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POLYHALOGENATED MONOTERPENES FROM THE RED ALGA *PLOCAMIUM CARTILAGINEUM*

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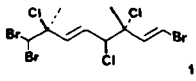
Abstract—Mixtures of polyhalogenated monoterpenes, first observed among the constituents of the digestive gland of the sea hare *Aplysia californica*, have been isolated from *Plocamium* species. The structures of eleven polyhalogenated monoterpenes from *Plocamium cartilagineum* have been determined by spectroscopic methods. All structures are based on the 3,7-dimethyl-1,5,7-octatriene skeleton.

During investigations of the chemical constituents of the sea hare *Aplysia californica*, we found that a major portion of the ether extract consisted of a complex mixture of polyhalogenated monoterpenes.[1] We have previously described the isolation and structural elucidation of (3*R*, 4*S*, 7*S*) - 3,7 - dimethyl - 1,8,8 - tribromo - 3,4,7 - trichloro - 1(*E*),5(*E*) - octadiene (1)[2] and 7 - chloro-3,7 - dimethyl - 1,4,6 - tribromo - 1(*E*) - octen - 3 - ol (2)[3] but found that the majority of the polyhalogenated monoterpenes were isolated as a complex mixture which was less polar than the tribromo-trichloromonoterpene 1. When it became apparent that the majority of the chemical constituents of the digestive gland of *A. californica* were derived from red algae, we screened the local species by silica gel TLC and found two sources of polyhalogenated monoterpenes, *Plocamium cartilagineum* (Dixon),[4] which also contained the tribromo-trichloromonoterpene 1, and *Plocamium violaceum* (Farlow).[5] Because the polyhalogenated monoterpene mixture from *Aplysia* was too complex, we have studied the non-polar materials from each alga. In this paper we wish to describe the structure eludication of a family of polyhalogenated monoterpenes which occur as the least polar fraction from *Plocamium cartilagineum*.



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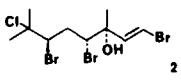

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Plocamium cartilagineum, collected intertidally (−0·2 to −1 m) at Bird Rock, La Jolla, was air-dried and ground to a powder. The gas chromatographic trace (Fig. 1) of the crude pentane extract shows the complexity of the polyhalogenated monoterpene mixture. The polyhalogenated monoterpenes were separated from hydrocarbons and from tribromo-trichloromonoterpene 1 by florisil chromatography. Rechromatography of one fraction on preparative alumina TLC gave pure compound 11, the major component of the mixture. The major fraction from florisil chromatography was rechromatographed on neutral alumina (grade 3) to give pure samples of 11 and the trichloro-tribromomonoterpene 1, together with eleven fractions which exhibited partial separation of the remaining compounds. Selected fractions were re-chromatographed on reverse phase high performance liquid chromatography to obtain pure samples of 6 and 3 and four pairs of diastereoisomers. The diastereoisomeric pairs were separated by preparative alumina TLC to obtain pure samples of the remaining compounds.

The molecular formulae of all new compounds (Fig. 2) were determined by high resolution mass spectrometry. The low resolution mass spectrum of 1 exhibited base peaks at *m/e* 167, 169, 171 (3:4:1) which were attributed to fragment 14. A similar array of peaks at *m/e* 167, 169, 171 was encountered in compounds 7–13, whereas compounds 3–6 exhibited base peaks at *m/e* 89, 91 (3:1) corresponding to fragment 15. The proton NMR spectrum of each compound contained signals having chemical shifts and coupling constants consistent with the presence of the partial structure 14 or 15.

14 15

A second simple subdivision of the compounds was made on the basis of the number of Me signals which appeared in the NMR spectra. Thus, compounds 7, 8, 12 and 13, having two Me groups, were separated from the remaining compounds, which had one Me group but contained more Cl atoms. Every compound had a UV absorption band in the region 233–257 nm, which was assigned to a diene system having various alkyl and halogen substituents. Since the molecular formulae indicated three unsaturation equivalents, every compound must have a linear monoterpene skeleton containing a conjugated diene and an isolated olefinic group.

Examination of the NMR spectra revealed that compounds 7, 8, 12 and 13 might be closely related to the

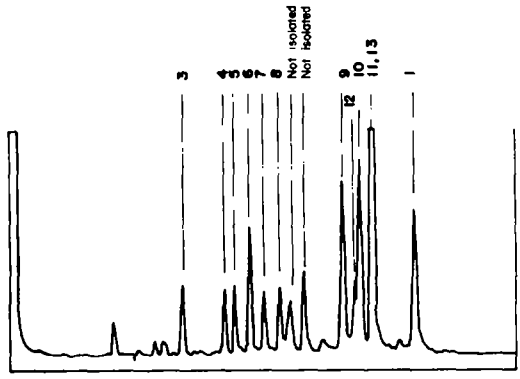


Fig. 1. Gas chromatographic trace of crude extract of *P. cartilagineum*. (Numbers correspond to structures described in text.)

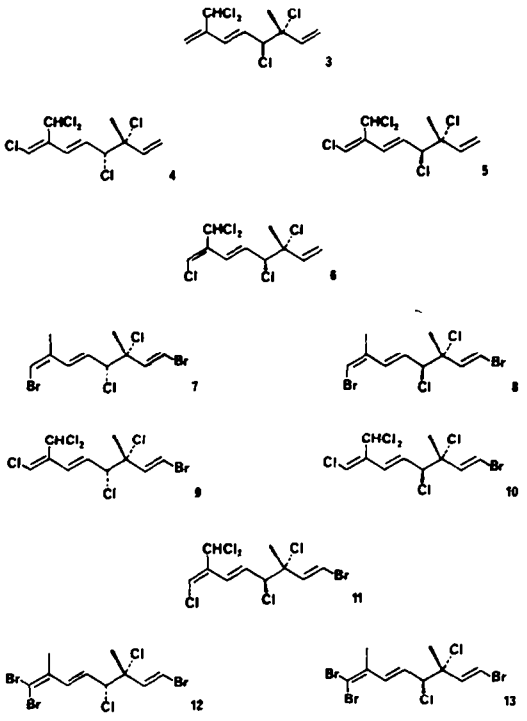
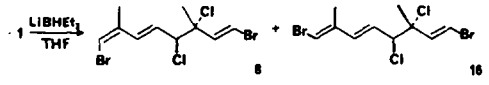


Fig. 2. Structures of new halogenated monoterpenes isolated from *P. cartilagineum*.

tribromo-trichloromonoterpene **1**, differing by the loss of either BrCl or HCl. Treatment of the tribromo-trichloromonoterpene **1** with lithium triethylborohydride in THF at 23° resulted in the reductive elimination of BrCl to obtain two isomeric products, one of which was identical in all respects to **8**. The second product **16** was



the expected geometrical isomer about the $\Delta^{7,8}$ double bond. Comparison of the chemical shifts of the Me signals (C-10) with the chemical shifts of the Me signals in (*Z*) and (*E*) 1-bromopropene[6] revealed that compound **8** was (3*R*, 4*S*) - 1,8 - dibromo - 3,4 - dichloro - 3,7 - dimethyl - 1(*E*),5(*E*),7(*Z*) - octatriene. Further support for this assignment was obtained by comparing the chemical shifts of the proton at C-8 (H_I) with calculated values.[7] The NMR spectrum of the other naturally-occurring $C_{10}H_{12}Br_2Cl_2$ isomer **7** was not identical with that of the 7(*E*) product **16** but was consistent with the interpretation that **7** and **8** were diastereoisomeric about C-3 and C-4. Thus, compound **7** must be 3,4 - *threo* - 1,8 - dibromo - 3,4-dichloro-3,7-dimethyl-1(*E*),5(*E*),7(*Z*)-octatriene.

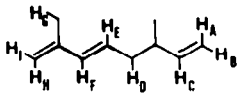
The NMR spectra of the two $C_{10}H_{11}Br_3Cl_2$ isomers **12** and **13** did not contain a singlet at about δ 6·16 ppm due to the C-8 vinyl proton (H_I), suggesting the presence of two bromine substituents at C-8. Since the coupling constants (J = 13·5–16·6 c/s) indicated that all olefinic bonds have the (*E*) geometry, the isomers **12** and **13** must be diastereoisomeric about C-3 and C-4. The relative stereochemistry at C-3 and C-4 was assigned on the basis of the following observations: Compounds **12** and **7** both had a Me signal at δ 1·79 ppm in the NMR spectrum and a positive optical rotation, while compounds **13** and **8** had the Me signal at δ 1·73 ppm and a negative optical rotation. Thus, compound **12** was 3,4 - *threo* - 3,4 - dichloro - 3,7 - dimethyl - 1,8,8 - tribromo - 1(*E*),5(*E*),7 - octatriene and compound **13** was 3,4 - *erythro* - 3,4 - dichloro - 3,7 - dimethyl - 1,8,8 - tribromo - 1(*E*),5(*E*),7 - octatriene.

The structure of **3**, the least halogenated of the metabolites, was assigned on the basis of its NMR spectrum, which showed two singlets at δ 5·35 and 5·52 ppm due to the terminal methylene group (C-8), a third singlet at δ 6·26 ppm (H_G) with the expected chemical shift for a dichloromethine proton, a 3-proton AMX pattern at δ 5·24 (H_B), 5·36 (H_H) and 6·04 (H_C) ppm due to the terminal vinyl group and a second AMX pattern at δ 4·46 (H_D), 6·18 (H_E) and 6·29 (H_F) ppm due to the chloromethine proton and the two vinyl protons on the adjacent disubstituted olefinic bond. The relative stereochemistry at C-3 and C-4 was again assigned on the basis of the chemical shift of the C-9 Me group (δ 1·73 ppm) and a negative optical rotation. Compound **3** was thus shown to be 3,4 - *erythro* - 3,4 - dichloro - 7 - dichloromethyl - 3 - methyl - 1,5(*E*),7 - octatriene.

The remaining six compounds could be separated into two groups of three, according to the presence of partial structures **14** and **15**, as indicated by the base peaks in the low resolution mass spectra. The NMR spectra of all six compounds contained singlets assigned to the vinyl proton at C-8 (H_H or H_I) and to a dichloromethine proton (H_G). The chemical shifts of the protons at C-6 (H_F) and C-10 (H_G) indicated the stereochemistry of the $\Delta^{7,8}$ double bond was (*E*) for compounds **6** and **11** and (*Z*) for the remaining four compounds, which were further subdivided into two pairs of diastereoisomers. The coupling constants (J = 13·5–16·5 c/s) for protons on the remaining olefinic linkages indicate that all have (*E*) geometry. The negative optical rotations of **6** and **11**, together with the chemical shift of the Me group in the NMR spectra, indicate that both **6** and **11** should be placed in the *erythro* series. Compounds **6** and **11** were thus shown to be 3,4 - *erythro* - 7 - dichloromethyl - 3 - methyl - 3,4,8 - trichloro - 1,5(*E*),7(*E*) - octatriene and 3,4 - *erythro* - 1 - bromo - 7 - dichloromethyl - 3 - methyl - 3,4,8 - trichloro - 1(*E*),5(*E*),7(*E*) - octatriene, respectively. Using the same criteria of optical rotations and Me group chemical shifts, the remaining four compounds were assigned the structures 3,4 - *threo* - 7 - dichloromethyl - 3 - methyl - 3,4,8 - trichloro - 1,5(*E*),7(*Z*) - octatriene (**4**), 3,4 - *erythro* - 7 - dichloromethyl - 3 - methyl - 3,4,8 - trichloro - 1,5(*E*),7(*Z*)-octatriene (**5**), 3,4 - *threo* - 1 - bromo - 7 - dichloromethyl-3 - methyl - 3,4,8 - trichloro - 1(*E*),5(*E*),7(*Z*) - octatriene (**9**) and 3,4 - *erythro* - 1 - bromo - 7 - dichloromethyl - 3 - methyl - 3,4,8 - trichloro - 1(*E*),5(*E*),7(*Z*) - octatriene (**10**).

The 220 MHz high resolution NMR spectra of compounds **4**, **5** and **10** contain examples of virtual coupling.[8] A simple first-order analysis of the multiplicity of H_D in each of these compounds leads to an erroneous interpretation involving the assignment of large allylic coupling constants (J_{DF} = 1·5–3·5 Hz). All new compounds possess an isolated linear 3-spin system in which the chemical shift of H_D is far removed from H_E and H_F. In most cases, $|\nu_E - \nu_F| \gg J_{EF}$ and the system is susceptible to first-order analysis. However, in the spectrum of compound **5**, $\nu_E = \nu_F$, allowing H_E and H_F to behave as a net spin system (I = 0 or 1) capable of coupling to H_D rather than as two individual protons (each with I = 0 or $\frac{1}{2}$) of which only H_E can couple to H_F. Consequently, H_D appears as a

Table 1. Spectroscopic data for new halogenated monoterpenes isolated from *P. cartilagineum*



#	λ_{max}	$[\alpha]_D^{25}$ ($CHCl_3$)	CH_3	CH_3	δ (ppm) / J (Hz)								
					H_A	H_B	H_C	H_D	H_E	H_F	H_G	H_H	H_I
1	--	-50.2°	1.75	1.95	6.55	Br	6.43	4.51	6.07	6.13	--	--	--
					J_{AC} = 14.0				J_{DE} = 6.5 J_{EF} = 15.0				
3	233	-5.7°	1.73	--	5.36	5.24	6.04	4.46	6.18	6.29	6.26	5.35	5.52
					J_{AC} = 17.0 J_{BC} = 10.5				J_{DE} = 7.5 J_{EF} = 15.0				
4	245	+34.6°	1.77	--	5.43	5.29	6.04	4.49	6.24	6.23	6.88	6.23	Cl
					J_{AC} = 16.5 J_{BC} = 11.0				J_{DE} = 7.6 J_{EF} = 16.0				
5	243	+5.1°	1.73	--	5.38	5.25	6.03	4.48	6.31	6.30	6.90	6.27	Cl
					J_{AC} = 17.0 J_{BC} = 10.5				J_{DE} = 7.5 J_{EF} = 16.6				
6	245	-39.3°	1.74	--	5.37	5.25	6.04	4.51	6.41	6.56	6.73	Cl	6.33
					J_{AC} = 17.0 J_{BC} = 10.5				J_{DE} = 7.5 J_{EF} = 16.0				
7	254	+62.8°	1.79	1.92	6.54	Br	6.43	4.51	5.82	6.76	--	Br	6.15
					J_{AC} = 13.5				J_{DE} = 9.0 J_{EF} = 16.0				
8	254	-46.0°	1.73	1.92	6.51	Br	6.40	4.53	5.87	6.80	--	Br	6.17
					J_{AC} = 14.0				J_{DE} = 9.0 J_{EF} = 15.5				
9	244	+4.7°	1.81	--	6.54	Br	6.39	4.49	6.22	6.31	6.89	6.27	Cl
					J_{AC} = 13.5				J_{DE} = 7.5 J_{EF} = 15.5				
10	242	-4.4°	1.74	--	6.52	Br	6.38	4.49	6.29	6.32	6.90	6.28	Cl
					J_{AC} = 14.0				J_{DE} = 7.4 J_{EF} = 15.6				
11	247	-22.9°	1.74	--	6.52	Br	6.40	4.52	6.43	6.58	6.74	Cl	6.33
					J_{AC} = 13.5				J_{DE} = 8.0 J_{EF} = 16.5				
12	257	+44.1°	1.79	2.03	6.54	Br	6.41	4.47	5.84	6.74	--	Br	Br
					J_{AC} = 13.5				J_{DE} = 9.0 J_{EF} = 15.5				
13	257	-34.7°	1.73	2.04	6.50	Br	6.36	4.48	5.90	6.74	--	Br	Br
					J_{AC} = 14.0				J_{DE} = 8.5 J_{EF} = 15.5				

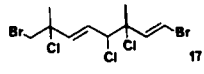
triplet. In compounds **4** and **10**, $\nu_F - \nu_E$ is small compared with J_{EF} such that H_D appears as a quartet.

The presence of the signal due to the C-8 vinyl proton (H_H) in the same region as the signals due to H_E and H_F further complicated our interpretation of the spectra. For this reason, the exact chemical shifts for the four protons (H_D, H_E, H_F and H_H) were calculated using the Nicolet ITRCAL (iterative NMR calculation) program.

The retention times of the halogenated monoterpenes on VPC (Fig. 1) roughly follow the order of increasing halogenation and molecular weight. For each of the pairs of diastereoisomers, the *threo* isomer was eluted before the *erythro* isomer on both VPC and on alumina TLC. For each pair of geometrical isomers at the $\Delta^{7,8}$ double bond, the (*Z*) isomer was eluted before the (*E*) isomer on both VPC and on alumina TLC.

The presence of so many compounds and particularly the relationship between the tribromotrichloromonoterpene **1** and compounds **7**, **8**, **12** and **13** made us suspect that some of these compounds might be artifacts. In a recent study[9] of the variations of the metabolites of single plants with depth, season and sexual status, we have shown that all the compounds described are natural products.

From the biosynthetic viewpoint, the halogenated monoterpenes must be divided into two groups according to the substitution at C-10. The dichlorotribromomonoterepenes **12** and **13** might be derived from the tribromo-trichloromonoterpene **1**, but the formation of two diastereoisomers from a single compound is puzzling. Similarly, the dibromo-dichloromonoterpenes **7** and **8** might be derived from the dibromotrichloromonoterpene **17**, which has recently been isolated from *A. californica*.[10]



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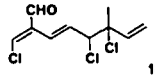

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During the preparation of this manuscript, the structure of a related aldyhyde, cartilagineal (**18**) was described.[11] The aldehyde is undoubtedly related to the pentachloromonoterpene **6**, but we feel that speculation on their biosynthetic relationship would be premature. We are currently investigating the more polar monoterpenes from *P. cartilagineum* and some monoterpenes obtained from *A. californica*, which performs the task of concentrating minor algal metabolites, to provide a full array of metabolites from which biosynthetic relationships may be inferred.

EXPERIMENTAL

UV spectra were recorded on a Hitachi Perkin-Elmer Model 124 spectrophotometer. Optical rotations were determined on a

Perkin-Elmer Model 141 polarimeter with a one decimeter microcell (1 ml) thermostated at 25·0°. NMR spectra were recorded on a Varian HR-220 spectrometer. High resolution mass spectrometry was performed by Beth Irwin, Department of Chemistry, UCLA. Low resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer system. All solvents used were either spectroquality or redistilled prior to use.

Collection and extraction. Plocamium cartilagineum was collected intertidally (−0·2 to −1 m) at Bird Rock, La Jolla, in Nov. 1973. The air-dried alga (3 kg) was ground in a Wiley mill and extracted with distilled pentane or hexane in a Soxhlet apparatus. The solvent was removed under reduced pressure to give 19·7 g of dark-yellow oil.

Florisil column chromatography. The crude extract (18·8 g) was applied to a 4 × 50 cm florisil column (J. T. Baker, 100/200 mesh) and the non-polar oil eluted with distilled hexane. Fraction 1 contained non-halogenated hydrocarbons (0·2 g); fractions 2, 3 and 4 contained a complex mixture of polyhalogenated monoterpenes (7·3, 3·9 and 0·9 g, respectively); and fractions 5–7 were relatively pure **1** (0·7 g total).

Purification of florisil chromatography fraction 3. Oil from fraction 3 (1·638 g) was subjected to preparative layer chromatography on alumina plates (20 × 20 × 0·15 cm) prepared from EM aluminum oxide PF-254 type E. Sample loading of 100 mg per plate and multiple development with pentane permitted resolution of two major bands (visualized by UV). The band with lower R_f yielded pure **11** (659 mg). The more mobile band yielded a mixture of four compounds.

Alumina column chromatography of florisil chromatography fraction 2. Halogenated monoterpene mixture (7·0 g) was applied to a neutral alumina column, activity III (2·5 × 93 cm). Elution with distilled hexanes yielded eleven fractions of halogenated monoterpene mixtures of various compositions (3·450 g total) and six fractions of **11** (1·335 g), followed by **1**.

Reverse phase high performance liquid chromatography. Selected chromatography fractions were further fractionated by reverse phase high performance liquid chromatography on a Waters ALC-201 liquid chromatograph, using a 2 × 2 ft × 3/8 in. o.d. column of Waters Bondapak C_{18}/Porasil B (37–75 μ) with acetonitrile/water eluent. Each fraction collected was extracted 3 times with equal volumes of pentane. Combined pentane layers were dried over Na_2SO_4 and the solvent evaporated at reduced pressure to yield, in most cases, pairs of diastereoisomers. When subjected to reverse phase HPLC using acetonitrile:water (65:35), the more mobile band (314 mg) from the PLC of florisil chromatography fraction 3 yielded pure **3** (6·4 mg), pure **6** (63·7 mg), and diastereomeric pair **9** and **10** (149·9 mg). Under the same conditions, alumina column chromatography fraction 4 (350·8 mg) yielded 3 pairs of diastereoisomers **4** and **5** (102·5 mg), **7** and **8** (48·0 mg), and **12** and **13** (78·0 mg). Using 60:40 acetonitrile/water eluent, alumina column chromatography fraction 9 (404·9 mg) was fractionated into pure **6** (102·2 mg), geometrical isomers **9** and **11** (81·1 mg), and diastereoisomers **9** and **10** (69·8 mg).

Separation of diastereoisomeric pairs. Pairs of diastereoisomers obtained by HPLC were separated by preparative layer chromatography on PF-254 alumina plates developed with pentane. The mixture of **4** and **5** (102·5 mg) gave **4** (30·8 mg) and **5** (7·5 mg). The mixture of **7** and **8** (48·0 mg) gave **7** (10·4 mg) and **8** (8·3 mg). The mixture of **12** and **13** (78·0 mg) gave **12** (26·1 mg) and **13** (28·4 mg). The mixture of **9** and **10** (69·8 mg) gave **9** (25·4 mg) and **10** (25·9 mg).

3,4 - Erythro - 3,4 - *dilchloro* - 7 - *dichloromethyl* - 3 - *methyl* - 1,5(E),7 - *octatriene* (**3**). λ_{max} (pentane) 233 nm; $[\alpha]_D^{25}$ −5·7° (*c* 0·2, $CHCl_3$); NMR (CCl_4) δ 1·73 (s, 3H), 4·46 (d, 1H, J = 7·5 Hz), 5·24 (d, 1H, J = 10·5 Hz), 5·35 (s, 1H), 5·36 (d, 1H, J = 17·0 Hz), 5·52 (s, 1H), 6·04 (d of d, 1H, J = 17·0, 10·5 Hz), 6·18 (d of d, 1H, J = 15·0, 7·5 Hz), 6·26 (s, 1H), 6·29 (d, 1H, J = 15·0 Hz). Mass spectrum, *m/e* 272, 274, 276 (M^+), 183, 185, 187 ($C_6H_6Cl_3^+$, base peak 89, 91 ($C_4H_6Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{12}Cl_4^{35}$: 271·9693. Obs: 271·9693 ± 0·0003.

3,4 - Threo - 7 - *dichloromethyl* - 3 - *methyl* - 3,4,8 - *trichloro* - 1,5(E),7(Z) - *octatriene* (**4**). λ_{max} (pentane) 245 nm; $[\alpha]_D^{25}$ +34·6° (*c* 1·6, $CHCl_3$); NMR (CCl_4) δ 1·77 (s, 3H), 4·49 (d of d, 1H, J = 7·6 Hz), 5·29 (d, 1H, J = 11·0 Hz), 5·43 (d, 1H, J = 16·5 Hz), 6·04 (d of d, 1H, J = 16·5, 11·0 Hz), 6·23 (s, 1H), 6·24 (m, 1H, J = 16·5, 11·0 Hz), 6·23 (s, 1H), 6·24 (m, 1H, J = 16·0, 7·6 Hz), 6·28 (m, 1H, J = 16·0 Hz), 6·88 (s, 1H). Mass spectrum, *m/e* 306, 308, 310, 312, 314 (M^+), 217, 219, 221, 223 ($C_6H_5Cl_4^+$), base peak 89, 91 ($C_4H_6Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{11}Cl_5^{35}$: 305·9303. Obs: 305·9306 ± 0·0006.

3,4 - Erythro - 7 - *dichloromethyl* - 3 - *methyl* - 3,4,8 - *trichloro* - 1,5(E),7(Z) - *octatriene* (**5**). λ_{max} (pentane) 243 nm; $[\alpha]_D^{25}$ +5·1° (*c* 0·4, $CHCl_3$); NMR (CCl_4) δ 1·73 (s, 3H), 4·48 (d of d, 1H, J = 7·5 Hz), 5·25 (d, 1H, J = 10·5 Hz), 5·38 (d, 1H, J = 17·0 Hz), 6·03 (d of d, 1H, J = 17·0, 10·5 Hz), 6·27 (s, 1H, 6·30 (m, 1H, J = 16·6 Hz), 6·31 (m, 1H, J = 16·6, 7·5 Hz), 6·90 (s, 1H). Mass spectrum, *m/e* 306, 308, 310, 312, 314 (M^+), 217, 219, 221, 223 ($C_6H_5Cl_4^+$), base peak 89, 91 ($C_4H_6Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{11}Cl_5^{35}$: 305·9303. Obs: 305·9301 ± 0·0006.

3,4 - Erythro - 7 - *dichloromethyl* - 3 - *methyl* - 3,4,8 - *trichloro* - 1,5(E),7(E) - *octatriene* (**6**). λ_{max} (pentane) 246 nm; $[\alpha]_D^{25}$ −39·3° (*c* 1·1, $CHCl_3$); NMR (CCl_4) δ 1·74 (s, 3H), 4·51 (d, 1H, J = 7·5 Hz), 5·25 (d, 1H, J = 10·5 Hz), 5·37 (d, 1H, J = 17·0 Hz), 6·04 (d of d, 1H, J = 17·0, 10·5 Hz), 6·33 (s, 1H), 6·41 (d of d, 1H, J = 16·0, 7·5 Hz), 6·56 (d, 1H, J = 16·0 Hz), 6·73 (s, 1H). Mass spectrum, *m/e* 306, 308, 310, 312, 314 (M^+), 217, 219, 221, 223 ($C_6H_5Cl_4^+$), base peak 89, 91 ($C_4H_6Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{11}Cl_5^{35}$: 305·9303. Obs: 305·9303 ± 0·0006.

3,4 - Threo - 1,8 - *dibromo* - 3,4 - *dichloro* - 3,7 - *dimethyl* - 1(E),5(E),7(Z) - *octatriene* (**7**). λ_{max} (pentane) 254 nm; $[\alpha]_D^{25}$ +62·8° (*c* 0·4, $CHCl_3$); NMR (CCl_4) δ 1·79 (s, 3H), 1·92 (d, 3H, J = 1·5 Hz), 4·51 (d, 1H, J = 9·0 Hz), 5·82 (d of d, 1H, J = 16·0, 9·0 Hz), 6·15 (br s, 1H), 6·43 (d, 1H, J = 13·5 Hz), 6·54 (d, 1H, J = 13·5 Hz), 6·76 (d, 1H, J = 16·0 Hz). Mass spectrum, *m/e* 360, 362, 364, 366, 368 (M^-), 193, 195, 197 ($C_6H_7BrCl^+$), 167, 169, 171 ($C_4H_5BrCl^-$), base peak 114, 116 ($C_6H_7Cl^+$), base peak 114, 116 ($C_6H_7Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{12}Br_2{}^{79}Cl_2{}^{35}$: 359·8684. Obs: 359·8682 ± 0·0007.

3,4 - Erythro - 1,8 - *dibromo* - 3,4 - *dichloro* - 3,7 - *dimethyl* - 1(E),5(E),7(Z) - *octatriene* (**8**). λ_{max} (pentane) 254 nm; $[\alpha]_D^{25}$ −46·0° (*c* 0·3, $CHCl_3$); NMR (CCl_4) δ 1·73 (s, 3H), 1·92 (d, 3H, J = 1·5 Hz), 4·53 (d, 1H, J = 9·0 Hz), 5·87 (d of d, 1H, J = 15·5, 9·0 Hz), 6·17 (br, s, 1H), 6·40 (d, 1H, J = 14·0 Hz), 6·51 (d, 1H, J = 14·0 Hz), 6·80 (d, 1H, J = 15·5 Hz). Mass spectrum, *m/e* 360, 362, 364, 366, 368 (M^+), 193, 195, 197 ($C_6H_7BrCl^+$), 167, 169, 171 ($C_4H_5BrCl^+$), base peak 114, 116 ($C_6H_7Cl^+$). High resolution mass measurement. Calcd for $C_{10}H_{12}Br_2{}^{79}Cl_2{}^{35}$: 359·8684. Obs: 359·8682 ± 0·0007.

3,4 - Threo - 1 - *bromo* - 7 - *dichloromethyl* -3 - *methyl* - 3,4,8 - *trichloro* - 1(E),5(E),7(Z) - *octatriene* (**9**). λ_{max} (pentane) 244 nm; $[\alpha]_D^{25}$ +4·7° (*c* 1·1, $CHCl_3$); NMR (CCl_4) δ 1·81 (s, 3H), 4·49 (d, 1H, J = 7·5 Hz), 6·22 (d of d, 1H, J = 15·5, 7·5 Hz), 6·27 (s, 1H), 6·31 (d, 1H, J = 15·5 Hz), 6·39 (d, 1H, J = 13·5 Hz), 6·54 (d, 1H, J = 13·5 Hz), 6·89 (s, 1H). Mass spectrum *m/e* 384, 386, 388, 390, 392 (M^+), 217, 219, 221, 223, 225 ($C_6H_4Cl_4^+$), 167, base peak 169, 171 ($C_4H_5BrCl^+$). High resolution mass measurement. Calcd for $C_{10}H_{10}Br^{79}Cl_5{}^{35}$: 383·8409. Obs: 383·8706 ± 0·0008.

3,4 - Erythro - 1 - *bromo* - 7 - *dichloromethyl* - 3 - *methyl* - 3,4,8 - *trichloro* - 1(E),5(E),7(Z) - *octatriene* (**10**). λ_{max} (pentane) 242 nm; $[\alpha]_D^{25}$ −4·4° (*c* 1·1, $CHCl_3$); NMR (CCl_4) δ 1·74 (s, 3H), 4·49 (d of d, 1H, J = 7·4 Hz), 6·28 (s, 1H), 6·29 (m, 1H, J = 15·6, 7·4 Hz), 6·32 (m, 1H, J = 15·6 Hz), 6·38 (d, 1H, J = 14·0 Hz), 6·52 (d, 1H, J = 14·0 Hz), 6·90 (s, 1H). Mass spectrum, *m/e* 384, 386, 388, 390, 392 (M^+), 217, 219, 221, 223, 225 ($C_6H_5Cl_4^+$), 167, base peak 169, 171 ($C_4H_5BrCl^+$). High resolution mass measurement. Calcd for $C_{10}H_{10}Br^{79}Cl_5{}^{35}$: 383·8409. Obs: 383·8406 ± 0·0008.

3,4 - Erythro - 1 - *bromo* - 7 - *dichloromethyl* - 3 - *methyl* - 3,4,8 - *trichloro* - 1(E),5(E),7(E) - *octatriene* (**11**). λ_{max} (pentane) 247 nm; $[\alpha]_D^{25}$ −22·9° (*c* 0·9, $CHCl_3$); NMR (CCl_4) δ 1·74 (s, 3H), 4·52 (d, 1H, J = 8·0 Hz), 6·33 (s, 1H), 6·40 (d, 1H, J = 13·5 Hz), 6·43 (d of d, 1H, J = 16·5, 8·0 Hz), 6·52 (d, 1H, J = 13·5 Hz), 6·58 (d, 1H, J = 16·5 Hz), 6·74 (s, 1H). Mass spectrum, *m/e* 384, 386, 388, 390, 392 (M^+), 217, 219, 221, 223, 225 ($C_6H_5Cl_4^+$), 167, base peak 169, 171 ($C_4H_5BrCl^+$). High resolution mass measurement. Calcd for $C_{10}H_{10}Br^{79}Cl_5{}^{35}$: 383·8409. Obs: 383·8406 ± 0·0004.

3,4 - Threo - 3,4 - *dichloro* - 3,7 - *dimethyl* - 1,8,8 - *tribromo* -

1(E),5(E),7 - *octatriene* (12). λ_{max} (pentane) 257 nm; $[\alpha]_D^{25}$ +44·1° (*c* 1·2, $CHCl_3$); NMR (CCl_4) δ 1·79 (s, 3H), 2·03 (s, 3H), 4·47 (d, 1H, J = 8·7 Hz), 5·84 (d of d, 1H, J = 15·5, 8·7 Hz), 6·41 (d, 1H, J = 13·5 Hz), 6·54 (d, 1H, J = 13·5 Hz), 6·74 (d, 1H, J = 15·5 Hz). Mass spectrum, *m/e* 438, 440, 442, 444, 446 (M^+), 271, 273, 275, 277 ($C_6H_6Br_2Cl^+$), 192, base peak 194, 196 ($C_6H_6BrCl^+$), 167, 169, 171 ($C_4H_5BrCl^+$). High resolution mass measurement. Calcd for $C_{10}H_{11}Br_3{}^{79}Cl_2{}^{35}$: 437·7789. Obs: 437·7788 ± 0·0004.

3,4 - Erythro - 3,4 - *dichloro* - 3,7 - *dimethyl* - 1,8,8 - *tribromo* - 1(E),5(E),7 - *octatriene* (13). λ_{max} (pentane) 257 nm; $[\alpha]_D^{25}$ −34·7° (*c* 1·1, $CHCl_3$); NMR (CCl_4) δ 1·73 (s, 3H), 2·04 (s, 3H), 4·48 (d, 1H, J = 8·5 Hz), 5·90 (d of d, 1H, J = 15·5, 8·5 Hz), 6·36 (d, 1H, J = 14·0 Hz), 6·50 (d, 1H, J = 14·0 Hz), 6·74 (d, 1H, J = 15·5 Hz). Mass spectrum, *m/e* 438, 440, 442, 444, 446 (M^+), 271, 273, 275, 277 ($C_6H_6Br_2Cl^+$), 192, base peak 194, 196 ($C_6H_6BrCl^+$), 167, 169, 171 ($C_6H_6BrCl^+$). High resolution mass measurement. Calcd for $C_{10}H_{11}Br_3{}^{79}Cl_2{}^{35}$: 437·7789. Obs: 437·7788 ± 0·0004.

Reductive elimination of BrCl *from* (3R, 4S, 7S) - 3 - *dimethyl* - 1,8,8 - *tribromo* - 3,4,7 - *trichloro* - 1(E),5(E) - *octadiene* (1). Lithium triethylborohydride (1 M in THF) was syringed into a stirred soln of 1 (80·8 mg, 0·168 mmole) in dry THF under a N_2 at 23°. Addition was continued until the VPC showed that less than 10% starting material remained (0·4 ml total addition). The solvent was removed under reduced pressure and water (10 ml) was added. The soln was extracted with pentane (3 × 15 ml) and the combined pentane extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure to yield a mixture of two compounds. The mixture was applied to an alumina chromatography column (activity III, 1 × 56 cm) and pure 3,4 - *erythro* - 1,8 - dibromo - 3,4 - dichloro - 3,7 - dimethyl - 1(*E*),5(*E*),7(*Z*) - octatriene (9·8 mg, identical to the natural product 8) was eluted with distilled hexanes. Subtraction of the NMR spectrum of compound 8 from the synthetic mixture (above) yielded a spectrum from which the structure 3,4 - *erythro* - 1,8 - dibromo - 3,4 - dichloro - 3,7 - dimethyl - 1(*E*),5(*E*),7(*E*) - octatriene (16) was deduced. 220 MHz NMR (CCl_4) δ 1·70 (s, 3H), 1·95 (brs, 3H), 4·41 (d, 1H, J = 9·0 Hz), 5·80 (d of d, 1H, J = 15·5, 9·0 Hz), 6·30 (d, 1H, J = 15·5 Hz), 6·38 (d, 1H, J = 14·0 Hz), 6·38 (brs, 1H), 6·49 (d, 1H, J = 14·0 Hz).

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