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NON-TERPENOID C-15 METABOLITES FROM THE RED SEAWEED *LAURENCIA PINNATIFIDA*[1]

A. G. GONZÁLEZ,* J. D. MARTÍN, V. S. MARTÍN, M. NORTE, R. PÉREZ and J. Z. RUANO
Department of Organic Chemistry, University of La Laguna, Institute of Organic Natural Products, La Laguna, Tenerife, Canary Islands, Spain

and

S. A. DREXLER and J. CLARDY*
Department of Chemistry, Cornell University, Ithaca, NY 14853, U.S.A.

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Abstract—The structures and absolute configurations of three halogenated vinyl acetylenes which are natural products from the red alga *Laurencia pinnatifida* (Gmal. Lamour) are described. The structure of *trans*-pinnatifidenyne **2** was determined by spectral, chemical and X-ray diffraction analyses. The structure of *cis*-pinnatifidenyne **1** is based on spectral comparison and chemical interconversion with the *trans*-isomer **2**. The structure of the acyclic trienyne **8** was secured as: (6*R*,7*R*)-3-*cis*,9-*cis*,12-*cis*,6-acetoxy,7-chloropentadeca-3,9,12-trien-1-yne by synthesis from *cis*-pinnatifidenyne **1**. The reactivity of these compounds to various conditions of catalytic hydrogenation has been examined in detail.

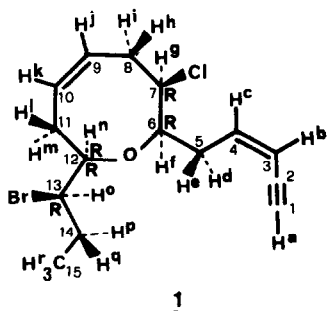
Our chemical studies on the marine alga *Laurencia* (Rhodomelaceae, Rhodophyta) have been concerned with assessing the diversity of halogen-based secondary metabolite biosynthesis in this genus. As part of this program we have described the structures of several halogenated sesquiterpenoids[2] which have been important in understanding terpenoid biogenesis in this alga.

Of the large number of metabolites isolated from algae of the *Laurencia* genus, most are halogenated sesquiterpenes[3] but a smaller group consists of halogenated cyclic ethers characterized by a straight-chain C_{15} carbon skeleton and a terminal enyne function.[4] The latter appear to be restricted to *Laurencia*, related compounds found in *Aplysia*[5] (opisthobrach molluscs) probably having a dietary origin in *Laurencia*.

In the present work we describe, among others, the isolation from *L. pinnatifida* (Gmal.) Lamour of two new C_{15} halogenated acetylenic cyclic ethers, designated as *cis*-pinnatifidenyne and *trans*-pinnatifidenyne for which we propose formulae **1** and **2**.

Cis-*Pinnatifidenyne* **1**, m.p. 47.5–48.5°, $\{\alpha\}_D^{25}+39$ (c, 13.8 $CHCl_3$) was obtained in high yield (0.05% dry weight) by column chromatography of an ether extract of the alga. Purified, neat samples of **1** deteriorated slowly at room temperature and hence no combustion analysis was obtained. The high resolution mass spectrum of *cis*-pinnatifidenyne indicated an elemental composition of $C_{15}H_{20}BrClO$. The presence of a conjugated terminal enyne group similar to that present in laureatin, a related compound,[4] was indicated by IR(KBr) absorption 3300 and 2100 cm^{-1} and UV absorption at λ_{max} (EtOH) 222.6 nm (ϵ = 13.200). The ^{1}H-NMR spectrum of **1** (Table 2) presented signals which could be assigned to a *cis*-enyne function, two non-conjugated olefinic protons, two α-ether protons and two α-halogen protons. The ^{13}C-NMR spectrum of **1** (Table 1) revealed that, in addition to the acetylene carbons, two disubstituted double bonds were also present in the molecule.

Trans-*Pinnatifidenyne* **2**, m.p. 57–58°, $\{\alpha\}_D^{25}+62$ (c, 8.9, $CHCl_3$), was isolated by chromatography as a more polar constituent (0.025% dry weight). Mass spectral analysis established that this new halogenated ether has the same elemental composition $C_{15}H_{20}BrClO$ as *cis*-pinnatifidenyne **1**; indeed, the fragmentation patterns of **1** and **2** were virtually identical. The presence in **2** of a terminal acetylene group conjugated with a double bond was indicated by IR (3300, 2115 cm^{-1}) and UV data (λ_{max} 224 nm, shoulder 232 nm; ϵ 16.400, 11.000). The larger extinction coefficient in the UV spectrum of **2** relative to that of **1** suggested the *trans* geometry for the double bond of the enyne group. Comparison of the ^{13}C- and ^{1}H-NMR spectra of **1** and **2** revealed great similarity in structure between the two compounds and at the same



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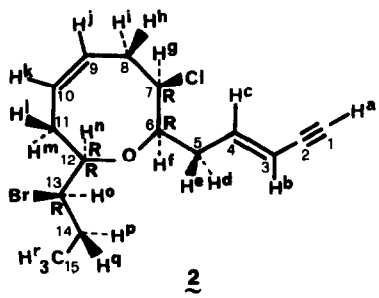

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Table 1. ^{13}C-NMR assignments for *cis*- and *trans*-pinnatifidenyne and related[a,b]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15
1	82.6	80.0	111.1	140.6	35.0	79.9	64.8	34.4	128.8	130.9	30.2	83.4	61.0	27.1	12.8
2	76.8	n/o	112.1	141.3	37.7	79.5	64.5	34.3	128.8	130.9	30.5	83.3	61.0	27.4	12.8
3	14.0	22.6	31.8	25.9	34.0	82.6	62.1	31.2	25.1	23.9	30.6	82.6	61.1	26.8	12.6
4	82.9	79.8	111.7	140.0	35.0	81.3	59.8	34.5	52.8	52.5	32.2	81.7	60.3	26.8	12.7
5	76.9	n/o	112.1	141.5	37.6	81.4	60.1	34.6	52.7	52.5	32.4	81.9	60.4	26.8	12.8
6	14.0	22.5	31.8	25.5	34.3	81.7	60.1	34.6	53.0	52.7	32.0	82.2	60.5	26.6	12.8

[a] All spectra taken at 20 MHz in $CDCl_3$ soln. and reported in PPM downfield from TMS.

[b] Assignments were aided by off-resonance decoupling of each compound and direct analysis of non-protonated carbon centres.

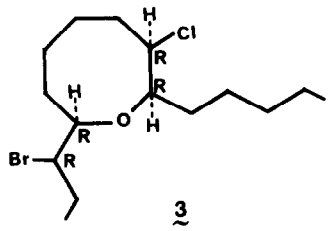
n/o: not observed.

time confirmed that the enyne double bond of **1** is *cis* and of **2** is *trans* (see Tables).

Catalytic hydrogenation of **1** afforded an oily octahydro derivative **3** ($C_{15}H_{28}BrClO$), which is identical, included the optical rotation, with that obtained from **2**. This confirmed that both compounds are identical with respect to carbon skeleton, size and location of the ether ring, type halogen substitution and stereochemistry of all substituents. The complete structure and absolute configuration of *trans*-pinnatifidenyne were determined by single crystal X-ray diffraction. A suitable single crystal was obtained by recrystallization from a hexane–ether mixture. Compound **2** crystallized in the triclinic space group P1 with $a = 5.454(4)$, $b = 8.882(7)$, $c = 10.072(7)$Å, $\alpha = 105.97(6)$, $\beta = 68.86(6)$ and $\gamma = 75.64(7)°$ and one molecule of $C_{15}H_{20}BrClO$ per unit cell. The structure was solved routinely by the heavy atom method using the 1010 (85%) unique observed ($F_o^2 \geq 3\sigma(F_o^2)$) reflections. The current residual is 0.084 for the structure and significantly higher for the enantioner.[6] Figure 1 is a stereoscopic drawing of the molecule in which the absolute configuration is represented.

The identical location of the endocyclic double-bond in both isomers was established by selective epoxidation of **1** (or **2**) to give the epoxiderivative **4** (or **5**) which was hydrogenated to give the hexahydroderivative **6**.

Detailed spectral comparison of *cis*- and *trans*-pinnatifidenyne and derivatives with the previously described vinyl acetylenes: rhodophytin, chondriol and related natural compounds[7] serve as a basis for the



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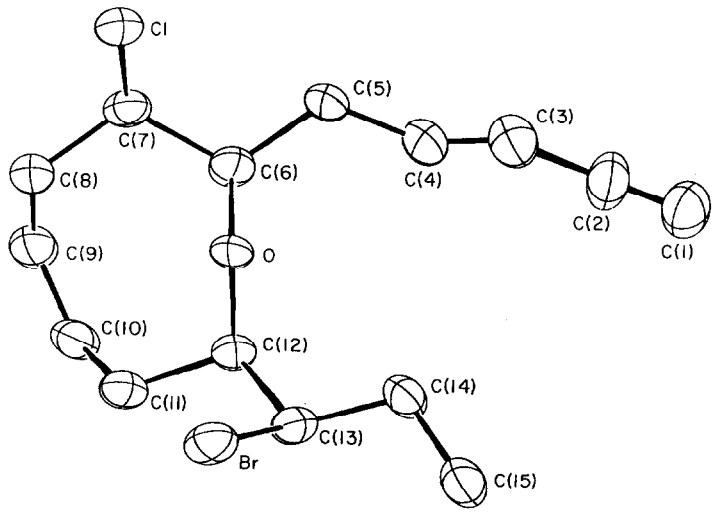


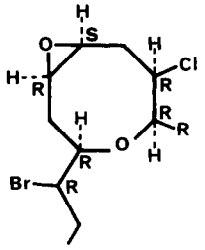
Fig. 1. A computer generated perspective drawing of the X-ray model of *trans*-pinnatifidenyne (**2**).

Table 2.

Proton(s) at carbon no.	H	δ	Multiplicity, J (Hz)	Proton(s) at carbon no.	H	δ	Multiplicity, J (Hz)
	^{1}H-NMR assignments for CIS-PINNATIFIDENYNE [a, b]				^{1}H-NMR assignments for TRANS-PINNATIFIDENYNE [a, b]		
1.....	H^a	3.13	d, J_{ab}=2.0	1.....	H^a	2.65	d, J_{ab}=1.6
2.....	-	-	-	2.....	-	-	-
3.....	H^b	5.57	dd, J_{ba}=2.0; J_{bc}=10.8	3.....	H^b	5.59	dd, J_{ba}=1.6; J_{bc}=15.7
4.....	H^c	6.03	dt, J_{cd}=J_{ce}=7.6; J_{cb}=10.8	4.....	H^c	6.14	dt, J_{cd}= J_{ce}=7.7; J_{cb}=15.7
5.....	H^d	2.82	dt, J_{dc}=J_{df}=7.6; J_{de}=14.2	5.....	H^d	2.40	dt, J_{dc}= J_{df}=7.7; J_{de}=14.1
	H^e	2.55	d of dd, J_{ed}=14.2; J_{ec}=7.6; J_{ef}=6.2		H^e	2.35	d of dd, J_{ed}=14.1; J_{ec}=7.7; J_{ef}=7.8
6.....	H^f	3.88	d of dd, J_{fe}=6.2; J_{fd}=7.6; J_{fg}=2.6	6.....	H^f	3.82	d of dd, J_{fe}=7.8; J_{fd}=7.7; J_{fg}=2.3
7.....	H^g	3.95	d of dd, J_{gf}=2.6; J_{gi}=4.2; J_{gh}=10.5	7.....	H^g	3.93	d of dd, J_{gf}=2.3; J_{gi}=3.0; J_{gh}=10.6
8.....	H^h	2.96	d of dd, J_{hg}=10.5; J_{hi}=12.1; J_{hj}=7.0	8.....	H^h	2.95	d of dd, J_{hg}=10.6; J_{hi}=12.3; J_{hj}=7.0
	H^i	2.51	d of dd, J_{ig}=4.2; J_{ih}=12.1; J_{ij}=1.1		H^i	2.53	d of dd, J_{ig}=3.0; J_{ih}=12.3; J_{ij}=1.2
9.....	H^j	5.69	d of dd, J_{ji}=1.1; J_{jh}=7.0; J_{jk}=10.2	9.....	H^j	5.69	d of dd, J_{ji}=1.2; J_{jh}=7.0; J_{jk}=10.5
10.....	H^k	5.91	d of dd, J_{kj}=10.2; J_{kl}=0.2; J_{km}=7.6	10.....	H^k	5.91	d of dd, J_{kj}=10.5; J_{kl}=0.1; J_{km}=7.9
11.....	H^l	2.63	d of dd, J_{lm}=14.0; J_{lk}=0.2; J_{ln}=10.2	11.....	H^l	2.63	d of dd, J_{lm}=14.2; J_{lk}=0.1; J_{ln}=10.5
	H^m	2.37	d of dd, J_{ml}=14.0; J_{mn}=3.0; J_{mk}=7.6		H^m	2.35	d of dd, J_{ml}=14.2; J_{mn}=3.1; J_{mk}=7.9
12.....	H^n	3.47	d of dd, J_{nm}=3.0; J_{nl}=10.2; J_{no}=4.1	12.....	H^n	3.46	d of dd, J_{nm}=3.1; J_{nl}=10.5; J_{no}=4.3
13.....	H^o	3.98	d of dd, J_{on}=4.1; J_{op}=3.4; J_{oq}=11.5	13.....	H^o	3.96	d of dd, J_{on}=4.3; J_{op}=3.6; J_{oq}=11.5
14.....	H^p	2.06	d of dq, J_{pq}=14.6; J_{po}=3.4; J_{pr}=7.2	14.....	H^p	2.01	d of dq, J_{pq}=14.5; J_{po}=3.6; J_{pr}=7.2
	H^q	1.79	d of dq, J_{qp}=14.6; J_{qo}=11.6; J_{qr}=7.2		H^q	1.80	d of dq, J_{qp}=14.5; J_{qo}=11.5; J_{qr}=7.2
15.....	H^r	1.08	t J_{rq}=7.2	15.....	H^r	1.07	t J_{rq}=7.2

[a] The spectra were recorded at 360 MHz in $CDCl_3$ solution. Chemical shifts are reported in PPM relative to TMS (o).

[b] Spin decoupling data support the proton assignments.



4 R = 

5 R = 

6 R = C_5H_{11}

structural proposal of **1** and **2** and the spectroscopic ^{13}C- and ^1H-NMR assignments (Tables 1 and 2).

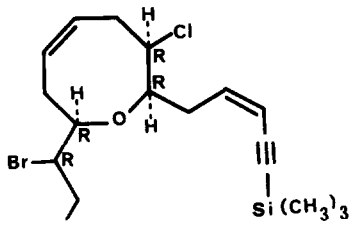
In addition several more polar halogenated compounds were identified in subsequent fractions of the lipid extract. From the hexane–ethyl acetate (5:1) eluent was isolated the chlorinated alcohol **8**, as a light mobile oil, $[\alpha]_D^{25}$ + 4.5 (c, 11.0; $CHCl_3$) in 0.0012% yield. Mass spectral analysis established the molecular formula $C_{17}H_{23}ClO_2$. The IR absorption of **8** showed the terminal acetylene (3300 cm^{-1}), ester group (1720 cm^{-1}), and multiple double bonds (3030 and 1640 cm^{-1}). The UV absorption λ_{max} (EtOH) 224 nm (ϵ 13.100) indicate the presence of a conjugated *cis*-enyne group similar to that present in *cis*-pinnatifidenyne **1**. The ^1H-NMR and ^{13}C-NMR spectral of **8** presented signals which could be assigned to one terminal acetylene group and three disubstituted double bonds. Treatment of compound **8** with K_2CO_3 in MeOH at 0° gave a mixture of the alcohol **9** and the epoxide **12**. Further treatment of **9** with K_2CO_3–MeOH at room temp gave **12** as the only product. The **8**→**9**→**10** transformation shows a *vic* O and Cl orientation.

In order to correlate chemically compound **8** with *cis*-pinnatifidenyne **1**, this compound was treated with Zn–AcOH–EtOH under different reaction conditions. Contrarily to reports of similar cases,[8] apart from the expected heterocyclic ring opening, partial hydrogenation of the acetylenic system also took place, the only isolable product obtained being the tetraolefinic derivative *cis,cis,cis* - 6*R* - hydroxy - 7*R* - chloro - pentadeca 1,3,9,12 - tetraene **13**. So as to protect the terminal acetylene, the trimethylsilyl derivative of **1**, compound **7**, was prepared, by treatment of **1** with n-BuMgBr–$ClSi(CH_3)_3$ in dry THF. Compound **7** was treated with Zn–AcOH–EtOH at room temp to give the 1 - trimethylsilyl derivative of *cis,cis,cis* - 6*R* - hydroxy - 7*R* - chloro - pentadeca - 3,9,12 - trien - 1 - yne **10**, which was acetylated with Ac_2O-py at room temp to give the acetate **11**. By treatment with sodium fluoride (in DMF, 40°, 4 hr,[9,10] compound **11** was readily converted into compound **8** in 94% yield, which was shown to be identical in all respects, included optical rotation, with the natural product. Hence compound **8** is (6*R*,7*R*) - 3 - *cis*,9 - *cis*,12 - *cis* - 6 - *acetoxy* - 7 - chloro - pentadeca - 3,9,12 - trien - 1 - yne.

EXPERIMENTAL

M.ps were determined on a Kofler block and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Model 237 spectrophotometer and ultraviolet spectra recorded on a Perkin–Elmer Model 137 or a Unicam SP 800. Optical rotations were determined for solutions in chloroform with a Perkin–Elmer 141 polarimeter. ^1H-NMR spectra were recorded on Perkin–Elmer R-12B (60 MHz) or R-32 (90 MHz) spectrometers, chemical shifts are reported relative to Me_4Si (δ0) and coupling constants are given in hertz; Q1/2 refers to the width of a band at half height. ^{13}C-NMR spectra were recorded on a Varian CFT-20 spectrometer. Low-resolution mass spectra were obtained from a Hewlett–Packard 5930-A mass spectrometer and high-resolution from a VG-Micromass ZAB-2F. Column and dry column chromatography were performed on silica gel 0.2–0.5 and 0.005–0.2 mm, respectively, and TLC and PLC on silica gel 6, all Merck products. Tlc pallates were developed by spraying with 6*N*-sulphuric acid and heating. All solvents were purified by standard techniques. Anhydrous sodium sulphate was used for drying solutions.

Collection and isolation. Laurencia pinnatifida was collected in April–May 1977, by hand, using SCUBA (−2 to −10 m) near Los Cristianos, Tenerife. Air dried seaweed (8.5 kg) was extracted with MeOH and the MeOH soln was concd *in vacuo*. The residue was percolated with ether and the ethereal soln washed with water. After evaporation of the solvent, a pale yellow oil (90 g) was obtained and chromatographed on Florisil (1500 g). One-litre fractions were collected employing the following elution scheme: hexane, fraction 1–10; benzene/hexane (1/1), fractions 11–14; benzene, fractions 15–24; ethyl acetate, fractions 25–32. Fractions exhibiting similar tlc profiles were combined. A portion (3.4 g) of combined fractions 8–19 (32 g) was chromato-



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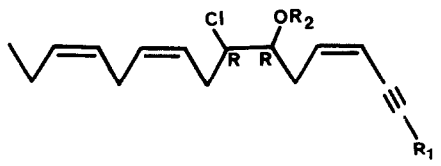
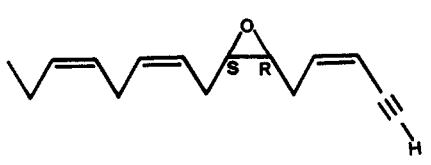


8 R_1 = H R_2 = Ac
9 R_1 = H R_2 = H
10 R_1 = $Si(CH_3)_3$ R_2 = H
11 R_1 = $Si(CH_3)_3$ R_2 = Ac



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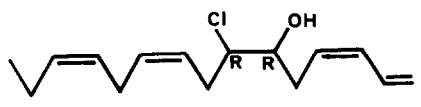

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graphed on 60 g of silica gel H using *n*-hexane-ethyl acetate (95:5) as solvent and collecting 20-ml fractions. *cis*Pinnatifidenyne (425 mg) crystallized from the material obtained in fractions 12–22 (620 mg). Fractions 27–32 yielded *trans*-pinnatifidenyne (118 mg). After 40 fractions had been collected, two 250-ml fractions were collected using n-hexane–ethyl acetate (5:1) and this yielded 11 mg of compound **8**. All attempts to crystallize compound **8** were unsuccessful.

cis-*Pinnatifidenyne* **1** was recrystallized from *n*-hexane: m.p. 47.5–48.5°, $\{\alpha\}_D^{25}$ + 39 (c, 13.8; $CHCl_3$); IR (KBr) 3300, 3040, 2100, 1450, 1380, 1320, 1300, 1100, 970, 800 and 740 cm^{-1}. Anal. Calc. for $C_{15}H_{20}BrClO$: mol wt calculated for $C_{15}H_{20}{}^{79}Br^{35}ClO$, 330.0921. Found (high resolution mass spectrum appeared at *m/e* 295, 297 (M^+–Cl); 265, 267, 269 (M^+–C_5H_5); 251, 253 (M^+–Br) and 209, 211 (M^+–C_3H_6Br).

Trans-*Pinnatifidenyne* **2** was crystallized from *n*-hexane: m.p. 57–58°C, $\{\alpha\}_D^{25}$ + 62 (c, 8.9, $CHCl_3$); IR (KBr) 3300, 3050, 2100, 1460, 1420, 1200, 1100 and 1050 cm^{-1}. Recrystallization from an ether/hexane mixture yielded large, colourless crystals which were utilized for X-ray crystallographic analysis. The molecular ion was extremely weak but could be detected by chemical ionization. Mass spectrometry with ammonia as the carrier gas led to an unambiguous molecular weight of 330, 332, 334, while mass spectrometry under all other conditions had furnished only M^+–Br. Anal. Calc. for $C_{15}H_{20}BrClO$: mol wt calculated for $C_{15}H_{20}{}^{35}Cl^{79}BrO$, 330.0921. Found: mol wt 330.0921. Significant peaks in the mass spectrum appeared at *m/e* 265, 267, 269 (M^+–C_5H_5); 251, 253 (M^+–Br), and 209, 211 (M^+–C_3H_6Br).

(6*R*,7*R*) - 3 - cis,9 - cis,12 - cis,6 - *acetoxy*,7 - *chloro* - *pentadeca* - 3,9,12 - *trien* - 1 - *yne* **8** was isolated as an oil, $\{\alpha\}_D^{25}$ + 4.54 (c, 11.0; $CHCl_3$); IR (film) 3300, 2990, 2955, 2920, 2870, 1730, 1430, 1370, 1220, 1030 and 960 cm^{-1}; UV (EtOH) 224 nm (ϵ = 13100). ^{1}H-NMR (90 MHz, CCl_4, δ-scale) 0.97 (3 H, t, J = 8 Hz), 2.01 (2 H, m), 2.06 (3 H, s), 2.50 (2 H, m), 2.73 (4 H, M), 3.08 (1 H, d, J = 2 Hz), 3.90 (1 H, m), 5.08 (1 H, m), 5.37 (4 H, m), 5.55 (1 H, dd, J = 2 and 8 Hz), and 5.95 (1 H, dt, J = 7 and 8 Hz). ^{13}C-NMR (20 MHz, $CDCl_3$) 14.2 (q), 20.6 (q), 20.9 (t), 25.8 (t), 32.3 (t), 32.5 (t), 75.45 (d), 78.64 (d), 81.77 (s), 83.74 (d), 111.8 (d), 124.6 (d), 126.5 (d), 131.7 (d), 132.4 (d), 138.9 (d). Mass spectrum: M^+ *m/e* 296, 294 ($C_{17}H_{23}ClO_2$). Further peaks at *m/e*: 201, 199 ($C_{10}H_{12}ClO_2$); 199 ($C_{15}H_{19}$), 193 ($C_{12}H_{17}O_2$); 171, 169 ($C_{10}H_{14}Cl$), 151 (($C_{10}H_{15}O$), 129 ($C_{10}H_9$) and 108 (C_8H_{12}).

Catalytic hydrogenation method. Between 10–100 mg of each compound to be hydrogenated was dissolved in 30 ml of anhyd diethyl ether and added to a 50 ml Erlenmeyer suction flask containing a catalytic amount of 10% Pd-C (10 mg) and a magnetic stirring bar. The reaction vessel was fitted with a balloon and septum, purged with hydrogen and the balloon filled. After stirring at 25°, the hydrogen was removed , the soln filtered and the ether evaporated to give, after thick-layer silica gel chromatography (plc), purified reaction products.

Octahydropinnatifidenyne **3**. (A) *From* cis-*pinnatifidenyne* **1**. Catalytic hydrogenation of **1** for 1.5 h gave the octahydro derivative **3** in 97% yield after plc (10% diethyl ether-n-hexane) purification: oil, $\{\alpha\}_D$ + 4.2 (c, 5.5, $CHCl_3$); IR ($CHCl_3$) 3000, 2960, 2860, 1450, 1415, 1345, 1310 and 1070 cm^{-1}. ^{1}H-NMR (60 MHz, $CDCl_3$) δ0.95 (bs, 3 H), 1.05 (3 H, t, J = 7 Hz), 3.70 (2 H, m), 3.95 (1H, m), 4.29 (1 H, dt, J = 9 Hz). Mass spectrum M^+ at *m/e* 342, 340, 338 ($C_{15}H_{28}BrClO$); 262, 260 (M^+–Br); 261, 259 (M^+–HBr); 219, 217 (M^+–C_3H_6Br). Anal. Calc. for $C_{15}H_{28}BrClO$: C, 52.87; H, 8.58; Br, 23.45; Cl, 10.40. Found: C, 53.12; H, 8.42; Br, 23.31; Cl, 10.51.

(B) *From* trans-*pinnatifidenyne* **2**. Hydrogenation of **2** for 2 hr in the same manner as described above for **1** gave in 92% yield after plc purification the octahydro derivative **3**: oil, $\{\alpha\}_D$ + 4.5 (c, 2.32, $CHCl_3$). IR, NMR and MS same as described in (A) above.

Cis-*Pinnatifidenyne*-8,9-*epoxide* **4**. *m*-Chloroperbenzoic acid (190 mg) in dry benzene (10 ml) was added dropwise to a soln of *cis*-pinnatifidenyne **1** (300 mg) in benzene (10 ml) with stirring. After 2 hr, calcium hydroxide was added to remove the excess of peracid; the soln was then filtered and evaporated. The residue obtained was applied to one large preparative plate and this was eluted four times with light petroleum–ether (20:1). The major band afforded *cis*-pinnatifidenyne-8,9-epoxide **4** (190 mg, 63%): oil, $\{\alpha\}_D^{25}$ + 45.2 (c, 12.3, $CHCl_3$); IR (film) 3280, 2950, 2120, 1650, 1450, 1380, 1200 and 1100 cm^{-1}. ^{1}H-NMR (60 MHz, $CDCl_3$) δ1.03 (3H, t, J = 7.2 Hz), 3.2 (1 H, d, J = 2 Hz), 3.8 (4 H, M), 5.61 (1 H, d of dd, J = 10.7 and 2 Hz), 6.07 (1 H, dt, J = 10.7 and 7 Hz). Mass spectrum M^+–C_5H_5); 269, 267 (M^+–Br).

trans-*Pinnatifidenyne*-8,9-*epoxide* **5**. Treatment of *trans*-pinnatifidenyne **2** (120 mg) in dry benzene (10 ml) with *m*-chloroperbenzoic acid (100 mg) in benzene (10 ml) in the same manner as described above for **1** gave, after plc purification, *trans*-pinnatifidenyne-8,9-epoxide **5** (67 mg, 56%): oil, $\{\alpha\}_D^{25}$ + 87 (c, 11.8, $CHCl_3$). IR (film) 3290, 2930, 1450, 1380, 1070, 960 and 800 cm^{-1}. ^{1}H-NMR (60 MHz, CCl_4) δ1.07 (3 H, t, J = 7.2 Hz), 2.83 (1 H, d, J = 1.7 Hz), 3.85 (1 H, m), 5.59 (1 H, d of dd, J = 16.3 and 1.7 Hz), 6.16 (1 H, dt, J = 16.3 and 7 Hz). Mass spectrum M^+ at *m/e* 350, 348, 346 ($C_{15}H_{20}BrClO_2$); 285, 283, 281 (M^+–C_5H_5); 269, 267 (M^+–Br).

Hexahydropinnatifidenyne-8,9-*epoxide* **6**. (A) *From* cis-*pinnatifidenyne*-8,9-*epoxide* **4**. Catalytic hydrogenation of **4** over PtO_2 in ethyl acetate for 30 min gave the hexahydro derivative **6** in 87% yield after plc (10% diethyl ether-*n*-hexane) purification: colourless oil, $\{\alpha\}_D^{25}$ + 22.3 (c, 11.8, $CHCl_3$). IR ($CHCl_3$) 2950, 1650, 1465, 1435, 1390, 1290, 1270, 1240, 1190, 1160 and 970 cm^{-1}. Mass spectrum M^+ at *m/e* 356, 354, 352 ($C_{15}H_{26}BrCl_2O_2$); 285, 283, 281 (M^+–C_5H_{11}); 240, 238, 236 (M^+–$C_7H_{11}O$).

(b) *From* trans-*pinnatifidenyne*-8,9-*epoxide* **5**. Hydrogenation of **5** for 30 min in the same manner as described above for **4** gave in 82% yield after plc the hexahydro derivative **6**, colourless oil, $\{\alpha\}_D^{25}$ + 19.8 (c, 1.13, $CHCl_3$). IR, NMR and MS same as described in (A) above.

Treatment of (6R,7R) - 3,3 - cis,9 - cis,12 - cis - 6 - *acetoxy* - 7 - *chloro* - *pentadeca* - 3,9,12 - *trien* - 1 - *yne* **8** *with* K_2CO_3. Potassium carbonate (100 mg) was added to a magnetically stirred soln of compound **8** (45 mg, 0.15 mmol) in 30 ml of MeOH. After 2 hr at room temp, 50 ml of diethyl ether was added and the supernatant decanted from the solid. The solid residue was washed thoroughly 3 times with 10-ml portions of ether. The combined organic solution was passed through a short pad of Florisil and the solvent was removed by distillation. The residue was applied to one preparative plate and this was eluted 3 times with light petroleum–ether (20:1). The less polar band offered the epoxide **12**, as a colourless oil (25 mg). IR (film) 3290, 3000, 2950, 2920, 2880, 1715, 1450, 1450, 1575, 1260, 1110 and 960 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) 0.97 (3H, t, J = 7.5 Hz), 2.08 (2 H, m), 2.40 (2 H, m), 2.62 (2 H, m), 2.82 (2 H, m), 3.00 (2 H, m), 3.15 (1 H, d, J = 2 Hz), 5.44 (4 H, m), 5.73 (1 H, dd, J = 7 and 2 Hz), 6.11 (1 H, dt, J = 7 and 6 Hz). Mass spectrum M^+ at *m/e* 216 ($C_{15}H_{20}O$), 198 ($C_{15}H_{18}$), 151 ($C_{10}H_{15}O$), 133 ($C_{10}H_{13}$).

The second band offered the alcohol **9** as an oil (11 mg): IR (film) 3440, 3290, 3010, 2960, 2920, 2870, 1430, 1380, 1260, 1090 and 965 cm^{-1}. ^{1}H-NMR spectrum (90 MHz, $CDCl_3$): δ0.97 (3H, t, J = 7.5 Hz), 2.06 (2 H, m), 2.44 (2 H, m), 2.66 (2 H, m), 2.82 (2 H, m), 3.14 (1 H, d, J = 2 Hz), 3.86 (1 H, m), 3.92 (1 H, m), 5.42 (4 H, m), 5.64 (1 H, dd, J = 7 and 2 Hz), 6.16 (1 H, dt, J = 7 and 6 Hz). Mass spectrum M^+ at *m/e* 254, 252 ($C_{15}H_{21}ClO$), 217 ($C_{15}H_{21}O$), 199 ($C_{15}H_{19}$), 189, 187 ($C_{10}H_{16}ClO$), 171, 169 ($C_{10}H_{14}Cl$), 159, 157 ($C_9H_{14}Cl$), 151 ($C_{10}H_{15}O$), 145, 143 (C_7H_8ClO), 133 ($C_{10}H_{13}$), 129 ($C_{10}H_9$), 109 (C_8H_{13}), 95 (C_6H_7O), 65 (C_5H_5).

When the reaction was run at 0°, the alcohol **9**, was the only compound isolated (92%). When the reaction was left at room temp overnight the epoxide **12** was isolated in 97% yield.

Treatment of cis-*pinnatifidenyne* **1** *with* Zn–AcOH–EtOH. A soln of *cis*-pinnatifidenyne **1** (315 mg, 0.95 mmol) in EtON (10 ml)–AcOH (5 ml) was stirred while Zn dust (100 mg) was added portionwise during 15 min. The reaction mixture was kept at room temp for 2 hr. The Zn was filtered off and the filtrate was worked up in the normal way to yield a residue (215 mg) which was dissolved in *n*-hexane and chromatographed on a silica gel (40 g) column. Compound **13** was eluted with *n*-hexane–ethyl acetate (9:1) as a colourless oil (159 mg, 50.4%). IR (film) 3420, 3020, 2970, 2940, 1650, 1600, 1440, 1380, 1315, 1280, 1080, 1005, 975 and 915 cm^{-1}. UV λ_{max} (EtOH) 234 nm (ϵ = 13300). ^{1}H-NMR (90 MHz, CCl_4) δ0.97 (3 H, t, J = 7.2 Hz), 2.08 (2 H, m), 2.64 (6 H,

m), 3.77 (2 H, m), 5.35 (7 H, m), 6.05 (1 H, t, J = 7 Hz), 6.62 (1 H, dt, J = 7 and 6 Hz). Mass spectrum M^+ at *m/e* 256, 254 ($C_{15}H_{23}ClO$), 219 ($C_{15}H_{23}O$), 201 ($C_{15}H_{21}$).

Treatment of cis-*pinnatifidenyne* **1** *with* $ClSi(CH_3)_3$. A soln of *cis*-pinnatifidenyne **1** (783 mg, 2.36 mmol) in dry THF (5 ml) under nitrogen at 0° was stirred while *n*-butyl-magnesium bromide (779 mg, 4.72 mmol) in 10 ml of THF was slowly added. The addition took 30 min at 0°. Subsequently, stirring was continued for 15 min. Then 518 mg (4.72 mmol) of trimethylchlorosilane dissolved in 25 ml of dry THF was added in 15 min at 0° and stirring was continued for 30 min. The reaction mixture was poured into a concentrated aqueous soln of ammonium chloride. After work-up and chromatography on silica gel (50 mg) 769 mg of the 1-trimethylsilyl derivative of *cis*-pinnatifidenyne **7** (80%) were isolated as a colourless oil: IR (film) 3020, 2945, 2145, 1450, 1385, 1255, 1090, 1055, 1020 and 850 cm^{-1}. ^1H-NMR (60 MHz, CCl_4) δ0.17 (9 H, s), 1.06 (3 H, t, J = 7.2 Hz), 1.90 (2 H, m), 2.55 (6 H, m), 3.50 (2 H, m), 3.88 (2 H, m), 5.80 (4 H, m). Mass spectrum: M^+ at *m/e* 406, 404, 402 ($C_{18}H_{28}BrClOSi$); 325, 323 ($C_{18}H_{28}ClSOSi$); 269, 267, 265 ($C_{10}H_{15}BrClO$); 187, 185 ($C_{10}H_{14}ClO$); 145, 143 (C_7H_8ClO); 107 (C_7H_7O); 91 (C_7H_7); 73 (C_3H_9Si).

Treatment of **7** *with* Zn–AcON–EtOH. A soln of **7** (454 mg, 1.125 mmole) in EtOH (10 ml)–AcOH (5 ml) was stirred while Zn dust (120 mg) was added portionwise during 20 min. The reaction mixture was stirred at room temp overnight. The ZN was filtered off and the filtrate was added to a soln of $NaHCO_3$aq and the whole extracted with ether. The ether soln was washed with 2N NaOH and water, dried over Na_2SO_4 and the solvent evaporated. The crude product (362 mg) was chromatographed using benzene–$CHCl_3$ (1:1) as eluent to give the 1-triemethylsilyl derivative of *cis,cis,cis* - 6*R* - hydroxy - 7*R* - chloro-pentadeca - 3,9,12 - trien - 1 - yne, compound **10**, as an oil (264 mg, 0.81 mmole, 72%): IR (film) 3430, 3015, 2960, 2155, 1710, 1440, 1345, 1255, 1050, 970, 845, 755 and 705 cm^{-1}. ^1H-NMR (60 MHz, CCl_4): δ 0.22 (9 H, s), 0.96 (3 H, t, J = 7.5 Hz), 2.03 (2 H, m), 2.52 (4 H, m), 2.73 (2 H, m), 3.76 (1 H, m), 3.86 (1 H, m), 5.46 (4 H, m), 5.61 (1 H, dd, J = 7 and 2 Hz), 6.07 (1H, dt, J = 7 and 6 Hz). Mass spectrum: M^+ at *m/e* 326, 324 ($C_{18}H_{29}ClOSi$); 289 ($C_{18}H_{29}OSi$); 271 ($C_{18}H_{27}OSi$); 271 ($C_{18}H_{27}Si$); 271 ($C_{18}H_{27}Si$); 253, 251 ($C_{15}H_{20}ClO$); 197 ($C_{15}H_{17}$); 73 (C_3H_9Si).

Acetate **11**, from Ac_2O–Py at room temp overnight, colourless oil, IR (film) 3005, 2950, 2145, 1740, 1435, 1375, 1225, 1035, 970, 850, 765 and 705 cm^{-1}. ^1H-NMR (60 MHz, CCl_4): δ0.17 (9 H, s), 0.95 (3 H, t, J = 7.2 Hz), 2.01 (2 H, m), 2.06 (3 H, s), 2.48 (2 H, m), 2.60 (2 H, m), 2.72 (2 H, m), 3.90 (1 H, m), 5.11 (1 H, m), 5.45 (4 H, m), 5.56 (1 H, dd, J = 7.5 AND 2 Hz), 5.76 (1 H, dt, J = 6 and 7 Hz). Mass spectrum, *m/e* 308, 306 ($C_{18}H_{27}ClSi$); 271 ($C_{18}H_{27}Si$); 197 ($C_{15}H_{18}$); 171, 169 ($C_{10}H_{14}Cl$); 73 (C_3H_9Si).

Treatment of **11** *with* NaF *in* aq DMF. To a soln of the silylated trienyne **11** (65 mg, 0.18 mmole) in DMF (50 ml) was added excess of NaF in water. The reaction mixture was kept for 4 hr at 40°. After work-up with water and *n*-hexane the crude reaction product (58 mg) was chromatographed using benzene–$CHCl_3$ (5:1) as eluent to give 44 mg (0.15 mmole (94%) of: (6*R*,7*R*) - 3 - *cis*,9 - *cis*,12 - *cis*,6 - acetoxy - 7 - chloro - pentadeca - 3,9,12 - trien - 1 - yne **8** as a colourless oil, $\{\alpha\}_D$ +4.2 (c, 1.18, $CHCl_3$). The physical and spectrocopic data (tlc, glc, IR, PMR, MS) was identical with those obtained from the naturally occurring compound.

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