Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.04; H, 9.11.

Similarly, the reaction with diethyl sodiomalonate gave 64% of **1b**: bp 142–144 °C (10 Torr); IR (neat) 1751 and 1733 cm^{-1} [lit.[14] bp 136–139 °C (11 Torr)].

Alkyl 6-Methylheptanoates (2). Diester **1b** was converted by known procedures[15] to 6-methylheptanoic acid (**3**) in 95% yield, bp 85–88 °C (2 Torr); *p*-bromophenacyl ester, mp 67.5–67.6 °C [lit.[16] bp 128–129 °C (15 Torr); *p*-bromophenacyl ester, mp 67.7 °C]. Fischer esterification of **3** gave **2a**: bp 72.5–73.2 °C (11 Torr); IR (neat) 1745 cm^{-1} [lit.[17,18] bp 73 °C (10 Torr); IR (neat) 1739 cm^{-1}]. Similarly, **3** gave **2b** in 59% yield: bp 52–53 °C (2 Torr); IR (neat) 1739 cm^{-1} (lit.[19] bp 200.3 °C).

General Reaction Procedure. A. Analytical Scale. The following procedure was typical of that used for all experiments reported in Tables I and II.

To a 25-mL flask were added diester **1a** or **1b** (4.0 mmol), a salt (4.0 mmol), water (8.0 mmol), and Me_2SO (10 mL). The heterogeneous reaction mixture was refluxed for 1 h, cooled, transferred to a separatory funnel containing 100 mL of water, and extracted with three 15-mL portions of hexane. The combined hexane extract was washed once with water, dried (Na_2SO_4), filtered, and concentrated at reduced pressure on a rotary evaporator.

The residual oil was analyzed by GLC. Authentic samples of **1a, 1b, 2a,** and **2b** were used to calibrate the detector response and determine the retention times (in min): **2a,** 1.8; **2b,** 2.2; **1a,** 4.6; and **1b,** 6.6. It was established by control runs that the detectable limit of diester in a mixture of 1 and **2** was 0.8%. No peaks other than **1** and **2** were observed in the product mixture.

B. Preparative Scale. A mixture of **1a** (4.4 g, 0.020 mol), sodium cyanide (1.0 g, 0.020 mol), water (0.72 mL, 0.040 mol), and Me_2SO (50 mL) was refluxed for 1 h and worked up as above to give 2.3 g (72%) of **2a**: purity >99% by GLC.

Acknowledgment. The authors are indebted to Professor Krapcho for stimulating discussions and helpful suggestions.

Registry No.—**1a,** 62337-57-9; **1b,** 39953-95-2; **2a,** 2519-37-1; **2b,** 62337-58-0; **3,** 929-10-2; **3** *p*-bromophenacyl ester, 62337-59-1; 1-bromo-4-methylpentane, 626-88-0; dimethyl sodiomalonate, 18424-76-5; diethyl sodiomalonate, 996-82-7.

References and Notes

(1) A. P. Krapcho, G. A. Glynn, and B. J. Grenon, *Tetrahedron Lett.*, 215 (1967).
(2) A. P. Krapcho and A. J. Lovey, *Tetrahedron Lett.*, 957 (1973).
(3) A. P. Krapcho, E. G. E. Jahngen, Jr., A. J. Lovey, and F. W. Short, *Tetrahedron Lett.*, 1091 (1974).
(4) C. L. Liotta and F. L. Cook, *Tetrahedron Lett.*, 1095 (1974).
(5) (a) W. S. Johnson, C. A. Harbert, and R. D. Stipanovic, *J. Am. Chem. Soc.*, **90,** 5279 (1968); (b) J. Harley-Mason and Atta-ur-Rahman, *Chem. Ind. (London),* 1845 (1968); (c) A. P. Krapcho and B. P. Mundy, *Tetrahedron,* **26,** 5437 (1970); (d) W. Kirmse, J. Knist, and J.-J. Ratajczak, *Chem. Ber.,* **109,** 2296 (1976).
(6) (a) B. M. Trost and T. J. Dietsche, *J. Am. Chem. Soc.,* **95,** 8200 (1973); (b) B. M. Trost and L. Weber, *J. Org. Chem.,* **40,** 3617 (1975).
(7) (a) M. Asaoka, K. Miyake, and H. Takei, *Chem. Lett.,* 1149 (1975); (b) W. S. Johnson, C. A. Harbert, B. E. Ratcliffe, and R. D. Stripanovic, *J. Am. Chem. Soc.,* **98,** 6188 (1976).
(8) (a) F. Texier, E. Marchand, and R. Carrie, *Tetrahedron,* **30,** 3185 (1974); (b) D. H. Miles and B.-S. Huang, *J. Org. Chem.,* **41,** 208 (1976).
(9) B. A. Bierl, M. Beroza, and C. W. Collier, *J. Econ. Entomol.,* **65,** 659 (1972).
(10) (a) H. J. Bestmann and O. Vostrowsky, *Tetrahedron Lett.,* 207 (1974); (b) H. J. Bestmann, O. Vostrowsky, and W. Stransky, *Chem. Ber.,* **109,** 3375 (1976).
(11) A. P. Krapcho, J. M. Eldridge, E. G. E. Jahngen, Jr., A. J. Lovey, W. P. Stephens, and J. F. Weimaster, Abstracts, 172nd National Meeting of the American Chemical Society, San Francisco, Calif., Sept 1976, No. ORGN-196.
(12) T. M. Santosusso and D. Swern, *J. Org. Chem.,* **41,** 2762 (1976).
(13) R. Adams and R. M. Kamm, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N.Y., 1941, p 250.
(14) H. Kondo and H. Suzuki, *Ber.,* **69,** 2459 (1936).
(15) E. B. Vliet, C. S. Marvel, and C. M. Hsueh, "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 416.
(16) A. H. Milburn and E. V. Truter, *J. Chem. Soc.,* 3344 (1954).
(17) E. Rothstein and W. G. Schofield, *J. Chem. Soc.,* 4566 (1965).
(18) E. Wenkert, P. Bakuzis, R. J. Baumgarten, C. L. Leicht, and H. P. Schenk, *J. Am. Chem. Soc.,* **93,** 3208 (1971).
(19) P. A. Levene and C. H. Allen, *J. Biol. Chem.,* **27,** 433 (1916).

Eremofortin C. A New Metabolite Obtained from *Penicillium roqueforti* Cultures and from Biotransformation of PR Toxin

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Received January 17, 1977

Penicillium roqueforti is a fungal species of particular interest because of the toxic compounds recently isolated from the mycelium of this species. These compounds include the indole alkaloids[1,2] and the sesquiterpenoid metabolites such as PR toxin (**3**) and related compounds.[3,4] We report here the isolation and characterization of a new sesquiterpenoid compound, eremofortin C (**4**). This compound was obtained using two methods: direct isolation from *P. roqueforti* culture media and biotransformation of PR toxin and eremofortin A[4] (**1**) by liver mixed-function oxidases.[5,6]

Isolation and Characterization of Eremofortin C. Eremofortin C was isolated from the culture media of a *P. roqueforti* strain by chloroform extraction. The chloroform extract was chromatographed on silica gel and crystallized from ethyl ether. The structure **4** was assigned on the bases of spectral data and various chemical reactions. The spectral characteristics of the compound indicated that it was closely related to PR toxin (**3**) and eremofortin A (**1**).

The IR spectrum (KBr) showed a hydroxyl group (3420, 3350 cm^{-1}), an α,β-unsaturated ketone (1685 cm^{-1}), an isolated double bond (1650 cm^{-1}), and a conjugated double bond (1620 cm^{-1}). The mass spectrum of **4** showed a molecular ion at *m/e* 322. High-resolution mass spectral analysis indicated a molecular peak at *m/e* 322.14161 (calcd for $C_{17}H_{22}O_6$, 322.14163). The complex 250-MHz ^1H NMR spectrum appeared to be a superposition of the spectra of two acetylated compounds: δ CH_3COO 2.18 and 2.19 ppm, two multiplets centered at δ 5.18 and 5.25 (H-3), and two singlets at δ 6.02 and 6.44 (H-9).

The equilibrium suggested by these data was proved by variable temperature ^1H NMR studies. Ratios of the areas of the H-9 peaks were measured at different temperatures. That at δ 6.02 ppm was attributed to compound **4a** and that at δ 6.44 ppm to compound **4b** after comparison with values obtained for H-9 in compounds **1, 3,** and **6**.[3,4] Results are given in Table I. An increasing temperature seemed to promote the formation of compound **4b** (79% at 95 °C). A lowering of these temperatures resulted in the recovery of the initial ratio of the two compounds.

The structure was confirmed by the following chemical reactions. Sodium borohydride reduction of PR toxin (**3**) yielded a crystalline substance. Chromatographic behavior and spectroscopic data (IR, ^1H NMR, mass spectrum) showed that this compound was identical with naturally occurring eremofortin C(**4a** $\rightleftarrows$ **4b**). Acetylation of eremofortin C yielded a unique compound **2** which crystallized from ethyl ether. The structure of **2** was assigned on the bases of spectral data by comparison with the previously mentioned metabolites.[4]

In Vitro Metabolism of PR Toxin and Eremofortin A. Four metabolites were obtained during incubation of PR toxin and eremofortin A with the microsomal enzymes of rat hepatocytes. Their chemical structures are shown in Scheme I.

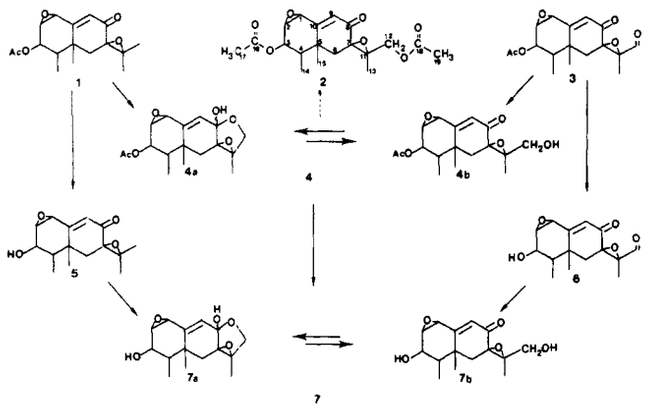
All the metabolites obtained from 10 mg of compounds **1** or **3** were isolated from the enzymatic reaction medium by

Table I. Effect of Temperature on Percent of Compound 4b in the Equilibrium 4a ⇄ 4b (in Pyridine-d_5)[a]

θ	20 °C	35 °C	50 °C	65 °C	80 °C	95 °C
% of 4b	61	67	69	73	77	79

[a] % 4b = (area of H-9 peak of 4b)/(area of H-9 peaks 4a + 4b) × 100.

Scheme I. Bioconversion of PR Toxin and Eremofortin A



Continuous lines: metabolic conversions
↓: metabolism not requiring $NADPH_2$
↘ ↙: metabolism requiring $NADPH_2$

Dotted lines ↓: chemical synthesis
⇄: chemical equilibrium

chloroform extraction. Reactions products were monitored by TLC and purified by silica gel column chromatography. Each metabolite isolated (a few milligrams) was crystallized and analyzed by mass spectroscopy and some by FT NMR spectroscopy (250 MHz). The structures were confirmed by chemical synthesis from known precursors.

Eremofortin C (4), eremofortin A alcohol (5), and PR alcohol (6), obtained from the enzymatic medium, were identified by direct comparisons with authentic specimens (chromatographic behavior, mass spectra, ^1H NMR spectra, and mixture melting points).

Eremofortin C Alcohol (7). The enzymatic product and saponification product from eremofortin C (4) showed similar chromatographic behavior. Low-resolution mass spectra were identical. The ^1H NMR spectrum (CD_3OD) showed an equilibrium between two compounds **7a** ⇄ **7b** measured on H-9 peaks: δ 5.95 ppm for **7a** and 6.42 for **7b**. Compound **7b** represented 75% of the mixture at 20 °C. Eremofortin C alcohol (7) was also obtained by sodium borohydride reduction of compound 6 and by enzymatic conversion of 5 and 6.

These results suggest an interesting biotransformation relationship between three compounds: eremofortin C (4), PR toxin (3) and eremofortin A (1). If similar relationships are found to exist during PR toxin biosynthesis by *Penicillium roqueforti* we could then hope to determine the biochemical pathway of *P. roqueforti* metabolites.

Experimental Section

Infrared spectra were obtained with a Perkin-Elmer 447 spectrometer, ^1H NMR spectra (250 MHz) were recorded with a Cameca spectrometer, variable temperature ^1H NMR spectra (90 MHz) with a Perkin-Elmer R-32 spectrometer, ^1H NMR spectra (60 MHz) with a Varian T-60 spectrometer, and ^{13}C NMR spectra (15, 1 MHz) with a JEOL FT 60 spectrometer.

Mass spectra were determined on an AEI Model MS 12 spectrometer for low resolution and MS 9 for high resolution (Laboratoire de Chimie Appliquée de l'Université de Bordeaux, 1 Bordeaux, France). Ultraviolet spectra were run on a Cary 11 spectrometer. A Perkin-Elmer 141 polarimeter was used for specific rotation. All melting points are uncorrected. Elemental microanalyses were carried out by the Centre de Microanalyse du CNRS, Thiais, France.

Isolation of Eremofortin C (4). NRRL 849, a *Penicillium roqueforti* strain, was grown in a culture medium containing 2% yeast extract and 15% sucrose. The culture flasks were incubated for 14 days at 25 °C in the dark without shaking. The mycelium was discarded and the culture medium extracted with chloroform. The dried, concentrated chloroform extract was chromatographed on a silica gel column. PR toxin and eremofortin C (4) were eluted with methanol–chloroform at proportion of 1:99 (v/v) and 2:98 (v/v), respectively. Each compound was monitored by TLC (elution solvent $CHCl_3$/MeOH, 95:5). Each was sprayed with a concentrated sulfuric acid reagent, examined with UV light at 365 nm, and then heated to 120 °C for 20 min.

Crystallization from ethyl ether gave a compound whose properties (IR, ^1H NMR) are described in the text: mp 122–126 °C; mass spectrum *m/e* 322 (M^+), 191, 177, 163, 149. Anal. Calcd for $C_{17}H_{22}O_6$ C, 63.34; H, 6.89. Found: C, 63.26; H, 6.92. The acetate of eremofortin C was prepared in acetic anhydride–pyridine solution at room temperature. 4 (140 mg) in 15 mL of solution gave 120 mg of pure acetate: mp 122–124 °C; $[\alpha]^{20}_D$ +161° (*c* 1.09, $CHCl_3$); UV λ_{max} 248 nm (ϵ 16 960); IR (KBr) 1745, 1740, and 1685 cm^{-1}; mass spectrum *m/e* 364 (M^+), 322, 291, 279, 205, 191, 177; ^1H NMR (60 MHz) δ ($CDCl_3$) H_3C-14 1.07 (d, 6.5 Hz), H_3C-13 1.4, H_3C-15 1.47, H_3C–COO 2.10 and 2.15, H-1 3.72 (d, 3 Hz), H-2 4 (m), H_2C-12 4.6, H-3 5.25 (m), H-9 6.55; ^{13}C NMR (15.1 MHz) ($CDCl_3$) δ (from Me_4Si) C-1 55.22 or 55.87 (d), C-2 55.22 or 55.87 (d), C-3 70.04 (d), C-4 41.84 (d), C-5 37.29 (s), C-6 42.36 (t), C-7 61.98 or 64.17 (s), C-8 192.96 (s), C-9 131.50 (d), C-10 161.39 (s), C-11 61.98 or 64.17 (s), C-12 65.36 (t), C-13 22.61 (q), C-14 10.39 (q), C-15 16.37 (q), C-16 and C-18 170.15 (s), C-17 and C-19 20.79 (q). Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.62; H, 6.64. Found: C, 62.49; H, 6.63.

Reduction of PR Toxin. PR toxin (240 mg) was reduced with 17 mg of $NaBH_4$ in 40 mL of MeOH at −5 °C for 20 min. The crude extract was purified on a silica gel column and gave 120 mg of PR toxin and 100 mg of eremofortin C, crystallized from ether. All spectroscopic data are identical with those previously obtained for naturally occurring eremofortin C (IR, mass spectrum, ^1H NMR), mp 122–126 °C, mixture melting point unchanged with eremofortin C (4).

Microsomal Preparations. Male rats (Wistar strain) weighing about 250 g were used for the experiment. They received an ip injection of 3-methylcholanthrene (20 mg/kg dissolved in corn oil) once a day for 3 consecutive days before killing. Livers were homogenized in 3 volumes of ice-cold 150 mM KCl and centrifuged at 4 °C for 20 min at 15 000 *g*. The pellets were discarded and the post-mitochondrial supernatant was removed and centrifuged for 90 min at 200 000 *g* (Beckman Ti Rotor). The microsomal pellets were washed twice with the following medium: 10 mM Tris HCl, pH 7.4, containing 0.5 mM $MgCl_2$ and 0.25 M sucrose. Microsomes were resuspended in this buffer and stored in liquid nitrogen. The amount of protein in the microsomal fraction was determined by the method of Lowry et al.[8] using bovine serum albumin as a standard.

Incubation Procedure. Incubations were carried out in conical glass flasks open to the air at 37 °C with gentle shaking for 1 or 2 h. The reaction mixture in 100 mL of Tris HCl buffer (10 mM Tris HCl, pH 7.4, 0.5 mM Mg Cl_2, 0.25 M sucrose) contained 150 mg of microsomal proteins and in some experiments 150 μM $NADPH_2$ (Boehringer). PR toxin or eremofortin A (10 mg in 450 μL of methanol) was added just before incubation. The reactions were stopped by addition of cold chloroform and the metabolites were extracted with chloroform. The dried, concentrated chloroform extract was analyzed by TLC using the system previously described. The metabolites were isolated using a stepwise gradient mixture of MeOH (0:100 to 20:80). A typical experiment with 10 mg of PR toxin and 150 μM of $NADPH_2$ produced 0.5 mg of compound 5, 3 mg of compounds 4 and 3, and 5 mg of compound 7. Each metabolite isolated was crystallized in the appropriate solvent and submitted to mass spectrum analysis.

Eremofortin A alcohol was obtained from eremofortin A by an incubation procedure without $NADPH_2$. Saponification of eremofortin A (50 mg) was carried out in a 0.02 M solution of potassium hydroxide in methanol–water (4:1 v/v, 10 mL) at 37 °C for 2 h. The reaction mixture was diluted with water and extracted with chloroform. The crude extract was crystallized from ethyl ether–isopropyl ether mixture (25 mg): mp 128–130 °C; $[\alpha]^{20}_D$ +143° (*c* 1.04, $CHCl_3$); UV $CHCl_3$ λ 246 nm (ϵ 13 200); IR (KBr) 3570, 3510, 3380, and 1685 cm^{-1}; mass spectrum *m/e* 264 (M^+), 235, 177, 149; high-resolution mass spectrum M^+ 264.13598 (calcd for $C_{15}H_{20}O_4$, 264.13615); ^1H NMR (60 MHz) ($CDCl_3$) δ H_3C-14 1.09 (d, 6.5 Hz), H_3C-12 1.28,

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.

References and Notes

(1) S. Ohomomo, T. Sato, T. Utagawa, and M. Abe, *Agric. Biol. Chem.*, **39**, 1333 (1975).
(2) P. M. Scott, M. A. Merrien, and J. Polonsky, *Experientia*, **32**, 140 (1976).
(3) R. D. Wei, H. K. Schnoes, P. A. Hart, and F. M. Strong, *Tetrahedron*, **31**, 109 (1975).
(4) S. Moreau, A. Gaudemer, A. Lablache-Combier, and J. Biguet, *Tetrahedron Lett.*, 833 (1976).
(5) A. H. Conney, *Pharmacol. Rev.*, **19**, 317 (1967).
(6) D. E. Hathway, S. S. Brown, L. F. Chassaud, and D. H. Hutson, "Foreign Compounds Metabolism in Mammals", Vol. 1 Chemical Society Specialist Report, London, 1970, p 315.
(7) C. De Duve, R. Wattiaux, and P. Baudhuin, *Adv. Enzymol.*, **24**, 291–358 (1962).
(8) O. H. Lowry, H. J. Rosebrough, A. L. Farr, and R. J. Randall, *J. Biol. Chem.*, **193**, 265–275 (1951).

Monoterpene Halogenation by the Red Alga *Placamium oregonum*

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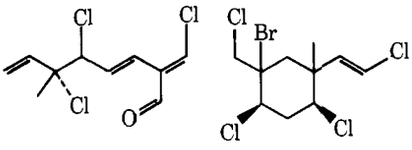
Received February 7, 1977

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

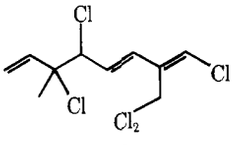
Four major constituents could be observed in approximately equal amounts in the reconstructed GC/MS trace (RGC) of the total ions from the crude $CHCl_3$ extract of *P. oregonum*.



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

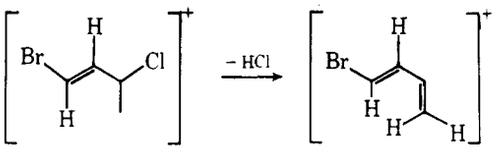
or

violacene[2b]



4[3]

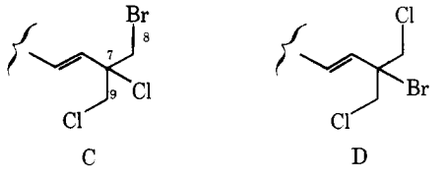
Comparison of this to the RGC for *m/e* 167 clearly showed that each of these components, along with a fifth minor one, contained a common C_4H_5ClBr structural unit A which fragmented to B by HCl loss. In addition, the mass spectra revealed that these five metabolites consisted of sets of isomers including 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