance of branched oxepanes in this seaweed [3], we were thus prompted to look for such elusive acetogenins with OH–C(7) moiety, in *L. microcladia* of Il Rogiolo. We report here on our successful isolation, from this seaweed, not only of such an acyclic $C_{15}$ acetogenin, but also of oxepanes that most likely descend biogenetically from it.

**2. Results and Discussion.** – Further examination of the chromatographic fractions from previous extracts *L. microcladia* [3] has now given three novel non-branched $C_{15}$ acetogenins with oxepane structure and one novel acyclic $C_{15}$ acetogenin (*Exper. Part*) which are presented below.

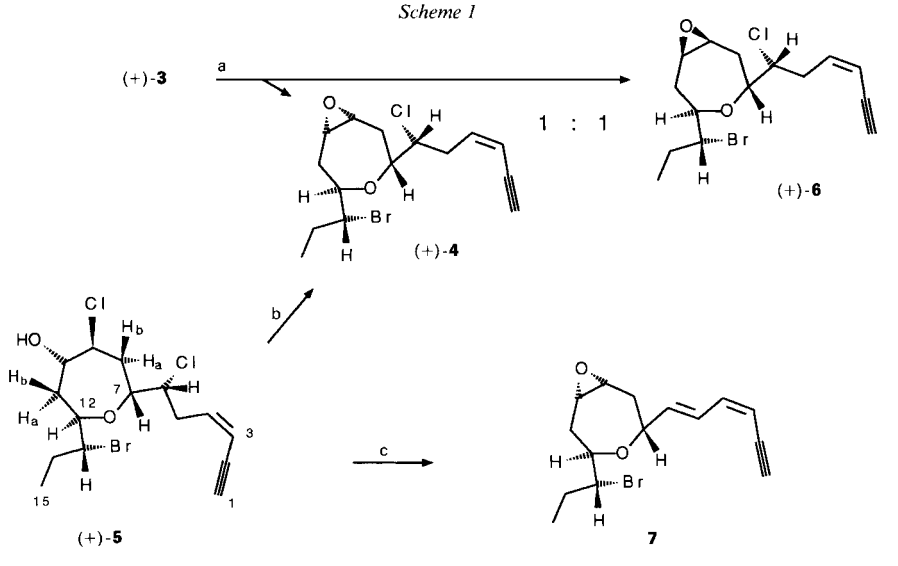
2.1. *Relative Configurations at the Seven-Membered Ring and Chemical Correlations of the Rogioloxepanes.* NMR and MS data (*Table* and *Exper. Part*) indicate for the first novel product isolated from *L. microcladia* the molecular formula $C_{15}H_{20}BrClO$. Since comparison with previous data [3a] immediately suggested an unbranched oxepane structure, to avoid difficulties with *Laurencia* taxonomy and biochemical variability [3b], this compound was called rogioloxepane A ((+)-**3**) referring to the place of collection of our seaweed.

Table. *$^{13}$C-NMR Data* ($CDCl_3$) *for Rogioloxepane A* ((+)-**3**), *B* ((+)-**4**), *C* ((+)-**5**), *and Prerogioloxepane* (**9**)

| C-atom | (+)-**3** | (+)-**4** | (+)-**5** | **9** |
|---|---|---|---|---|
| C(1) | 82.38 (*d*) | 82.50 (*d*) | 82.51 (*d*) | 82.75 (*d*) |
| C(2) | 79.96 (*s*) | 79.53 (*s*) | 79.86 (*s*) | not detected |
| C(3) | 110.66 (*d*) | 110.85 (*d*) | 110.84 (*d*) | 111.17 (*d*) |
| C(4) | 141.42 (*d*) | 140.97 (*d*) | 141.06 (*d*) | 140.43 (*d*) |
| C(5) | 34.92 (*t*) | 34.37 (*t*) | 35.17 (*t*) | 35.65 (*t*) |
| C(6) | 64.41 (*d*) | 62.86 (*d*) | 64.70 (*d*) | 65.63 (*d*) |
| C(7) | 77.03 (*d*) | 69.49 (*d*) | 72.20 (*d*) | 73.02 (*d*) |
| C(8) | 31.08 (*t*) | 32.74 (*t*) | 33.12 (*t*) | 32.55 (*t*) |
| C(9) | 128.17 (*d*) | 53.86 (*d*) | 60.50 (*d*) | 132.33 (*d*) |
| C(10) | 127.85 (*d*) | 53.44 (*d*) | 71.15 (*d*) | 124.11 (*d*) |
| C(11) | 32.63 (*t*) | 29.10 (*t*) | 33.72 (*t*) | 25.72 (*t*) |
| C(12) | 77.06 (*d*) | 75.58 (*d*) | 71.78 (*d*) | 131.90 (*d*) |
| C(13) | 62.78 (*d*) | 63.47 (*d*) | 63.10 (*d*) | 126.58 (*d*) |
| C(14) | 28.43 (*t*) | 29.07 (*t*) | 28.36 (*t*) | 20.58 (*t*) |
| C(15) | 12.78 (*q*) | 12.74 (*q*) | 12.73 (*q*) | 14.25 (*q*) |

All one-bond $^1$H,$^{13}$C correlations for rogioloxepane A ((+)-**3**) are established by $^{13}$C,$^1$H-COSY experiments, while the whole C-skeleton is established by the $^1$H,$^1$H-COSY spectrum (*Fig. 1*). The 1D-NMR spectra of rogioloxepane A ((+)-**3**; *Table* and *Exper. Part*) resemble those for rogiolenyne D ((+)-**1**) [3b], except for the absence of the signals for the two diastereotopic protons ($\delta$(H) = 3.63 (*dd*) and 3.26 (*t*)) at C(15) ($\delta$(C(15)) = 33.65 (*t*)) and the methine proton ($\delta$(H) = 2.74 (*m*)) at C(11) ($\delta$(C(11)) = 47.58 (*d*)) of (+)-**1**, which are replaced, with (+)-**3**, by the signals $\delta$(H) = 2.71 (*m*) and 2.23 (*m*), attributable to the two diastereotopic protons at C(11) ($\delta$(C(11)) = 32.63 (*t*) and $\delta$(H) 3.91 (*ddd*)), attributable to *H*–C(13) ($\delta$(C(13)) = 62.78 (*d*)).

*Scheme 1*




a) 1. MCPBA/$CH_2Cl_2$; 2. HPLC (*Si-60*). b) $K_2CO_3$/MeOH, 5°, 2 h. c) $K_2CO_3$/MeOH, r.t., 24 h.

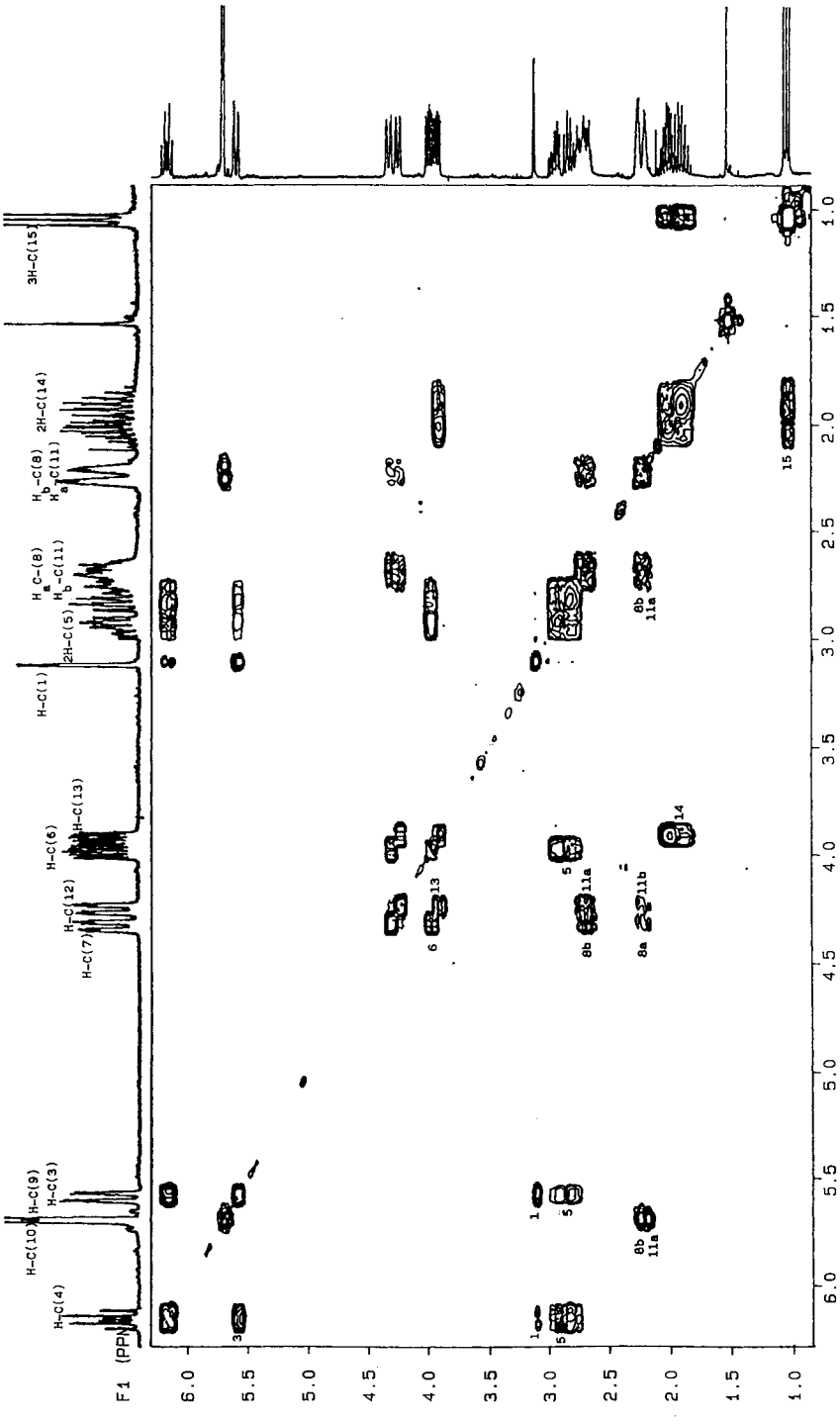



Fig. 1. *COSY 120° Contour plot for rogioloxepane A* ((+)-**3**). Numbering at the contour maps refers to the ordinate scale

Rogioloxepane A ((+)-**3**) is isomeric with isolaurepinnacin ((−)-**2**) [5a], the (*Z*)-configuration of the C(3)=C(4) bond being reflected in a $J(3,4) = 10.8$ Hz, while the *trans*-relationship between the two side chains is best established by chemical correlation with (+)-**5** (*Scheme 1*), where, as shown below, the *trans*-relationship rests unequivocally on NOE data and $Eu(fod)_3$-induced shift. The different configurational relationship between the side chains in the isomers is reflected in a large difference in the resonances of the H−C(7) and H−C(12) groups: downfield shift, by *ca.* 0.7 ppm, of the $^1H$ resonances, and upfield shift, by *ca.* 4 ppm, of the $^{13}C$ resonances for (+)-**3** (*Exper. Part* and *Table*) with respect to (−)-**2** [5a]. In contrast, $J$(H,H) values for coupling with either H−C(7) or H−C(12) are very similar in the two isomers; this suggests that the seven-membered ring takes a different conformation in the two isomers in order to place both side chains in the pseudoequatorial position in any case.

Two new compounds of higher polarity were also isolated from *L. microcladia*. Because of their close structural relationship with (+)-**3**, they have been called rogioloxepane B ((+)-**4**) and C ((+)-**5**; *Scheme 1*). NMR and MS data (*Table* and *Exper. Part*) indicate the molecular formula $C_{15}H_{20}BrClO_2$ for (+)-**4**, *i.e.* the same degree of unsaturation as, but one O-atom more, than (+)-**3**. This suggests that we are dealing with a product of epoxidation of (+)-**3** at a C=C bond; that epoxidation must have occurred at C(9)=C(10) bond is shown by the absence of the signals of H−C(9) and H−C(10) of (+)-**3**, replaced by $\delta(H) = 3.24$ and 3.18, which are correlated to the $\delta(C) = 53.86$ (*d*) and 53.44 (*d*), respectively.

Analogously, the molecular formula $C_{15}H_{21}BrCl_2O_2$ is indicated for (+)-**5**, suggesting one unsaturation less, but one H- and one Cl-atom more than with either (+)-**3** or (+)-**4**. This implies opening of the epoxy moiety of (+)-**5** by $Cl^-$ to form a chlorohydrin; that attack by $Cl^-$ must have occurred at C(9) is indicated by one-bond heteronuclear correlation of H−C(9) (which is unequivocally assigned by selective irradiation at H−C(8)) with the C-atom with $\delta(C) = 60.50$ (*d*). That H−C(9) occupies the pseudoequatorial position is indicated by its small vicinal couplings ($J = 2.7$ and 4.6 Hz) and *W* coupling (1.6 Hz) with $H_a$−C(11). Similar evidence indicates that also H−C(10) occupies the pseudoequatorial position (*W* coupling between H−C(10) and $H_b$−C(8) is observed). The *trans*-relationship between the two side chains is unequivocally established by two series of experiments. First, NOE effects were observed at $H_b$−C(11) (on irradiation at H−C(7)) and at $H_a$−C(8) (on irradiation at H−C(12)). Second, on addition of $Eu(fod)_3$, H−C(12) underwent a larger deshielding than H−C(7).

The above conclusions find further support in the chemical transformations indicated in *Scheme 1*. Thus, epoxidation of (+)-**3** led to a 1:1 mixture of rogioloxepane B ((+)-**4**) and its unnatural isomer isorogioloxepane B ((+)-**6**) with inverted configuration at the C-atoms involved in the epoxy moiety. Moreover, mild alkaline treatment of (+)-**5** for short times led to (+)-**4**. On prolonged treatment, epoxide ring closure from the chlorohydrin portion was followed by dehydrochlorination in the enyne chain, leading to the unnatural dehydrochlororogioloxepane B (**7**). The presence of the additional C=C bond and its configuration are supported by the $^1H$-NMR pattern for the dienyne system (*Exper. Part*).

2.2. *Conformational Analysis and Relative Configurations at the Side Chains of the Rogioloxepanes.* A rationalization of the stereochemical course of the epoxidation of rogioloxepane A ((+)-**3**) and, in analogy with the rogioloxepanes [3b], the assignment of

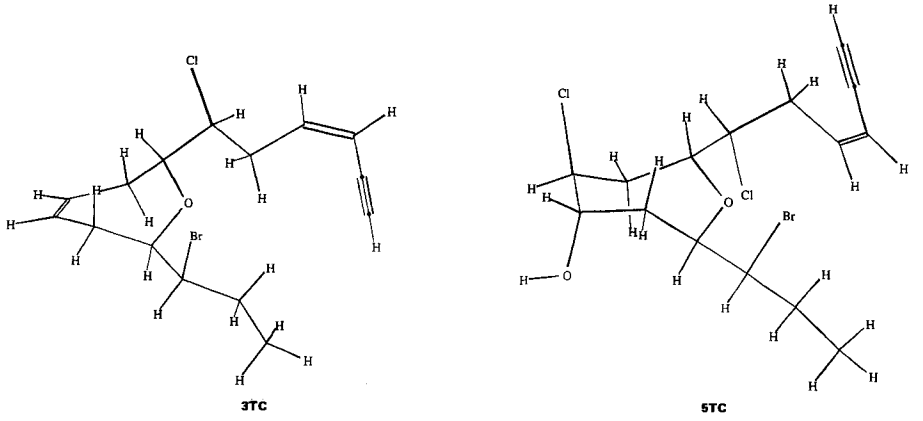



Fig. 2. a) *Preferred twist-chair conformation of rogioloxepane A* (**3TC**); b) *preferred twist-chair conformation of rogioloxepane C* (**5TC**), *as inferred from molecular-mechanics calculations*

the relative configurations at the halogen-bearing positions of the side chains require assessment of the preferred conformations. This has been attempted through molecular-mechanics calculations [17] which resulted in the displays at *Fig. 2* for (+)-**3**. According to this analysis, in the preferred conformation **3TC** the 2,3,6,7-tetrahydrooxepin ring is a twist chair, while the side chains are pseudoequatorially disposed. The near equivalence of the two faces of the C(9)=C(10) bond explains the lack of stereoselectivity in the epoxidation of (+)-**1** (*Scheme 1*).

As concerns the configuration at the side chains, molecular-mechanics calculations have been carried out for both the *threo*- and the *erythro*-configurations. In the *threo*-case, the preferred conformation turns out to have the values +64° and −62° for the dihedral angles H–C(7)–C(6)–H and H–C(12)–C(13)–H, respectively, while all other conformations with gauche H–C(7)–C(6)–H and H–C(12)–C(13)–H protons contribute significantly. In contrast, in the *erythro*-case the less strained conformation has these protons in *'anti'*-relationship. Values of $J(7,6)$ and $J(13,12)$ as low as 2.5–3 Hz are in accordance with the *threo*-assignment which is also in line with expectations from *anti* addition at the (*Z*)-C(12)=C(13) bond of the precursor.

In the lowest-energy rigid chair form, the longest side chain takes the pseudoequatorial position, while the shortest chain is constricted in the pseudoaxial position; this results in 4.7 Kcal·mol$^{-1}$ higher strain energy than with **3TC**. In contrast, our molecular-mechanics calculations indicate that with isolaurepinnacin ((−)-**2**) [5a], the rigid chair, where both side chains are in pseudoequatorial position, is preferred by 5.8 Kcal·mol$^{-1}$ over the twist-chair form.

Similar calculations indicate that the less strained conformer of rogioloxepane C ((+)-**5**) takes preferentially the twist-chair form **5TC** (*Fig. 2*).

2.3. *Absolute Configuration of the Rogioloxepanes.* We have recently found practical [3b] to establish the absolute configuration of C(11)-branched oxepane (rogiolenyne) [3b] *via Mosher*'s NMR method [18] applied to the MTPA esters. Followings this line [3b], the diastereoisomeric MTPA esters (+)-**8a** and (+)-**8b** were prepared from (+)-**5**. The H-NMR data for (+)-**8a** reveal upfield shift of the signals for the protons at both the ring

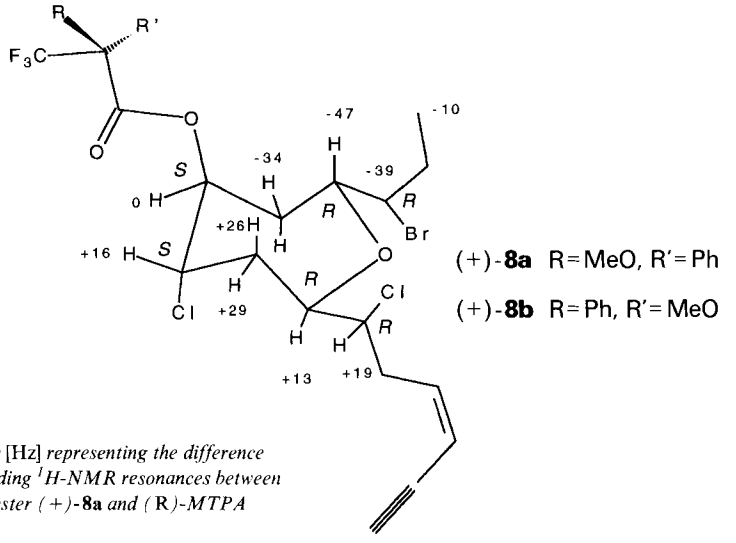



Fig. 3. *The values* [Hz] *representing the difference for the corresponding* $^1$*H-NMR resonances between the (*S*)-MTPA ester (+)-***8a*** and (*R*)-MTPA (+)-***8b***

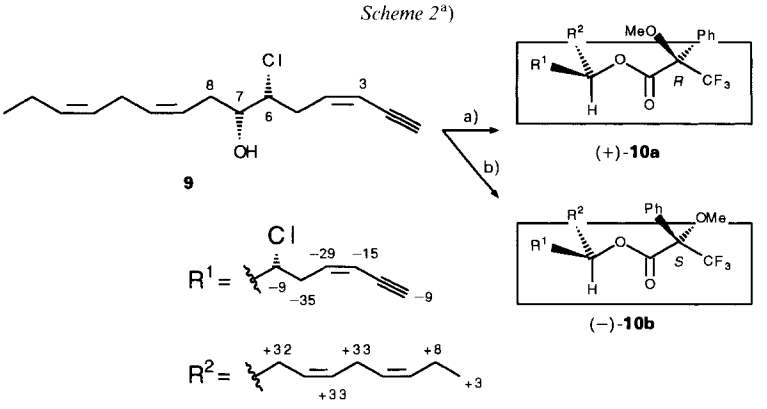
segment C(11)–C(12) and the C(13)–C(15) side chain on it, while, with (+)-**8b**, the signals for the protons at both the opposite ring segment C(8)–C(7) and side chain are those which undergo upfield shift (*Exper. Part* and *Fig. 3*). As these shifts are attributable to the diamagnetic effect of the Ph group [18b], the (*S*)-configuration at C(10) of rogioloxepane C ((+)-**3**) is established[2]). All other chiral centers at the oxepane ring of this compound are assigned as in *Fig. 3* on the basis of the relative configurations established above. It must be warned to this regard that the assignments of the absolute configuration at the ring positions are based on unequivocal NMR data, while the assignments at the side chains, being based on the fitting of averaged NMR data with calculations, can not have the same high degree of reliability.

2.4. *Prerogioloxepane* (**9**): *Structure, Absolute Configuration, and Preferred Conformation.* NMR and MS data (*Table* and *Exper. Part*) indicate the molecular formula $C_{15}H_{21}ClO$ for a product of intermediate polarity, that we have isolated from *L. microcladia*. NMR signals for a conjugated enyne terminal group and for two further disubstituted C=C bonds, and the absence of Br, indicate an acyclic compound which, having structural requirements for the immediate biogenetic precursor of rogioloxepane A ((+)-**3**), was called prerogioloxepane (**9**). The H–C(6)–Cl group is unequivocally assigned from the typical $\delta$(C) = 65.63 (*d*), the $^1$H,$^{13}$C(6) heteronuclear correlation, and the proton correlation of H–C(6) with 2H–C(5).

The absolute configuration at carbinyl C-atom was established *via Mosher*'s NMR method [18] along the lines followed above with (+)-**3**. Thus, the MTPA esters (+)-**10a** and (–)-**10b** were prepared as indicated in *Scheme 2*. As expected [18b] and further supported by molecular-mechanics calculations, the plane containing the $CF_3$ group, the ester C=O group, and the carbinyl H-atom bisects the two chains, C(6)–C(1) and C(8)–C(15). The $^1$H-NMR data for (+)-**10a** indicate an upfield shift of the signals for the

[2]) The same conclusions are attained by a similar analysis of the $^{13}$C-NMR signals.

*Scheme 2*[a])




a) 1. (+)-(*S*)-MTPA-Cl/pyridine, r.t., 24 h; 2. HPLC (CN).
b) 1. (−)-(*R*)-MTPA-Cl/pyridine, r.t., 24 h; 2. HPLC (CN).

[a]) The values given for $R^1$ and $R^2$ represent the difference [Hz] in the corresponding $^1$H-NMR resonances between (−)-**10b** and (+)-**10a**.

protons at the whole C(8)–C(15) chain, while with (−)-**10b** the signals for the protons at the whole C(6)–C(1) chain are those that undergo upfield shift (*Exper. Part* and *Scheme 2*). Since such shifts can be assigned to the diamagnetic effect of the Ph group [18b], prerogioloxepane (**9**) must have (*R*)-configuration at C(7). *threo*-Configuration at C(6)–C(7) is in accordance with the low value $J(6,7) = 3.2$ Hz, like with the rogioloxepanes.

Molecular-mechanics calculations indicate that **9** takes preferentially the folded conformation which is displayed in *Fig. 4*.

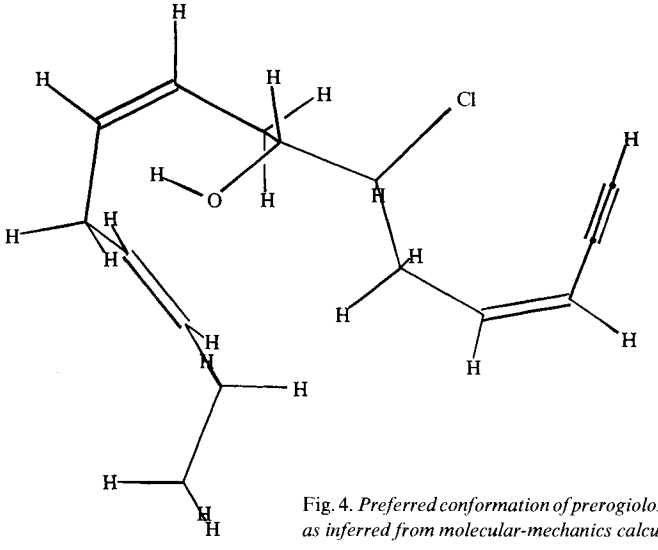
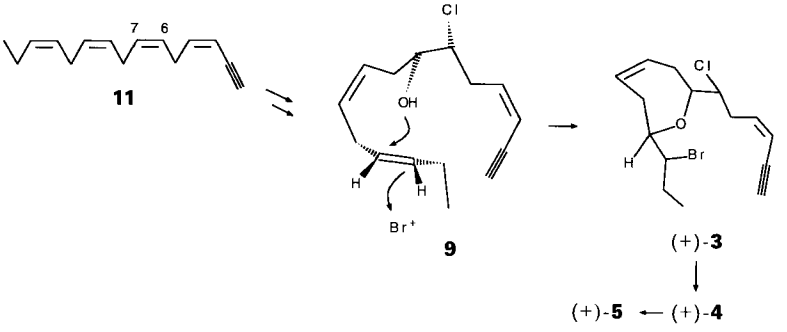



Fig. 4. *Preferred conformation of prerogioloxepane* (**9**), *as inferred from molecular-mechanics calculations*

2.5. *The Biogenesis.* It can be envisaged (*Scheme 3*) that laurencenyne (**11**), which was found in *Laurencia okamurai* collected off the coast of Goza, Japan [19], is also produced by *L. microcladia* of Il Rogiolo but is depleted, however, to form a 6,7-*cis*-epoxide which undergoes $Cl^-$ attack to give prerogioloxepane (**9**). As deduced above (*Fig. 4*), this compound preferentially exists in the folded conformation that is most apt to undergo $Br^+$-aided intramolecular cyclization affording rogioloxepane A ((+)-**3**; *Scheme 3*). This

Scheme 3. *Hypothetical Biogenesis*




is a preferred pathway to OH–C(7) attack at C(13) with C(12) attack to $Br^+$ like, presumably, in the route to laurepinnacin [5a]. That rogioloxepane B ((+)-**4**) and rogioloxepane C((+)-**5**) descend biogenetically from rogioloxepane A ((+)-**3**), as indicated in *Scheme 3*, finds chemical analogy in the reactions indicated in *Scheme 1*.

We thank Mr. *A. Sterni* for recording the mass spectra and, for financial support, both M.P.I. (Progetti 40%) and, in part, C.N.R., Roma.

## Experimental Part

1. *General.* See [3]. Moreover: $^1$H-NMR at 299.94 MHz (the coupling pattern of many protons has been elucidated by differential decoupling irradiations [20]); 90/120 $^1$H,$^1$H-COSY [21] were carried out with (+)-**3**, (+)-**5**, (+)-**6**, and (+)-**10a**. NOE stands for differential NOE. $^{13}$C-NMR at 75.43 MHz; multiplicities from DEPT [22]; H-bearing C-atoms for compounds (+)-**3**, (+)-**5**, and (+)-**8b** were assigned from $^{13}$C,$^1$H-COSY [23]. Inverse detection *via* the heteronuclear multiple-quantum coherence pulse sequence [24a] was carried out, with the dedicated *Varian* probe [24b], on compound **9**.

2. *Isolation.* The residue (0.38 g) from evaporation of the combined *Fr. 4* and *5* of the 54 fractions obtained before from *L. microcladia* extracts [3a] was subjected to reversed-phase flash chromatography with MeOH/$H_2O$ gradient elution collecting various fractions. The residue (0.03 g) from *Fr. 3* was subjected to HPLC (CN) with hexane to give rogioloxepane A ((+)-**3**; $t_R$ 5.8 min; 11 mg, 0.02%). The residue (0.11 g) from the combined *Fr. 11–18* was subjected to reversed-phase HPLC with MeCN/$H_2O$ 65:35, followed by HPLC (*Si-60*; hexane/$Et_2O$ 75:25) to give rogioloxepane B ((+)-**4**) ($t_R$ 9.1 min; 2 mg, 0.004%). The residue (0.06 g) from *Fr. 25–30* was subjected to HPLC (CN; hexane/i-PrOH 99:1) to give prerogioloxepane (**9**; $t_R$ = 8.5 min; 4 mg, 0.007%). The residue (0.230 g) from *Fr. 36* was subjected to HPLC (CN; hexane/i-PrOH 97:3), followed by HPLC (*Si-60*; hexane/$Et_2O$ 65:35) to give rogioloxepane C ((+)-**5**; $t_R$ 16.5 min; 15 mg, 0.03%).

3. *Rogioloxepane A (= (+)-(2R,7R)-2-(1-Bromopropyl)-7-[(Z)-1-chlorohex-3-en-5-ynyl]-2,3,6,7-tetrahydrooxepin*; (+)-**3**). Colorless oil. $[\alpha]_D$ = +21 ($c$ = 0.20, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.13 (*dd*, $J$(1,3) = 2.3, $J$(1,4) = 1.0, H–C(1)); 5.58 (*ddt*, $J$(3,4) = 10.8, $J$(3,1) = 2.3, $J$(3,5a) ≈ $J$(3,5b) = 1.4, H–C(3)); 6.16 (*dtd*,

$J(4.3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.2$, $J(4,1) = 1.0$, H–C(4)); 2.94, 2.80 (*2dddd*, $J_{gem} = 14.9$, $J(5a,4) = 7.2$, $J(5a,3) = 1.4$, $J(5a,6) = 5.0$, and $J_{gem} = 14.9$, $J(5b,4) = 7.2$, $J(5b,3) = 1.4$, $J(5b,6) = 9.2$, resp., 2 H–C(5)); 3.98 (*ddd*, $J(6,5b) = 9.2$, $J(6,5a) = 5.0$, $J(6,7) = 2.9$, H–C(6)); 4.32 (*ddd*, $J(7,8a) = 10.4$, $J(7,6) = 2.9$, $J(7,8b) = 1.5$, H–C(7)); 5.70 (*m*, H–C(9), H–C(10)); 2.23 (*m*, $H_b$–C(8), $H_a$–C(11)); 2.71 (*m*, $H_a$–C(8), $H_b$–C(11)); 4.24 (*ddd*, $J(12,11b) = 10.4$, $J(12,13) = 2.7$, $J(12,11a) = 1.5$, H–C(12)); 3.91 (*ddd*, $J(13,14a) = 9.4$, $J(13,14b) = 4.5$, $J(13,12) = 2.7$, H–C(13)); 1.91 (*ddq*, $J_{gem} = 14.6$, $J(14a,13) = 9.4$, $J(14a,15) = 7.3$, $H_a$–C(14)); 2.00 (*ddq*, $J_{gem} = 14.6$, $J(14b,13) = 4.5$, $J(14b,15) = 7.3$, $H_b$–C(14)); 1.05 (*t*, $J(15,14) = 7.3$, 3 H–C(15)). MS: 296, 294 (5, 5, $[M-HCl]^{+\cdot}$), 253, 251 (1.6, 3, $[M-Br]^+$), 219, 217 (22, 22, $[M-C_6H_6Cl]^+$), 129 (50), 91 (80), 67 (100).

4. *Rogioloxepane B (= (+)-(1S,3R,5R,7R)-3-(1-Bromopropyl)-5-[(Z)-1-chlorohex-3-en-5-ynyl]-4,8-dioxabicyclo[5.1.0]octane;* (+)-**4**). Colorless oil. $[\alpha]_D = +8$, $[\alpha]_{435} = +20$ ($c = 0.04$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.13 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.9$, H–C(1)); 5.59 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 6.13 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 2.89, 2.74 (*2dddd*, $J_{gem} = 15.2$, $J(5a,4) = 7.3$, $J(5a,3) = 1.6$, $J(5a,6) = 4.9$, and $J_{gem} = 15.2$, $J(5b,4) = 7.3$, $J(5b,3) = 1.4$, $J(5b,6) = 9.2$, resp., 2 H–C(5)); 4.00 (*ddd*, $J(6,5b) = 9.2$, $J(6,5a) = 4.9$, $J(6,7) = 3.0$, H–C(6)); 4.12 (*dt*, $J(7,8a) = 9.4$, $J(7,8b) \approx J(7,6) = 3.0$, H–C(7)); 2.29 (*m*, $H_a$–C(8)); 2.19 (*m*, $H_b$–C(8)); 3.24 (*td*, $J(9,10) = J((9,8a) = 3.5$, $J(9,8b) = 5.2$, H–C(9)); 3.18 (*td*, $J(10,9) = J(10,11a) = 3.5$, $J(10,11b) = 1.5$, H–C(10)); 2.24 (*m*, $H_a$–C(11)); 2.42 (*dd*, $J_{gem} = 16.1$, $J(11b,12) = 10.0$, $J(11b,10) = 1.5$, $H_b$–C(11)); 3.78 (*ddd*, $J(12,11b) = 10.0$, $J(12,13) = 2.4$, $J(12,11a) = 1.6$, H–C(12)); 3.87 (*ddd*, $J(13,14a) = 8.8$, $J(13,14b) = 5.4$, $J(13,12) = 2.4$, H–C(13)); 1.96 (*m*, 2 H–C(14)); 1.03 (*t*, $J(15,14) = 7.3$, 3 H–C(15)). MS: 312, 310 (1, 1, $[M-HCl]^{+\cdot}$), 269, 267 (2, 6, $[M-Br]^+$), 235, 233 (11, 11, $[M-C_6H_6Cl]^+$), 91 (48), 41 (100).

5. *Rogioloxepane C (= (+)-(2R,4S,5S,7R)-2-(1-Bromopropyl)-5-chloro-7-[(Z)-1-chlorohex-3-en-5-ynyl]-oxepan-4-ol*; (+)-**5**). Colorless oil. $[\alpha]_D = +23$ ($c = 0.11$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.13 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 1.0$, H–C(1)); 5.58 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 6.13 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.2$, $J(4,1) = 1.0$, H–C(4)); 2.96, 2.84 (*2dddd*, $J_{gem} = 14.9$, $J(5a,4) = 7.2$, $J(5a,3) = 1.4$, $J(5a,6) = 5.0$, and $J_{gem} = 14.9$, $J(5b,4) = 7.2$, $J(5b,3) = 1.4$, $J(5b,6) = 9.2$, resp., 2 H–C(5)); 3.99 (*ddd*, $J(6,5b) = 9.6$, $J(6,5a) = 4.7$, $J(6,7) = 2.5$, H–C(6)); 4.38 (*dt*, $J(7,8a) = 10.5$, $J(7,8b) \approx J(7,6) = 2.5$, H–C(7)); 2.66 (*ddd*, $J_{gem} = 15.8$, $J(8a,7) = 10.5$, $J(8a,9) = 2.7$, $H_a$–C(8)); 2.02 (*ddd*, $J_{gem} = 15.8$, $J(8b,7) = 2.5$, $J(8b,9) = 4.6$, $H_b$–C(8)); 4.28 (*m*, H–C(9)); 4.20 (*m*, H–C(10)); 2.45 (*ddd*, $J_{gem} = 15.7$, $J(11b,12) = 10.5$, $J(11b,10) = 1.8$, $H_b$–C(11)); 2.00 (*ddd*, $J_{gem} = 15.7$, $J(11a,12) = 2.0$, $J(11a,10) = 4.6$, $H_a$–C(11)); 4.29 (*ddd*, $J(12,11b) = 10.5$, $J(12,13) = 3.0$, $J(12,11a) = 2.0$, H–C(12)); 3.94 (*ddd*, $J(13,14a) = 10.0$, $J(13,14b) = 4.0$, $J(13,12) = 3.3$, H–C(13)); 1.91 (*ddq*, $J_{gem} = 14.6$, $J(14a,13) = 9.4$, $J(14a,15) = 7.3$, $H_a$–C(14)); 2.00 (*ddq*, $J_{gem} = 14.6$, $J(14b,13) = 4.5$, $J(14b,15) = 7.3$, $H_b$–C(14)); 1.05 (*t*, $J(15,14) = 7.3$, 3 H–C(15)). *W* Couplings were more easily discernible from $^1$H-NMR ($C_6D_6$): 1.60 (*dddd*, $J_{gem} = 15.8$, $J(8b,7) = 2.1$, $J(8b,9) = 5.4$, $J(8b,10) = 1.6$, $H_b$–C(8)); 1.52 (*tdd*, $J_{gem} = 15.4$, $J(11a,10) = 5.4$, $J(11a,12) \approx J(11a,9) = 1.6$, $H_a$–C(11)). MS: 348, 346 (6, 4, $[M-HCl]^{+\cdot}$), 305, 303 (2, 2, $[M-Br]^+$), 273, 271, 269 (6, 17, 15 $[M-C_6H_6Cl]^+$), 235, 233 (28, 28), 41 (100).

6. *Epoxidation of (+)-***3**. To (+)-**3** (5 mg, 0.015 mmol) in 1 ml of dry $CH_2Cl_2$ were added, at r.t., 7 mg of 65% *m*-chloroperoxybenzoic acid and 5 mg of solid $NaHCO_3$ followed by, after 2 h, 1 ml of 5% aq. $NaHCO_3$. This mixture was then percolated through a *Whatman* phase-separation filter, the filtrate was evaporated, and the residue was subjected to HPLC (*Si-60*; hexane/$Et_2O$ 3:1) to obtain, at $t_R$ 13.4 min, (+)-**6** and, at $t_R$ 12.3 min, (+)-**4** (2 mg each, 42% each).

*Isorogioloxepane B (= (+)-(1R,3R,5R,7S)-3-(1-Bromopropyl)-5-[(Z)-1-chlorohex-3-en-5-ynyl]-4,8-dioxabicyclo[5.1.0]octane*; (+)-**6**). Colorless oil. $[\alpha]_D = +4$, $[\alpha]_{435} = +11$ ($c = 0.04$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.11 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.9$, H–C(1)); 5.58 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 6.12 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 2.86 (*m*, 2 H–C(5)); 3.91 (*m*, H–C(6), H–C(13)); 4.08 (*ddd*, $J(7,8a) = 9.1$, $J(7,8b) = J(7,6) = 2.9$, H–C(7)); 2.20 (*m*, $H_b$–C(8), $H_a$–C(11)); 2.25 (*ddd*, $J_{gem} = 16.2$, $J(8a,7) = 9.1$, $J(8a,9) = 3.2$, $H_a$–C(8)); 3.25 (*td*, $J(9.10) = J(9,8a) = 3.5$, $J(9,8b) = 5.2$, H–C(9)); 3.18 (*td*, $J(10,9) = J(10,11a) = 3.5$, $J(10,11b) = 1.5$, H–C(10)); 2.41 (*ddd*, $J_{gem} = 16.2$, $J(11b,12) = 10.0$, $J(11b,10) = 1.6$ $H_b$–C(11)); 3.89 (*ddd*, $J(12,11b) = 10.0$, $J(12,13) = 2.4$, $J(12,11a) = 1.6$, H–C(12)); 1.70 (*ddq*, $J_{gem} = 14.6$, $J(14a,13) = 9.1$, $J(14a,15) = 7.3$, $H_a$–C(14)); 1.92 (*ddq*, $J_{gem} = 14.6$, $J(14b,13) = 4.8$, $J(14b,15) = 7.3$, $H_b$–C(14)); 1.04 (*t*, $J(15,14) = 7.3$, 3 H–C(15)). MS: 312, 310 (1, 1, $[M-HCl]^{+\cdot}$), 269, 267 (1, 3, $[M-Br]^+$), 235, 233 (10, 10, $[M-C_6H_6Cl]^+$), 91 (63), 55 (100).

7. *Treatment of (+)-***5** *with Base*. A suspension of (+)-**5** (2 mg) in 3% $K_2CO_3$/MeOH was stirred at 5° during 2 h, until disappearance of (+)-**5**. Standard workup afforded (+)-**4**, identical in every respect to natural rogiol-

oxepane B, in 83% yield after HPLC. Overnight stirring of (+)-**5** at r.t., under otherwise identical conditions, led to 7 in 65% yield, after HPLC.

*(1S,3R,5R,7R)-3-(1-Bromopropyl)-5-[(1E,3Z)-hexa-1,3-dien-5-ynyl]-4,8-dioxabicyclo[5.1.0]octane* (**7**): $^1$H-NMR ($CDCl_3$): 3.22 (*dd*, $J(1,3) = 2.4$, $J(1,4) = 0.9$, H–C(1)); 5.44 (*ddd*, $J(3,5) = 1.2$, $J(3,1) = 2.4$, $J(3,4) = 10.9$, H–C(3)); 6.45 (*tt*, $J(4,6) = J(4,1) = 1.1$, $J(4,5) \approx J(4,3) = 10.9$, H–C(4)); 6.87 (*tdd*, $J(5,7) = J(5,3) = 1.1$, $J(5,4) = 10.9$, $J(5,6) = 15.4$, H–C(5)); 6.08 (br. *dd*, $J(6,5) = 15.4$, $J(6,7) = 6.5$, H–C(6)); 4.60 (br. *q*, $J(7,8b) = J(7,8a) = J(7,6) = 6.5$, H–C(7)); 2.19 (*m*, $H_b$–C(8)); 2.29 (*m*, $H_a$–C(8)); 3.24 (*td*, $J(9,10) = J(9,8b) = 4.3$, $J(9,8a) = 0.8$, H–C(9)); 3.18 (*td*, $J(10,9) = J(10,11a) = 4.3$, $J(10,11b) = 1.4$, H–C(10)); 2.24 (*m*, Ha–C(11)); 2.44 (*dd*, $J_{gem} = 15.9$, $J(11b,12) = 10.2$, $J(11b,10) = 1.4$, $H_b$–C(11)); 3.77 (*ddd*, $J(12,11b) = 10.0$, $J(12,11a) = J(12,13) = 2.0$, H–C(12)); 3.84 (*ddd*, $J(13,14a) = 8.0$, $J(13,14b) = 6.0$, $J(13,12) = 2.6$, H–C(13)); 1.91 (*m*, 2 H–C(14)); 1.01 (*t*, $J(15,14) = 7.3$, 3 H–C(15)).

8. *Treatment of (+)-***5** *with MTPA-Cl.* To a soln. of (+)-**5** (6 mg, 0.015 mmol) in 0.2 ml of dry pyridine and 0.2 ml of $CCl_4$ were added 5 mol-equiv. of (+)-(*S*)-MTPA-Cl [18a]. The resulting soln. was allowed to stand at r.t. for 24 h and was then added of 3 ml of a sat. aq. $CuSO_4$ soln. and percolated through a *Whatman* phase-separation filter; the filtrate was evaporated and the residue was subjected to HPLC (CN; hexane/i-PrOH 97.5:2.5) affording the pure MTPA ester (+)-**8b** ($t_R$ 8.2 min; 3.9 mg, 63%), besides unreacted (+)-**5** ($t_R$ 14 min; 2 mg). Under otherwise identical conditions, (+)-**5** (6 mg) was reacted with (−)-(*R*)-MTPA-Cl [18a], leading to the pure MTPA ester (+)-**8a** ($t_R$ 8.5 min; 3.2 mg, 62%) besides unreacted (+)-**5** (2.7 mg).

*Data of (+)-***8a**. Colorless oil. $[\alpha]_D = +3$, $[\alpha]_{435} = +13$ ($c = 0.05$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.12 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 1.0$, H–C(1)); 5.59 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.3$, H–C(3)); 6.09 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.2$, $J(4,1) = 1.0$, H–C(4)); 2.86 (*m*, 2 H–C(5)); 3.90 (*ddd*, $J(6,7) = 2.6$, $J(6,5a) = 5.2$, $J(6,5b) = 9.2$, H–C(6)); 4.38 (*td*, $J(7,6) = J(7,8b) = 2.6$, $J(7,8a) = 10.4$, H–C(7)); 2.00 (*m*, $H_b$–C(8), $H_a$–C(11)); 2.51 (*ddd*, $J(8a,7) = 10.1$, $J(8a,9) = 2.1$, $J_{gem} = 15.7$, $H_a$–C(8)); 4.34 (*m*, H–C(9)); 5.42 (br. *t*, $J(10,9) \approx J(10,11a) = 4.2$, H–C(10)); 2.49 (*ddd*, $J(11b,10) = 2.1$, $J(11b,12) = 10.0$, $J_{gem} = 15.6$, $H_b$–C(11)); 3.96 (*ddd*, $J(12,11a) = 1.6$, $J(12,11b) = 10.2$, $J(12,13) = 2.6$, H–C(12)); 3.71 (*ddd*, $J(13,12) = 2.6$, $J(13,14a) = 4.3$, $J(13,14b) = 9.6$, H–C(13)); 1.91, 1.82 (2*ddq*, $J(14a,13) = 4.3$, $J_{gem} = 14.5$, $J(14a,15) = 7.3$, and $J(14b,13) = 9.6$, $J_{gem} = 14.5$, $J(14b,15) = 7.3$, resp., 2 H–C(14)); 0.99 (*t*, $J(15,14a) = J(15,14b) = 7.3$, 3 H–C(15)); 7.55–7.35 (series of *m*, 5 arom. H); 3.54 (*q*, $J = 1.3$, MeO). $^{13}$C-NMR ($CDCl_3$): 82.58 (*d*, C(1)); 79.90 (*s*, C(2)); 111.08 (*d*, C(3)); 140.64 (*d*, C(4)); 35.57 (*t*, C(5)); 64.72 (*d*, C(6)); 74.58 (*d*, C(7)); 32.61 (*t*, C(8)); 56.44 (*d*, C(9)); 72.56 (*d*, C(10)); 31.87 (*t*, C(11)); 71.61 (*d*, C(12)), 61.64 (*d*, C(13)); 27.51 (*t*, C(14)); 12.77 (*q*, C(15)); detected aromatic signals: 129.86 (*d*), 128.66 (*d*), 127.21 (*d*), 55.40 (*q*). MS: 566, 564, 562 (1.5, 5, 4, $[M-HCl]^+$), 489, 487, 485 (4, 12, 9, $[M-C_6H_6Cl]^+$), 368, 366, 364 (1, 2, 1.5, $[M-MTPAOH]^{+\cdot}$), 295, 293 (5, 5), 251, 249, (11, 20), 189 (100), 105 (50).

*Data of (+)-***8b**. Colorless oil. $[\alpha]_D = +20$, $[\alpha]_{435} = +45$ ($c = 0.05$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.11 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 1.0$, H–C(1)); 5.59 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.3$, H–C(3)); 6.09 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.2$, $J(4,1) = 1.0$, H–C(4)); 2.84 (*m*, 2 H–C(5)); 3.87 (*ddd*, $J(6,7) = 2.7$, $J(6,5a) = 5.2$, $J(6,5b) = 9.2$, H–C(6)); 4.33 (*td*, $J(7,6) = J(7,8b) = 2.7$, $J(7,8a) = 10.6$, H–C(7)); 1.90 (*dddd*, $J(8b,10) = 1.2$, $J(8b,7)$, $= 2.7$, $J(8b,9) = 5.7$, $J_{gem} = 15.7$, $H_b$–C(8)); 2.42 (*ddd*, $J(8a,7) = 10.7$, $J(8a,9) = 1.8$, $J_{gem} = 15.7$, $H_a$–C(8)); 4.29 (*m*, H–C(9)); 5.42 (br. *t*, $J(10,9) \approx J(10,11a) = 4.2$, H–C(10)); 2.47 (*ddd*, $J(11b,10) = 2.0$, $J(11b,12) = 10.2$, $J_{gem} = 15.7$, $H_b$–C(11)); 2.13 (*tdd*, $J(11a,9) = J(11a,12) = 1.5$, $J(11a,10) = 4.9$, $J_{gem} = 15.7$, $H_a$–C(11)); 4.12 (*ddd*, $J(12,11a) = 1.4$, $J(12,11b) = 10.2$, $J(12,13) = 3.0$, H–C(12)); 3.84 (*ddd*, $J(13,12) = 2.7$, $J(13,14a) = 3.3$, $J(13,14b) = 10.1$ H–C(13)); 2.00, 1.78 (2*ddq*, $J(14a,13) = 3.3$, $J_{gem} = 14.4$, $J(14a,15) = 7.2$, and $J(14b,13) = 10.1$, $J_{gem} = 14.4$, $J(14b,15) = 7.2$ resp., 2 H–C(14)); 1.02 (*t*, $J(15,14a) = J(15,14b) = 7.2$, 3 H–C(15)); 7.55–7.35 (series of *m*, 5 arom. H); 3.53 (*q*, $J = 1.0$, MeO). $^{13}$C-NMR ($CDCl_3$): 82.57 (*d*, C(1)); 79.84 (*s*, C(2)); 111.05 (*d*, C(3)); 140.71 (*d*, C(4)); 35,48 (*t*, C(5)); 64.85 (*d*, C(6)); 74.92 (*d*, C(7)); 33.32 (*t*, C(8)); 56.81 (*d*, C(9)); 72.31 (*d*, C(10)); 32.37 (*t*, C(11)); 71.33 (*d*, C(12)); 62.29 (*d*, C(13)); 28.22 (*t*, C(14)); 12.68 (*q*, C(15)); detected aromatic signals: 129.87 (*d*), 128.69 (*d*), 127.26 (*d*), 55.45 (*q*). MS: 566, 564, 562 (2.5, 9.4, 8.8, $[M-HCl]^+$), 489, 487, 485 (4, 12, 9, $[M-C_6H_6Cl]^+$), 368, 366, 364 (1, 2, 1.5, $[M-MTPAOH]^{+\cdot}$), 295, 293 (4, 4), 251, 249 (11, 20), 189 (100), 105 (50).

9. *Prerogioloxepane* (= *(7R,3Z,9Z,12Z)-6-Chloropentadeca-3,9,12-trien-1-yn-7-ol*; **9**). Colorless oil. $^1$H-NMR ($CDCl_3$): 3.14 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.9$, H–C(1)); 5.61 (*ddt*, $J(3,4) = 10.9$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 6.12 (*dtd*, $J(4,3) = 10.9$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 2.90, 2.86 (2*dddd*, $J_{gem} = 13.2$, $J(5a,4) = 7.3$, $J(5a,3) = 1.6$, $J(5a,6) = 5.9$, and $J_{gem} = 13.2$, $J(5b,4) = 7.3$, $J(5b,3) = 1.6$, $J(5b,6) = 7.9$, resp., 2 H–C(5)); 4.03 (*ddd*, $J(6,5b) = 7.9$, $J(6,5a) = 5.9$, $J(6,7) = 3.2$, H–C(6)); 3.71 (*ddq*, $J(7,OH) = J(7,8b) = J(7,8a) = 7.4$, $J(7,6) = 3.2$, H–C(7)); 2.42 (br. *t*, $J(8,7) = J(8,9) = 7.3$, 2 H–C(8)); 5.54 (*ttd*, $J(10,8a) = J(10,8b) = 1.4$, $J(10,11a) = J(10,11b) = 7.2$, $J(10,9) = 10.7$, H–C(10)); 2.82 (br. *t*, $J(11,12)$

$= J(11,13) = 7.3$, 2 H–C(11)); 5.28 (*ttd*, $J(12,14a) = J(12,14b) = 1.3$, $J(12,11a) = J(12,11b) = 7.0$, $J(12,13) = 10.7$, H–C(12)); 5.39 (*m*, H–C(9), H–C(13)); 2.05 (br. *quint.*, $J(14,15) = J(14,13) = 7.3$, 2 H–C(14)); 0.96 (*t*, $J(15,14) = 7.3$, 3 H–C(15)); 1.97 (*d*, $J(OH,7) = 7.4$, OH). The MS spectrum could not be obtained because of interfering impurities; the MTPA esters were obtained in pure form, however.

10. *Treatment of* **9** *with MTPA-Cl.* By the same procedure as described in *8*, **9** (1.5 mg) with (+)-(*S*)- or (–)-(*R*)-MTPA-Cl afforded, after HPLC (CN; hexane/i-PrOH 99.5:0.5), the MTPA ester (+)-**10a** ($t_R$ 6.7 min; 0.8 mg, 30%) or the isomer (–)-**10b** ($t_R$ 7.0 min; 0.8 mg, 30%), respectively.

*Data of the (+)-(R)-Ester (+)-***10a**. Colorless oil. $[\alpha]_D = +21$, $[\alpha]_{435} = +63$ ($c = 0.05$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.10 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.9$, H–C(1)); 5.62 (*ddt*, $J(3,4) = 10.9$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 6.07 (*dtd*, $J(4,3) = 10.9$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 2.77 (*m*, 2 H–C(5)); 4.10 (*ddd*, $J(6,5b) = 7.5$, $J(6,5a) = 6.5$, $J(6,7) = 4.0$, H–C(6)); 5.26 (*td*, $J(7,8b) = J(7,8a) = 6.4$, $J(7,6) = 4.0$, H–C(7)); 2.53 (*m*, 2 H–C(8)); 5.39–5.20 (series of *m*, H–C(9), H–C(12), H–C(13)); 5.44 (*ttd*, $J(10,8a) = J(10,8b) = 1.4$, $J(10,11a) = J(10,11b) = 7.2$, $J(10,9) = 10.7$, H–C(10)); 2.70 (*m*, 2 H–C(11)); 2.03 (br. *quint.*, $J(14,15) = J(14,13) = 7.3$, 2 H–C(14)); 0.94 (*t*, $J(15,14) = 7.3$, 3 H–C(15)); 7.60–7.40 (series of *m*, 5 arom. H); 3.58 (*q*, $J = 1.3$, MeO). MS: 236, 234 (0.7, 2, $[M-\text{MTPA}-\text{OH}]^{+\cdot}$), 207, 205 (1.5, 4.5), 199 (22, $[M-\text{MTPAOH}-\text{Cl}]^+$), 189 (100), 105 (64), 91 (69).

*Data of the (–)-(S)-Ester (+)-***10b**. Colorless oil. $[\alpha]_D = -12$, $[\alpha]_{435} = -40$ ($c = 0.05$, $CCl_4$). $^1$H-NMR ($CDCl_3$): 3.07 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.8$, H–C(1)); 5.57 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 5.98 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.0$, $J(4,1) = 0.8$, H–C(4)); 2.66 (*m*, 2 H–C(5)); 4.07 (*ddd*, $J(6,5b) = 7.7$, $J(6,5a) = 6.2$, $J(6,7) = 3.4$, H–C(6)); 5.24 (*dt*, $J(7,8b) = J(7,8a) = 6.5$, $J(7,6) = 3.4$, H–C(7)); 2.64 (*m*, 2 H–C(8)); 5.40 (*ttd*, $J(9,11a) = J(9,11b) = 1.5$, $J(9,8a) = J(9,8b) = 7.1$, $J(9,10) = 10.7$, H–C(9)); 5.55 (*ttd*, $J(10,8a) = J(10,18b) = 1.6$, $J(10,11a) = J(10,11b) = 7.4$, $J(10,9) = 10.7$, H–C(10)); 2.81 (*m*, 2 H–C(11)); 5.35–5.25 (*m*, H–C(12), H–C(13)); 2.05 (br. *quint.*, $J(14,15) = J(14,13) = 7.5$, 2 H–C(14)); 0.95 (*t*, $J(15,14) = 7.5$, 3 H–C(15)); 7.60–7.40 (series of *m*, 5 arom. H); 3.55 (*q*, $J = 1.2$, MeO). MS: practically superimposable to that of (+)-**10a**.

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