H_3C-13 1.40, H_3C-15 1.52, H-1 3.7 (m), H-2 3.95 (m), H-3 4.12 (m), H-9 6.4, mixture melting point of the two compounds unchanged.

PR alcohol (6) was obtained from PR toxin by an incubation procedure without $NADPH_2$ and was chemically synthesized from **3** by the procedure described above. All spectroscopic data are in good agreement with the data previously reported:[3] mp 152–154 °C and mixture melting point unchanged. The melting point given in ref 3 (113.5–115 °C) is the only difference observed from literature data.

Eremofortin C alcohol (7) was prepared by saponification of eremofortin C according to the procedure described above (poor yield) or by $NaBH_4$ reduction of PR alcohol according to the procedure described for the chemical synthesis of eremofortin C (**4**). **6** (48 mg) yielded 11 mg of crystallized eremofortin C alcohol (**7**) (from ethyl acetate): mp 170 °C, dec; IR (KBr) 3460, 3390, 1685 cm^{-1}; ^1H NMR (CD_3OD) see text, mass spectrum *m/e* 280 (M^+), 237, 191, 177, 149, 121, 91; high-resolution mass spectrum 280.13149 (calcd for $C_{15}H_{20}O_5$, 280.13106). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.17; H, 7.36.

Acknowledgments. We thank A. Butryn for technical assistance, Dr. M. H. Loucheux for variable temperature NMR measures, Dr. G. Bourgeois for measurement of the mass spectra, and Dr. C. Berrier for ^{13}C NMR spectral analysis.

Registry No.—**1**, 62445-06-1; **2**, 62375-73-9; **3**, 56299-00-4; **4b**, 62375-74-0; **5**, 62375-75-1; **7b**, 62375-76-2.

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Monoterpene Halogenation by the Red Alga *Placamium oregonum*

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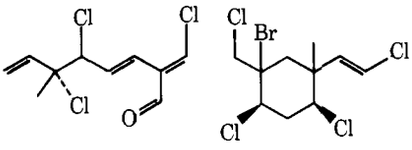
Several years ago we began to study the chemistry of the red seaweeds in the Plocamiaceae because extracts from some of its species were toxic to fish and insects.[1] This proved to be a rewarding venture in that several new natural products were characterized from the toxic extracts of *Placamium cartilagineum* (Dixon) and *Placamium violaceum* (Farlow) including cartilagineal (**1**),[1] plocamene A (**2**),[2] and plocamene B (**3**).[2a] Extending our work along a phyletic approach we discovered that *Placamium sandvicense* (J. Ag.) from Maui, Hawaii, was also a rich source of polyhalogenated monoterpenes including **4**.[3] Continuing our study of monoterpene halogenation by the Plocamiaceae we turned to *Placamium oregonum* (Doty) which ranges from the central California coast to the Pacific northwest. In the fall of 1975 we collected *P. oregonum* from Partridge Point, Whidbey Island, Wash., and, although its crude extract displayed very little toxicity in our bioassays, the GC/MS profile of semipure fractions did show several new polyhalogenated monoterpene constituents. Reported below are the structures of these metabolites along with evidence for their biogenesis.

Results and Discussion

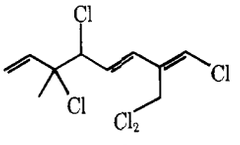
Four major constituents could be observed in approximately equal amounts in the reconstructed GC/MS trace (RGC) of the total ions from the crude $CHCl_3$ extract of *P. oregonum*.



cartilagineal (**1**)[1] plocamene A (**2**)[2a] plocamene B (**3**)[2a]

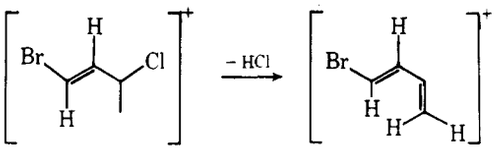
or

violacene[2b]



4[3]

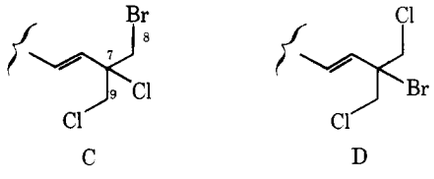
Comparison of this to the RGC for *m/e* 167 clearly showed that each of these components, along with a fifth minor one, contained a common C_4H_5ClBr structural unit A which fragmented to B by HCl loss. In addition, the mass spectra revealed that these five metabolites consisted of sets of isomers including two of formula $C_{10}H_{12}Cl_2Br_2$, two of formula $C_{10}H_{13}Cl_3Br_2$, and a single one of formula $C_{10}H_{12}Cl_4Br_2$. This



A [167/169/171] B [131/133]

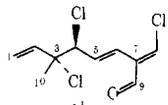
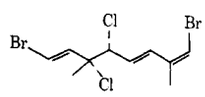
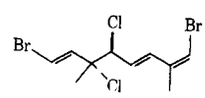
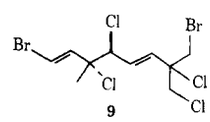
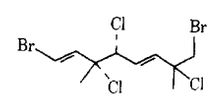
complex mixture was conveniently separated by HPLC on Porasil A, and the retention order on both HPLC and GLC was according to molecular weight.

The spectra of the lowest molecular weight isomers were consistent with structures **5** and **6** which were previously isolated from *Placamium cartilageineum*.[4] The highest molecular weight component did not show a mass spectral parent ion but it did show an $M^+ - Cl$ 395/397/399/401/403 ($C_{10}H_{12}Cl_3Br_2$) and $M^+ - Br$ 351/353/355/357 ($C_{10}H_{12}Cl_4Br$). It was concluded to have the gross structure of oregonene A (**9**) based upon the ^{13}C NMR spectrum, which showed four olefin carbons (Table I), and the ^1H NMR spectrum, which showed only a single methyl at δ 1.74 (s) and the trans vinyl AB at δ 6.49 (J = 14 Hz) associated with fragment A along with additional structural pieces including two $-CH_2X$ units at δ 3.76, 3.90 (AB, J = 11 Hz), 3.95 (s); and a $XCHCH{=}CH-$ at 4.49 (d, J = 6 Hz), 6.02 (d, J = 16 Hz), 6.16 (m, J = 16, 6 Hz). While the presence of mass spectrum fragment A supported the placement of a Br at C_1 and a Cl at C_3, a combination of ^1H and ^{13}C NMR data was needed to unambiguously locate the remaining halogens. The ^{13}C chemical shift position for halogenated isostructural carbons is very sensitive to the type of halogen substituent. For example in *trans*-2-butenyl halide the $-CH_2Br$ appears 12 ppm higher than the $-CH_2Cl$.[5] Therefore, comparison of the δ values (Table I) for C_1, C_3, and C_4 of **9** vs. the same carbons in **1**, **5**, and **6** supported the assignment of a Br at C_1 and Cls at C_3 and C_4 in **9**. The remaining three halogens could then be placed as shown in C or D.



C D

Table I. 25.1-MHz ^{13}C NMR Chemical Shifts

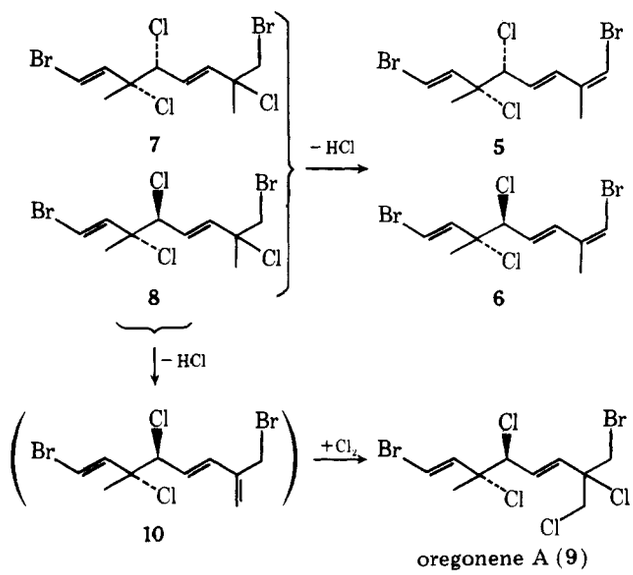
Carbon	 1	 5	 6	 9	 7
1	116.3 (t)	110.5	110.0	110.6	110.6
2	122.5 (d)	128.5	127.9	130.6	127.6
3	71.5 (s)	71.9	71.6	71.3	
4	69.5 (d)	69.1	69.0	67.1	67.8
5	134.0 (d)	133.2	133.0	133.8	137.1
6	139.5 (d)	137.6	138.7	138.9	137.9
7	137.3 (s)		135.4	68.9	
8	143.9 (d)	108.2	108.0	37.1	41.5
9	189.3 (d)	19.1	19.5	49.5	27.8
10	24.6 (q)	28.4	25.4	24.9	28.0

Based upon the symmetry properties of these fragments, C_8 and C_9 are in an enantiotopic-like environment for D, whereas they are heterotopic for C. The observable proton $\Delta\nu_{av8-9}$ = 0.07 ppm is more consistent with the latter rather than the former arrangement. Similarly the $\Delta\nu_{8-9}$ = 12.4 ppm fits the expected shift difference for a C–Br vs. a C–Cl and is thus also consistent only with partial structure C. The relative *R,S* stereochemistry for the C_3–C_4 dichlorides was assigned by the empirical relationship developed below. The vicinal dichloride stereochemistry in **5** (*R,R*) and **6** (*R,S*) had previously been assigned based upon the difference in proton shifts for the C_3 methyls equal to 0.06 ppm (δ 1.79 vs. 1.73) and by a comparison to the methyl shift of a precursor to **6** whose structure had been established by x ray.[4] A much larger methyl shift difference equal to 3 ppm (δ 28 vs. 25) can be observed for the different vicinal dichloride stereochemistries in ^{13}C NMR as exemplified by compounds **1**, **5**, and **6** in Table I. Both the proton and carbon shifts for the **9** C_3 CH_3 support the dichloride stereochemistry shown in Table I.

The major component of the $C_{10}H_{13}Cl_3Br_2$ isomers was assigned structure **7**. Again ^{13}C data were invaluable for the difficult job of unambiguously establishing the halogen regiochemistry. Thus, a Br could be located at C_1 and Cls at C_3 and C_4 based upon the ^{13}C shifts and mass spectral data. The remaining Br could be easily located at C_8 based upon the shift of C_8 (41.5 ppm), vs. 37.1 ppm for the C_8 Br in **9**, with the difference being approximately equal to the expected 2–4 ppm shielding from the γ substituent in the latter.[6] While this work was in progress this same structure was reported from the digestive gland extract of the sea hare *Aplysia californica*; however, the halogen regiochemistry was deduced by a combination of biogenetic and mass spectral analogies.[7] Finally, a tentative assignment of the minor component as **8** was based upon GC/MS data and the discussion below.

The various halocarbons **5–9** isolated in this research are closely related from a biogenetic view. This is evident from both the gross halogenation pattern and the C_3–C_4 chlorine stereochemistry. For example, diastereomers **5** and **6** are undoubtedly each derived from **7** and **8** by a regiospecific loss of HCl as shown in Scheme I. Alternative loss of HCl from **8** from the other possible direction can lead to **9** after enzymatic addition of Cl_2 to an intermediate such as **10**.

Scheme I



Experimental Section

The NMR spectra were recorded on a JEOL PS 100 pulsed FT spectrometer operating at 100 MHz for ^1H and 25.1 MHz for ^{13}C. GC/MS data were recorded on a Finnigan 4000 system equipped with a 3 ft × 0.125 in. glass column packed with 3% OV-17 on Chromosorb G and temperature programmed from 120 to 190 °C at 6 min. Routine low-resolution mass spectral data were recorded on a Hitachi Perkin-Elmer RMU-6E mass spectrometer. High-performance liquid chromatography (HPLC) was done on a Waters ALC 201 using Porasil columns 0.375 in. × 8 ft. All solvents were reagent grade and distilled for HPLC use. Low-boiling petroleum ether was used in all instances. Spectral grade solvents were used for NMR (Me_4Si standard) determinations. The ^{13}C assignments (Table I) were made based on the data of compound **1** and expected additivity effects.[6b] Our earlier assignments of the ^{13}C NMR of **1** for carbons 2, 5, and 6 were revised based upon comparisons to the data for compounds **5** and **6**.

Collections and Extractions. *Plocamium oregonum* was collected from Partridge Point, Whidby Island, Wash., during Sept 2–4, 1975. The algae were kept frozen until extraction. All samples were cold extracted twice with $CHCl_3$ and once with ETOH (95%) over a period of 3–7 days. The combined extract was then chromatographed through silica gel (Grace grade 62, 60–200 mesh, activated) using petroleum ether followed by petroleum ether/benzene (1:1). The resulting semipurified oil was then subjected to HPLC using petroleum ether/benzene (90:10).

Isolations. Following the procedure above for compounds **5**, **6**, and **7**, impure **8** and oregonene A (**9**) were isolated from the extraction of ca. 280 g (dry weight) of alga.

1,8-Dibromo-3,4-dichloro-3,7-dimethyl-1,5,7-octatriene (5) was obtained in HPLC fraction 8 (57 mg) as a clear, mobile oil. Its ^1H NMR [$CDCl_3$, i.e., methyl peaks at δ 1.78 (s) and 1.91, d, J = 2 Hz] and its mass spectrum [i.e., M^+ 360/362/364/366, ratio 32:100:86:26 (theory for Cl_2Br_2 38:100:90:32) for formula $C_{10}H_{12}Cl_2Br_2$] were identical with those in the literature.[4]

The dibromodichlorodimethyloctatriene 6 was obtained in HPLC fraction 9 (60 mg) as an oil. Its NMR [$CDCl_3$, i.e., methyl peaks at δ 1.74 (s) and 1.91, d, J = 2 Hz] and its mass spectrum were identical with those in the literature.[4]

1,8-Dibromo-3,4,7-trichloro-3,7-dimethyl-1,5-octadiene (7) was obtained in HPLC fraction 11 (43 mg) as a clear liquid. Its ^1H NMR ($CDCl_3$) showed two quaternary methyls δ 1.81 (s) and 1.86 (s); a $-CH_2X$ (s) 3.68; XCHCH=CH- (ABX) 4.43 (m, J = 7 Hz), 5.90 (m, J = 16 Hz), 5.98 (d, J = 16, 7 Hz); and a trans BrCH=CH- (AB) 6.45 (d, J = 14 Hz), 6.50 (d, J = 14 Hz). In benzene-d_6 the ABX for -C(Cl)HCH=CH- was clearly resolved: 4.0 (d, J = 7 Hz), 5.40 (d, J

= 16 Hz), 5.56 (dd, J = 16, 7 Hz). Its mass spectrum displayed no parent M^+ but showed fragments $M^+ - Cl$ 361/363/365/367, ratio 40:99:100:28 (theory for Cl_2Br_2 above); $M^+ - Br$ 317/319/321/323, ratio 48:100:68:16 (theory for Cl_3Br 51:100:65:18); 229/231/233; 193/195/197; 167/169/171; and 131/133.

The dibromotrichlorodimethyloctadiene 8 was obtained impure in HPLC fractions 12–13 (17 mg). It was tentatively identified by its GC/MS peak and its mass spectrum, which was identical with that above for 7.

Oregonene A (9) was obtained as a clear oil in HPLC fractions 14–15 (50 mg). Its ^1H NMR ($CDCl_3$) is described in the text and in benzene-d_6 the H_5 and H_6 multiplet was simplified to a doublet (J = 16 Hz) and a doubled doublet (J = 16, 6 Hz). Its mass spectrum showed no parent M^+ but displayed fragments: $M^+ - Cl$ 395/397/399/401/403, ratio 33:87:100:41 (theory for Cl_3Br_2 32:92:100:50); $M^+ - Br$ 351/353/355/357, ratio 39:100:90:34 (theory for Cl_4Br 44:100:83:33), 315/317/319; 228/230/232; 167/169/171; 131/133.

Several attempts were made to dehalogenate the C_7 and C_8 positions. The reaction conditions ($NaCNBH_3$, HMPT, 70 °C, 2 h)[8] that successfully didebrominated 1,2-dibromo-1-methylstyrene in 83% yield in our hands gave no reaction with oregonene A (9). More forcing conditions caused decomposition.

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Registry No.—**5**, 57766-75-3; **6**, 57766-76-4; **7**, 62447-48-7; **8**, 62447-49-8; **9**, 62416-32-4.

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(5) For *trans*-2-butenyl chloride, $-CH_2Cl$ 45.5 ppm, and for *trans*-2-butenyl bromine, $-CH_2Br$ 33.3 ppm.
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Deoxygenation of *N*-Nitrosodibenzylamine with Aryl Azides

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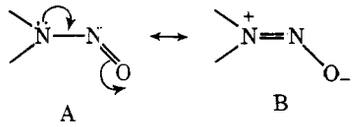
Recently a great deal of attention has been focused on *N*-nitrosamines because of their synthetic utility[1] as well as their carcinogenic[2,3] and carcinostatic[3] properties. The large contribution of dipolar form B to the structure of *N*-nitrosamines, clearly indicated by spectral data,[4] helps explain some of the chemistry of this class of compounds; thus, structure B suggests that *N*-nitrosamines may formally be regarded as *N*-oxides of *N*-nitrenes. These considerations coupled with our interest in novel methods to generate *N*-nitrenes,[5] led us

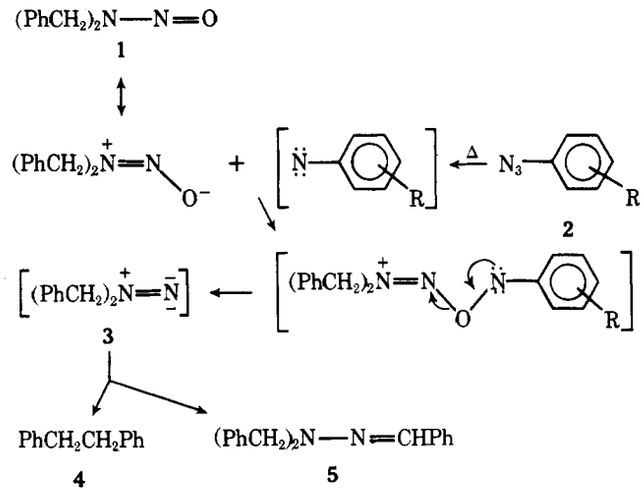


A B

to consider the "deoxygenation" of *N*-nitrosamines as a route to these reactive intermediates.

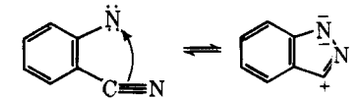
It was reported earlier[6] that the reaction of *N*-nitrosodibenzylamine (1) with iron pentacarbonyl resulted in the formation of products traceable to *N*-dibenzylaminonitrene (3). It was felt that electron-deficient species such as *C*-nitrenes should react with *N*-nitrosamines to yield *N*-nitrenes. This communication describes our results.

Since bibenzyl (4) and benzylidenedibenzylhydrazine (5) are known transformation products of *N*-dibenzylaminonitrene (3),[7] *N*-nitrosodibenzylamine (1) was selected as the substrate for our investigation. A solution of 1 in chlorobenzene was heated to reflux with a twofold excess of phenyl azide until nitrogen evolution ceased. Work-up of the reaction mixture gave 81.5% of recovered 1 along with trace amounts



of bibenzyl (4); thin-layer chromatography showed the presence of azoxybenzene.[8] Since the anticipated course of the reaction was predicated on the electron-deficient nature of the *C*-nitrenes, the reaction of 1 was carried out with aryl azides containing groups which should enhance the electron-deficient nature of the *C*-nitrenes derived from them.[9] 4-Nitrophenyl azide gave a 46% yield of bibenzyl (4), while only 48% of 1 was recovered. Similarly, 4-cyanophenyl azide afforded a 48% yield of 4, although a much larger amount (93.7%) of 1 was recovered. Unexpectedly, *p*-chlorophenyl azide gave *no* bibenzyl, while 79.5% of 1 was unreacted. The anomalous effect of the chlorine was further confirmed by the reaction of 2-chloro-4-nitrophenyl azide with 1 in which only 14% of 4 (compared with 4-nitrophenyl azide) was obtained and 1 was recovered in 63% yield. 2,3-Dichlorophenyl azide gave 4 and 5, albeit in low yield.[10]

With substituents in the 2 position, such as *o*-benzoyl and *o*-nitro, capable of reacting with the nitrene[11] to give stable compounds, little or no bibenzyl was obtained (see Table I, entries 8 and 9); 3-phenylanthranil and benzofuroxan were the major products, respectively. 2-Cyanophenyl azide provided a surprising contrast to the aforementioned azides; bibenzyl was isolated in as good a yield (47%) as those obtained from 4-nitro- and 4-cyanophenyl azides. This may be rationalized by the fact that the cyano group, being located ortho to the nitrene, may interact with and in a sense "store" the nitrene without forming a stable compound in contrast to the nitro and benzoyl groups (vide supra[11]). These data led to the



expectation that the synergistic effect of a cyano group in the 2 position coupled with that of a nitro group in the 4 position should result in providing us with a most efficient azide for