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Registry No. 9, 74164-09-3; 10, 74096-80-3; 11, 66940-40-7; 12, 66940-42-9; 13, 74096-81-4; 15, 74127-92-7; 16, 74096-82-5; 18, 74112-97-3; 19, 74096-83-6; 20, 74096-84-7; 21, 74096-85-8; 22, 74096-86-9; 25, 74096-87-0; 26, 74096-88-1; 27, 74112-98-4; 28, 74096-89-2; 29, 74112-99-5.

Cyclic Monoterpenoid Feeding Deterrents from the Red Marine Alga *Ochtodes crockeri*

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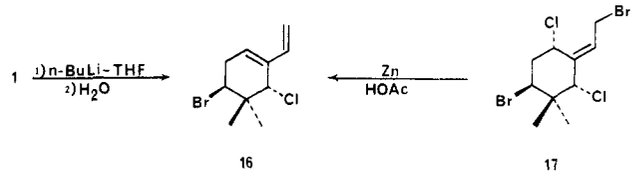
Thirteen new cyclic halogenated and oxygenated monoterpenoids along with chondrocoles A and C have been isolated from the red marine alga *Ochtodes crockeri* Setchell and Gardner from the Galapagos Islands. These new compounds have been characterized by combined spectral and chemical methods, and on the basis of laboratory feeding experiments, they appear to function as herbivore feeding deterrents in the natural environment.

Unlike other marine organisms, red seaweeds (Rhodophyta) of the families Plocamiaceae and Rhizophyllidaceae (Gigartinales) produce halogenated monoterpenoids. Within these families, the genera *Plocamium*,[2] *Chondrococcus*,[2] and *Ochtodes*[3] are known to contain large amounts of both acyclic and cyclic polyhalogenated monoterpenes. While the biological functions of these compounds are not well understood, several previously reported monoterpenes exhibit antimicrobial activity[3], and some are toxic.[4] In this paper we wish to describe the structures of 13 new cyclic monoterpenoids from the red seaweed *Ochtodes crockeri* and, further, to provide evidence that in *Ochtodes* these compounds function as herbivore feeding deterrents.

The marine alga *O. crockeri* Setchell and Gardner grows abundantly and without evidence of predation throughout the Galapagos Islands, despite the intense feeding pressure of many endemic herbivores including the voracious marine iguana *Amblrhyncus cristatus*. Collections of *O. crockeri* were made from locales near Isla Santa Cruz and Isla Isabela of the Archipelago de Colon (Galapagos Islands) in 1977 and 1978. The freshly collected algae were stored in 2-propanol and subsequently repeatedly extracted with chloroform/methanol (1:1). The combined extracts were chromatographed on silica gel, and fractions were subsequently purified by high-pressure LC (μ-Porasil) to yield compounds **1**–**15** (in order of their elution from silica gel). Compounds **1** and **4**–**15** (see Chart I) were recognized as new monoterpenoids, whereas **2** and **3**, chondrocoles A and C, had been previously isolated from the related alga *Chondrococcus hornemanni* (Mertens) Schmitz from Hawaii.[5] The structures of these new terpenoids were assigned, including relative stereochemistries,[6] by spectral analysis (^{1}H and ^{13}C NMR data, Tables I and II) including data obtained from suitable derivatives. Compounds **1**–**15** possess a monoterpenoid ring system present in three of four synergistic sex pheromones produced by the male boll weevil, *Anthonomus grandis* Bohemon.[7,8]

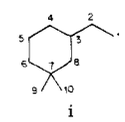
The diene **1** was isolated as 3% of the organic extract and analyzed for $C_{10}H_{13}Br_2Cl$ by high-resolution mass spectrometry. The three degrees of unsaturation were accounted for by two conjugated double bonds [λ_{max} 242 nm (ϵ 5300)] and one carbocyclic ring. Characteristic axial and equatorial ^{1}H NMR coupling constants for the α-bromine (C-6) methine proton (Table I) strongly suggested the presence of a six-membered ring. Futhermore, the proton chemical shifts, and a vicinal 14-Hz olefinic coupling constant, indicated a disubstituted *E* olefin to be placed at C-1–C-2. Treatment of the diene **1** with *n*-BuLi in THF at −78 °C resulted in lithium–bromine exchange which, after protonation, yielded the debromodiene **16**.



16 17

Compound **16** was also produced by treatment of the previously described monoterpene ochtodene (**17**)[2] with Zn in acetic acid. Mass spectral analysis of **16** clearly established the presence of one bromine and one chlorine atom, illustrating that the olefinic halogen at C-1 in diene **1** is bromine. Since diene **16** was identical as produced from both **1** and **17**, compound **1** must possess an equa-

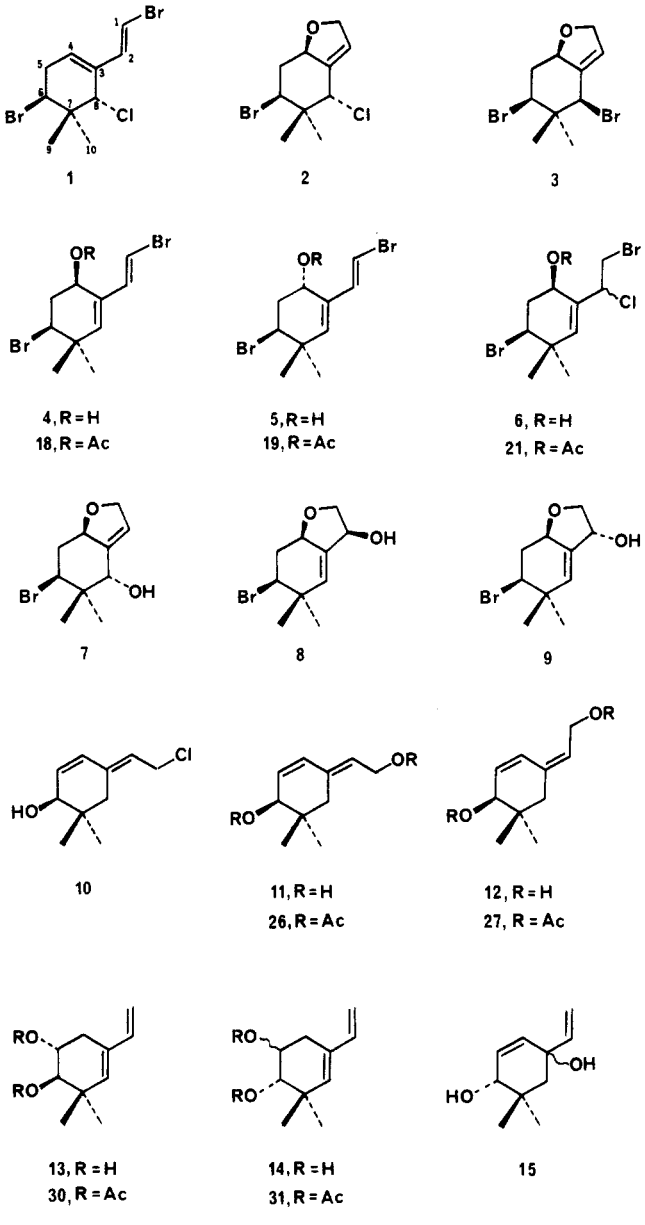
(1) To whom correspondence should be addressed.
(2) D. J. Faulkner, *Tetrahedron*, **33**, 1 (1978), and reference cited therein.
(3) O. J. McConnell and W. Fenical, *J. Org. Chem.*, **43**, 4238 (1978).
(4) P. Crews, E. Kho-Wiseman, and P. Montana, *J. Org. Chem.*, **43**, 116 (1978).
(5) B. J. Burreson, F. X. Woolard, and R. E. Moore, *Chem. Lett.*, 1111 (1975).
(6) The structures assigned compounds **1** and **4**–**15** are drawn to indicate relative stereochemistry only. The convenion *R** and *S** is used in the experimental section to indicate these assignments. See IUPAC Tentative Rules for Stereochemistry: *J. Org. Chem.*, **35**, 2849 (1970).
(7) J. H. Tumlinson, D. D. Hardee, R. C. Guelder, A. C. Thompson, P. A. Hedin, and J. P. Minyard, *Science* (*Washington, DC*), **166**, 1010 (1969).
(8) We wish to suggest the name ochtodane (i) for this recently recognized monoterpene ring sytem and the numbering sequence below which is based upon geraniol.



i

0022-3263/80/1945-3401$01.00/0

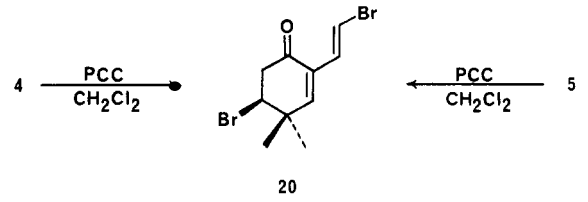
Chart I



torial bromine at C-6 and an axial chlorine substituent at C-8 in analogy to ochtodene.[3]

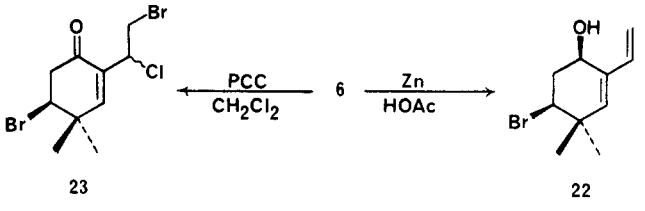
Compounds **2** and **3**, chondrocoles A and C,[5] were isolated as 3 and 2% of the extract of *O. crockeri*, respectively. The identities of these monoterpenoids were confirmed by comparisons with authentic samples,[9] and by analysis of spectral data (Tables I and II). ^{13}C and ^{1}H NMR features for **2** and **3** were highly comparable with several other monoterpenoids isolated and provided a sound foundation for subsequent assignments.

Compounds **4** and **5** (3 and 2% of the extract) were recognized as isomeric alcohols by their highly comparable spectral characteristics. Both compounds yielded a molecular ion which analyzed for $C_{10}H_{15}OBr_2$, and they exhibited identical UV absorptions at 240 nm (ϵ 17 000), revealing the presence of a consistent diene chromophore. As in **1**, both **4** and **5** exhibited 14-Hz coupling constants for the bromine-substituted *E* double bond at C-1, C-2. Treatment of **4** and **5** with acetic anhydride in pyridine gave the acetates **18** and **19**, confirming that **4** and **5** were alcohols and allowing the ^{1}H NMR assignments of the methine protons at C-4. Location of the C-4 methine bands in the ^{1}H NMR spectra of **4** and **5** and the data from spin-decoupling experiments allowed assignment of the isolated four-spin system involving carbons 4–6. Pyridinium chlorochromate (PCC) oxidation of both **4** and **5** yielded the same (including optical rotation) α,β-unsaturated ketone **20**. Therefore, the absolute stereochemistries



at C-6 in **4** and **5** are identical. Chemical shift and coupling constant data for the C-6 methine proton confirmed the pseudoequatorial bromine substituent. The relative stereochemistries at C-4 in these alcohols were determined from ^{1}H NMR features of the acetates **18** and **19**. The C-4 proton from acetate **18** shows couplings of 8 and 6 Hz, while acetate **19** shows couplings of 3 and 3 Hz. Thus the C-4 methine in **18** was assigned as pseudoaxial and that in **19** as pseudoequatorial. The C-4 hydroxyl substituents were, therefore, assigned as pseudoequatorial in **4** and pseudoaxial in **5**. In support of the pseudoaxial hydroxyl assignment in **5**, the C-6 pseudoaxial proton is shifted 0.35 ppm, illustrating the expected 1,3-diaxial interaction.

Alcohol **6**, isolated as 4% of the extract, analyzed for $C_{10}H_{15}OBr_2Cl$ and lacked the diene chromophores observed in **4** and **5**. The alcohol formed a monoacetate, **21**, thus allowing the delineation of the C-4 methine proton in its ^{1}H NMR spectrum. The primary halogen at C-1 was assigned as bromine on the basis of its ^{13}C NMR shift of 40.5 ppm (off-resonance triplet), well below the value of 50 ppm or greater expected for carbons bearing a primary chlorine.[10] Treatment of **6** with Zn/HOAc afforded the expected vicinal elimination at C-1, C-2, yielding the diene **22**. Diene **22** showed mass spectral features for a single

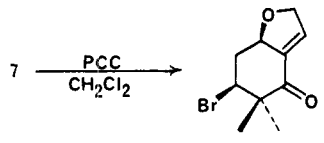


bromine atom, illustrating that the vicinal elimination involved a chlorine atom at C-2. PCC oxidation of **6** yielded the α,β-unsaturated ketone **23** [λ_{max} 235 nm (ϵ 8800)]. Spectral analysis of **23** confirmed the location of the carbonyl at C-4 and the C-3, C-8 placement of the olefin. The stereochemical assignments for **6** were derived from spin-decoupling experiments (Table I).

The alcohol **7** was isolated as 2% of the organic extract and determined, by mass spectrometry, to have the molecular formula $C_{10}H_{15}O_2Br$. The striking similarity between **7** and chondrocole A (**2**) allowed the formulation of its basic structure. Placement of the hydroxyl at C-8 was indicated by the facile conversion of **7** to the α,β-unsaturated ketone **24** [λ_{max} 253 nm (ϵ 5200)] via PCC oxidation. The stereochemistry of the C-8 hydroxyl was assigned as axial on the basis of both the 1,3-diaxial deshielding effects on the C-6 proton and the ^{13}C NMR γ-shielding effects

(9) We thank Professor R. E. Moore, University of Hawaii, for providing authentic samples of chondrocoles A and C.

(10) J. J. Sims, A. F. Rose, and R. R. Izac, in "Marine Natural Products", Vol. II, P. J. Scheuer, Ed., Academic Press, New York, 1979, Chapter 5.



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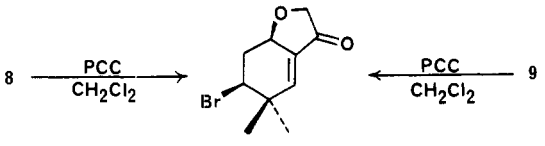
upon the methyl carbons C-9 and C-10.[11] Further analysis of the ^1H NMR spectrum with Eu(fod)$_3$-induced shifts (Experimental Section) allowed the complete assignment shown in Table I.

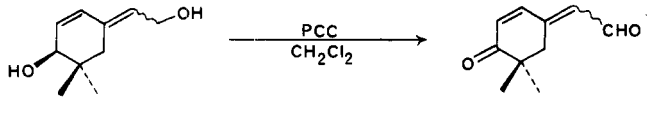
Two alcohols, **8** and **9**, isomeric with **7** ($C_{10}H_{15}O_2Br$) were also components of *O. crockeri* (3 and 2% of the extract). That the alcohols were epimeric at the hydroxyl-bearing center was confirmed by oxidation of each alcohol to the identical α,β-unsaturated ketone **25** [λ_{max} 234 nm (ϵ 8400)].



25

The ^1H NMR characteristics clearly illustrated that the enone functionality in **25** encompassed C-2, C-3, and C-8. In the alcohols, the stereochemistries of the C-2 hydroxyls were assigned on the basis of the 1,3-diaxial-type deshielding interaction experienced by the axial methine proton at C-4. In alcohol **8**, this proton appears at δ 4.12, while in **9** this proton is shifted to δ 4.44. Hence, the hydroxyl in alcohol **8** is assigned trans to the C-4 methine proton, and in **9** it is assigned cis.

Three compounds, the chloro alcohol **10** and the isomeric diols **11** and **12**, all of which showed very similar ^1H NMR spectra, were isolated as 2, 4, and 3% of the extract, respectively. The diols **11** and **12** each analyzed for $C_{10}H_{16}O_2$, and UV absorptions at 238 nm (ϵ 19 400) for **11** and 238 nm (ϵ 10 600) for **12** suggested each to possess the heteroannular diene chromophore. Acetylation yielded the diacetates **26** and **27**. ^1H NMR spectra of each confirmed the presence of one primary and one secondary alcohol. The placement of primary alcohols at C-1, the diene chromophores at C-2 through C-5, and the equatorial secondary hydroxyls at C-6 was made possible through ^1H NMR decoupling studies and from an analysis of ^{13}C NMR chemical shift data.[10] The *gem*-dimethyl carbons attached to C-7 exhibit diagnostic γ-shielding effects corresponding to the type and stereochemistries of adjacent substituents. Assignments of the stereochemistries of the C-2, C-3 double bonds in **11** and **12** remained. In alcohol **11**, the C-8 protons are nonequivalent and form an AB quartet with bands at δ 2.06 and 2.31. In **12** the C-8 protons appear as a 2-hydrogen singlet at δ 2.13. Also, in **12** the C-4 olefin proton is deshielded by 0.33 ppm relative to that in **11**. These shifts indicate that the hydroxyl is in proximity to C-8 in alcohol **11**, thus requiring the C-2, C-3 *E* configuration. In **12**, the hydroxyl approaches C-4, thus requiring the *Z* configuration. For comparison of these effects at higher oxidation states, alcohols **11** and **12** were oxidized to the isomeric keto aldehydes **28** and **29**. Here again,



11, E
12, Z

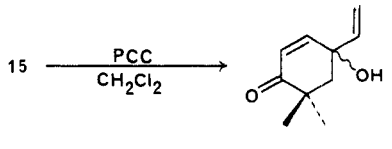
28, E
29, Z

large shifts are evident at both C-4 and C-8. In **28** the C-8 protons appear 0.40 ppm to lower field than those in **29**, and in **29** the C-4 proton is deshielded by 1.0 ppm, thus supporting the *E* and *Z* assignments for **11** and **12**, respectively.

The chloro alcohol **10** had ^1H and ^{13}C NMR features similar to those of the diol **11**. The major differences were the spectral characteristics derived from the halogen-bearing carbon, C-1. Although facile loss of the C-1 allylic halogen precluded mass spectral assignment of this element from isotopic data, the ^{13}C NMR shift for C-1 (65.5 ppm, triplet) strongly indicated that the halogen was chlorine. The C-2, C-3 olefin stereochemistry was assigned as *E* based upon the favorable ^1H NMR spectral comparison of **10** with **11** and not with **12**.

Three diols, **13–15**, were isolated as the most polar components of *O. crockeri* in 3, 2, and 2% yields, respectively. Diols **13** and **14** each analyzed for $C_{10}H_{16}O_2$ and were recognized as isomeric conjugated dienediols from their spectral features [**13**, λ_{max} 230 nm (ϵ 12 200); **14**, λ_{max} 230 nm (ϵ 11 800)]. The isolated vinyl groups were recognized from their ^1H NMR features, and from decoupling studies. Acetylation of **13** to yield **30** allowed the placement of secondary hydroxyl groups at both C-5 and C-6 in this diol. A singlet olefin proton at δ 5.59 allowed the olefin to be assigned at the C-3, C-8 position rather than at C-3, C-4. The stereochemistry of the vicinal diol was assigned as trans (C-5 pseudoequatorial/C-6 pseudoequatorial) on the basis of the ^{13}C NMR γ-shielding effects on the C-9 and C-10 methyl groups (Table II) and on the C-5, C-6 (axial–axial) methine proton coupling of 8 Hz. Similar arguments apply in the structure assignment of diol **14**. However, in **14** the diol stereochemistry clearly differed. The C-6 hydroxyl was assigned as pseudoaxial due to the ^{13}C shift of one methyl group from 19.0 to 24.8 ppm. The C-6 methine proton showed a coupling to the C-5 proton of 4 Hz which is consistent with pseudoaxial–pseudoequatorial or pseudoequatorial–pseudoequatorial values. Hence, by NMR analysis the stereochemistry at C-5 cannot be unambiguously assigned.

The final compound isolated, the diol **15**, was isomeric with **13** and **14** but lacked the conjugated diene chromophore. An isolated vinyl group was present, however, as indicated by the characteristic ^1H NMR absorptions, which required the placement of a tertiary hydroxyl at C-3. This placement was substantiated by the presence of a ^{13}C off-resonance singlet at 75.3 ppm. The isolated C-8 methylene was observed in the ^1H NMR spectrum as an AB doublet of doublets (δ 1.69, 1.80; J = 14 Hz). Further spectral analysis suggested that C-4 through C-6 compromise an allylic alcohol constellation. Of the two alternatives (hydroxyl at C-4 or C-6), the 6-hydroxyl substitution is preferred. ^{13}C NMR γ-shielding effects on the C-9 and C-10 methyl groups are minimal, suggesting that the C-6 hydroxyl is either absent or pseudoaxial. PCC oxidation of **15** yielded an α,β-unsaturated ketone assigned as structure **32**. Analogous to the spectral behavior of bra-



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silenol,[12] transformation of the hydroxyl to the ketone at

(11) P. Crews and E. Kho-Wiseman, *Tetrahedron Lett.*, 2483 (1978).

(12) M. O. Stallard, W. Fenical, and J. Kittredge, *Tetrahedron*, **34**, 2077 (1978).

Table I. ^{1}H NMR Data for *Ochtodes* Monoterpenoids[a]

H's at	compounds						
	1	2	3	4	5	6	7
C-1	6.54[b] (d, 14)	4.72 (dd, 2, 5)	4.66 (dd, 5, 2)	6.56[b] (d, 14)	6.50[b] (d, 14)	3.81 (dd, 12, 10), 3.76 (dd, 12, 6)	4.75 (dd, 5, 2)
C-2	6.63[b] (d, 14)	6.97 (d, 2)	5.90 (d, 2)	6.60[b] (d, 14)	6.61[b] (d, 14)	4.36 (dd, 10, 6)	5.72 (d, 2)
C-4	5.65 (dd, 3, 5.5)	4.78 (ddd, 11, 6, 2)	4.60 (m)	4.51 (dd, 12, 5)	4.39 (dd, 4, 3)	5.04 (dd, 8, 4)	4.94 (ddd, 10, 6, 2)
C-5$_{ax}$	2.68 (ddd, 19, 11, 3)	1.95 (ddd, 13, 12, 11)	2.10 (ddd, 13, 12, 11)	2.71 (ddd, 12, 5, 3)	2.39 (m)	2.70 (ddd, 12, 4, 3)	2.05 (ddd, 12.5, 12, 10)
C-5$_{eq}$	2.86 (ddd, 5.5, 6, 19)	2.94 (ddd, 12, 6, 4)	2.60 (ddd, 12, 6, 4)	2.31 (ddd, 12, 12, 10)	2.30 (m)	2.27 (ddd, 12, 12, 8)	2.60 (ddd, 12, 6, 4)
C-6	4.54 (dd, 6, 11)	4.40 (dd, 13, 4)	4.00 (dd, 13, 4)	4.16 (dd, 10, 3)	4.34 (m)	4.10 (dd, 12, 3)	4.40 (dd, 12, 2.5)
C-8	4.38 (s)	4.65 (s)	4.46 (s)	5.62 (s)	5.64 (s)	5.70 (s)	4.25 (s)
C-9	1.08 (s)	1.07 (s)	1.09 (s)	1.15 (s)	1.09 (s)	1.12 (s)	1.03 (s)
C-10	1.30 (s)	1.32 (s)	1.36 (s)	1.27 (s)	1.18 (s)	1.22 (s)	1.36 (s)

[a] Recorded in $CDCl_3$ solution at 220 MHz with Me_4Si as internal standard. Multiplicities and coupling constants (in hertz) are in parentheses. [b] Assignments may be reversed.

C-6 resulted in a 0.2-ppm downfield shift in both adjacent methyl groups to δ 1.20 and 1.27, respectively. These shifts would be less likely if the ketone was positioned at C-4; however, we feel the alternative structure cannot be rigorously excluded. No data could be interpreted to suggest the hydroxyl stereochemistry at C-3.

The biological activities of all new compounds were determined against the herbivorous marine damselfish *Pomacentrus coeruleus*. The toxicities of these new monoterpenoids and their efficiacies as feeding deterrents are listed in Table III. The halogenated terpenoids 1 and 4–7 showed moderate toxicities and/or strong sedative effects in the 5–10 μg/mL range, with toxicity being defined as death produced within 1 h.

While not all showed toxicity, these compounds showed distinct feeding inhibition properties down to the 100-ppm level, and this activity was independent of halogen substitution. Since these compounds comprise about 15 000 ppm of the dry weight of *O. crockeri*, it is most likely that these metabolites function in nature by deterring herbivorous predators.

Experimental Section

^{1}H NMR spectra were recorded on a Varian HR-220 spectrometer with computerized Fourier transform and spin-decoupling capabilities. ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer, and chemical shifts are expressed as δ values in parts per million relative to δ_{Me4Si} 0. Coupling constants (J) are given in hertz. Infrared spectra were obtained on a Perkin-Elmer Model 137 sodium chloride spectrophotometer. UV spectra were recorded on a Perkin-Elmer 124 spectrophotometer, and optical rotations were measured on a Perkin-Elmer 141 polarimeter. Low-resolution mass spectra were obtained on a Hewlett-Packard 5930A mass spectrometer, and high-resolution mass spectra were obtained through the Department of Chemistry at UCLA. All high-pressure liquid chromatographic separations were obtained by using a Waters Model 6000 high-pressure liquid chromatograph with a 2.1 ft × $^1/_4$ in column with μ-Porasil as the support.

Isolation. *Ochtodes crockeri* was collected from several locales in the Galapagos Islands in 1977 and 1978, stored in 2-propanol and extracted with $CHCl_3$–methanol (1:1). The combined extracts were chromatographed on a silica gel column (Grace grade 62) with a solvent gradient system of increasing polarity from isooctane to dichloromethane to ethyl acetate. Column fractions were subsequently further chromatographed by high-pressure LC using isooctane and ethyl acetate solvent mixtures.

Acetylation. All acetates were produced by treating approximately 10 mg of the natural products in 0.5 mL of pyridine with a slight excess of acetic anhydride. The reactions were stirred at room temperature for 4–8 hours, and excess reactants were removed under vacuum.

Oxidation. Oxidations of all compounds were carried out by using pyridinium chlorochromate.[13] Approximately 10 mg of the natural product was dissolved in 2–5 mL of dichloromethane. Reagent (1.5 equiv) was added and the reaction stirred at room temperature for approximately 2 h. (The reaction was followed by TLC.) The mixture was filtered through a small silica gel pipet column to remove excess reagent, and the CH_2Cl_2 was removed in vacuo.

1,6(*S)-Dibromo-8(*S**)-chloro-1(*E*),3(*Z*)-ochtodiene (1).**[6] Isooctane elution from silica gel column chromotography and final purification with isooctane by high-pressure LC yielded 1: $[\alpha]^{20}_D$ +16.7° (*c* 5.4, $CHCl_3$); IR ($CHCl_3$) 1600 cm^{-1} UV (MeOH) λ_{max} 242 nm (ϵ 5300); mass spectrum (for $C_{10}H_{13}Br_2Cl$), *m/e* (relative intensity) 326 (1), 328 (2.3), 330 (1.4); high-resolution mass measurement obsd for $C_{10}H_{13}{}^{79}Br_2{}^{35}Cl$ *m/e* 325.9074, requires *m/e* 325.9074.

6(*S)-Bromo-8(*S**)-chloro-1,3(*Z*)-ochtodiene (16).** Diene 1 (15 mg, 4.6 × 10^{-5}mol) and 1 equiv of *n*-BuLi were combined in THF at −78 °C and stirred for 15 min. An excess of dilute HOAc was carefully added, and the solution was extracted with ether. The ether extract was washed with saturated $NaHCO_3$ and dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo. The diene obtained (16) was identical with the diene obtained by Zn/HOAc reduction of ochtodene.[3]

6(*S)-Bromo-8(*R**)-chloro-1,4(*R**)-oxido-2(*E*)-ochtodene (Chondrocole A, 2) and 6(*S**),8(*S**)-Dibromo-1,4(*R**)-oxido-2(*E*)-ochtodene (Chondrocole C, 3).** The previously described ethers 2 and 3 were coeluted on column chromatography with 5% CH_2Cl_2 in isooctane. Further purification by high-pressure LC with 1% EtOAc in isooctane yielded pure chondrocole A (2) and chondrocole C (3) as determined by comparison of their spectral features (see Tables I and II) with those from authentic samples.[9]

1,6(*S)-Dibromo-1(*E*),3(8)(*Z*)-ochtodien-4(*R**)-ol (4) and 1,6(*S**)-Dibromo-1(*E*),3(8)(*Z*)-ochtodien-4(*S**)-ol (5).** They were eluted in the same silica gel column fraction with 5% CH_2Cl_2 in isooctane. Further purification by high-pressure LC with 1.5% ethyl acetate in isooctane yielded pure 4 ($[\alpha]^{20}_D$ −45.4° (*c* 2.5, $CHCl_3$)) and 5 ($[\alpha]^{20}_D$ −71.2° (*c* 3.2, $CHCl_3$)) both with the following: IR ($CHCl_3$) 3500, 1600 cm^{-1}; UV (MeOH) λ_{max} 240 nm

(13) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).

compounds							
8	9	10	11	12	13	14	15
3.76 (dd, 10, 6), 3.94 (dd, 10, 3.5)	3.75 (dd, 10, 3), 4.11 (dd, 10, 5)	4.08 (d, 7)	4.28 (d, 7)	4.25 (d, 7)	5.15 (d, 18), 5.05 (d, 11)	5.20 (d, 18), 5.05 (d, 11)	5.46 (dd, 18, 1), 5.29 (dd, 11, 1)
4.67 (dd, 6, 3.5)	4.57 (dd, 5, 3)	5.55 (d, 7)	5.75 (d, 7)	5.45 (d, 7)	6.33 (dd, 18, 11)	6.36 (dd, 18, 11)	6.18 (dd, 18, 11)
4.12 (dd, 10, 5)	4.44 (dd, 8, 6)	6.08 (d, 10)	6.10 (d, 10)	6.43 (d, 10)	2.08 (br)	2.12 (d, 17), 1.86 (d, 17)	5.58 (s)
2.12 (ddd, 14, 12, 10) 2.63 (ddd, 12, 5, 2.5)	2.00 (ddd, 12, 12, 8) 2.63 (ddd, 12, 5, 2.5)	5.66 (dd, 10, 3)	5.70 (dd, 10, 3)	5.74 (dd, 10, 3)	4.13 (d, 8)	4.33 (bs)	5.58 (s)
4.05 (dd, 14, 2.5)	4.06 (dd, 12, 2.5)	3.93 (d, 3)	3.95 (d, 3)	3.95 (d)	3.33 (d, 8)	3.48 (d, 4)	4.00 (s)
5.67 (s)	5.68 (s)	2.04 (d, 15), 2.26 (d, 15)	2.06 (d, 15), 2.31 (d, 15)	2.13 (s)	5.59 (s)	5.54 (s)	1.69 (d, 14), 1.80 (d, 14)
1.17 (s)	1.14 (s)	0.89 (s)	0.90 (s)	0.87 (s)	0.88 (s)	0.89 (s)	1.05 (s)
1.17 (s)	1.16 (s)	0.98 (s)	1.00 (s)	0.97 (s)	1.09 (s)	1.10 (s)	1.10 (s)

(ϵ 17 000); low-resolution mass spectrum (for $C_{10}H_{14}OBr_2$), *m/e* (relative intensity) 308 (1), 310 (2), 312 (1); high-resolution mass measurement obsd *m/e* 307.9409, requires *m/e* 307.9412.

Ketone **20**: $[\alpha]^{20}_D$ +15.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3 H, s), 1.33 (3 H, s), 3.04 (1 H, d, *J* = 10), 3.04 (1 H, d, *J* = 6), 4.31 (1 H, dd, *J* = 10, 6), 6.66 (1 H, d, *J* = 14), 6.69 (1 H, s), 7.18 (1 H, d, *J* = 14); UV (MeOH) λ_{max} 275 nm (ϵ 4200); low-resolution mass spectrum (for $C_{10}H_{12}OBr_2$), *m/e* (relative intensity) 306 (1), 308 (2), 310 (1).

Acetate **18**: ^1H NMR ($CDCl_3$) δ 1.11 (3 H, s), 1.21 (3 H, s), 2.09 (3 H, s), 2.35 (2 H, m), 4.26 (1 H, dd, *J* = 8, 4), 5.51 (1 H, dd, *J* = 3, 3), 5.78 (1 H, s), 6.20 (1 H, d, *J* = 14), 6.58 (1 H, d, *J* = 14); IR ($CHCl_3$) 1720, 1600 cm^{-1}.

Acetate **19**: ^1H NMR ($CDCl_3$), δ 1.16 (3 H, s), 1.21 (3 H, s), 2.08 (3 H, s), 2.21 (1 H, ddd, *J* = 12, 12, 8), 2.78 (1 H, ddd, *J* = 12, 6, 3), 4.26 (1 H, dd, *J* = 12, 3), 5.57 (1 H, dd, *J* = 8, 6), 5.76 (1 H, s), 6.15 (1 H, d, *J* = 14), 6.54 (1 H, d, *J* = 14); IR ($CHCl_3$) 1720, 1600 cm^{-1}.

2-Chloro-1,6(*S)-dibromo-3(8)(*Z*)-ochtoden-4(*R**)-ol (6).** Elution of the silica gel column with 5% dichloromethane in isooctane and high pressure LC purification with 2% ethyl acetate in isooctane gave pure **6**: $[\alpha]^{20}_D$ −26.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3500 cm^{-1}; low-resolution mass spectrum (for $C_{10}H_{15}OBr_2Cl$), *m/e* (relative intensity): 344 (1), 346 (2.3), 348 (1.4). Anal. Calcd: Br, 43 (inaccurate due to small sample size). Found: Br, 39.1.

Acetate **21**: ^1H NMR ($CDCl_3$) δ 1.14 (3 H, s), 1.22 (3 H, s), 2.05 (3 H, s), 2.27 (1 H, ddd, *J* = 14, 12, 8), 2.72 (1 H, ddd, *J* = 12, 4, 3), 3.70 (2 H, d, *J* = 7), 4.08 (1 H, dd, *J* = 14, 3), 4.57 (1 H, t, *J* = 7), 5.60 (1 H, dd, *J* = 8, 4), 5.86 (1 H, s).

Ketone **23**: $[\alpha]^{20}_D$ +25.0° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.33 (3 H, s), 1.37 (3 H, s), 3.06 (2 H, m), 3.76 (1 H, dd, *J* = 10, 5), 3.80 (1 H, dd, *J* = 10, 7), 4.36 (1 H, dd, *J* = 10, 5), 5.05 (1 H, dd, *J* = 7, 5); IR ($CHCl_3$) 1680 cm^{-1}; UV (MeOH) λ_{max} 235 nm (ϵ 8800); low-resolution mass spectrum (for $C_{10}H_{13}OBr_2Cl$), *m/e* (relative intensity) 342 (1), 344 (2.3), 346 (1.4).

6(*S)-Bromoochto-1,3(8)-diene-4(*R**)-ol (22).** Diene **22** was prepared by adding zinc dust (0.1 g, 0.154 mol) to **6** (0.01 g, 2.9 × 10^{-5}mol) and stirring in 2 mL of dry acetic acid at room temperature. After the mixture was stirred for 1 h, 10 mL of diethyl ether was added, the mixture was filtered, and the filtrate was washed with ether. The solvent was removed in vacuo to yield **22**: $[\alpha]^{20}_D$ −20.8° (*c* 0.6, $CHCl_3$); ^1H NMR δ 1.22 (3 H, s), 1.25 (3 H, s), 2.32 (1 H, ddd, *J* = 12, 11, 7), 2.69 (1 H, ddd, *J* = 12, 7, 3), 4.11 (1 H, dd, *J* = 11, 3), 4.57 (1 H, dd, *J* = 7, 7), 5.15 (1 H, d, *J* = 11), 5.44 (1 H, d, *J* = 18), 5.61 (1 H, s), 6.18 (1 H, dd, *J* = 18, 11); IR ($CHCl_3$) 3600 cm^{-1}; UV (MeOH) λ_{max} 230 nm (ϵ 10 000); low-resolution mass spectrum (for $C_{10}H_{15}OBr$), *m/e* (relative intensity) 230 (1), 232 (1).

6(*S)-Bromo-1,4(*R**)-oxido-2(*Z*)-ochtoden-8(*S**)-ol (7).** Elution from silica gel with dichloromethane and high-pressure LC purification with 20% ethyl acetate in isooctane gave **7**: $[\alpha]^{20}_D$ +30.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3500, 1200 cm^{-1}; low-resolution mass spectrum (for $C_{10}H_{15}O_2Br$), *m/e* (relative intensity) 246 (1), 248 (1); high-resolution mass measurement obsd *m/e* 246.0258, requires *m/e* 246.0256.

Ketone **24**: $[\alpha]^{20}_D$ −80.0° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.16 (3 H, s), 1.25 (3 H, s), 2.36 (1 H, ddd, *J* = 12, 12, 10), 2.77 (1 H, ddd, *J* = 12, 6, 4), 4.16 (1 H, dd, *J* = 12, 4), 4.70 (1 H, dd, *J* = 5, 1), 4.84 (1 H, ddd, *J* = 10, 6, 2), 6.6 (1 H, d, *J* = 1); IR ($CHCl_3$) 1690 cm^{-1}; UV (MeOH) λ_{max} 253 nm (ϵ 5200); low-resolution mass spectrum (for $C_{10}H_{13}O_2Br$), *m/e* (relative intensity) 244 (1), 246 (1).

A lanthanide induced shift study using $Eu(fod)_3$ was performed on the natural product **7** in order to confirm relative stereochemistry and overall structure (see ref 3 for experimental details). The data in Table IV were obtained.

6(*S)-Bromo-1,4(*R**)-oxido-3(8)(*E*)-ochtoden-2(*S**)-ol (8) and 6(*S**)-Bromo-1,4(*R**)-oxido-3(8)(*E*)-ochtoden-2(*R**)-ol (9).** Compounds **8** and **9** were eluted with the same Silica gel column fraction with 100% CH_2Cl_2 and purified by high-pressure LC with 22% ethyl acetate in isooctane to give **8** ($[\alpha]^{20}_D$ −64.6° (*c* 0.7, $CHCl_3$)) and **9** ($[\alpha]^{20}_D$ −55.0° (*c* 1.0, $CHCl_3$)) both with the following: IR ($CHCl_3$) 3600, 1200 cm^{-1}; low-resolution mass spectrum (for $C_{10}H_{15}O_2Br$) *m/e* (relatiive intensity) 246 (1), 248 (1); high-resolution mass measurement obsd *m/e* 246.0256, requires *m/e* 246.0256.

Ketone **25**: $[\alpha]^{20}_D$ −60.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.23 (6 H, s), 2.18 (1 H, ddd, *J* = 12, 5, 7), 2.72 (1 H, ddd, *J* = 12, 7, 2), 4.09 (2 H, d, J_{AB} = 15), 4.10 (1 H, dd, *J* = 12, 5, 2), 4.6 (1 H, dd, *J* = 7, 7), 6.5 (1 H, s); IR ($CHCl_3$) 1710, 1660 cm^{-1}; UV (MeOH) λ_{max} 234 nm (ϵ 8400); low-resolution mass spectrum (for $C_{10}H_{13}O_2Br$), *m/e* (relative intensity) 244 (1), 246 (1).

1-Chloro-2(*E*),4-ochtodien-6(*R)-ol (10).** The diene **10** was eluted from the silica gel column with 5% ethyl acetate in dichloromethane and was further purified by high-pressure LC with 25% ethyl acetate in isooctane: $[\alpha]^{20}_D$ +5.7° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3500, 1600 cm^{-1}; UV (MeOH) λ_{max} 238 nm (ϵ 21 000); low-resolution mass spectrum (for $C_{10}H_{14}O$) *m/e* 150 (M^+ − HCl).

2(*E*),4-Ochtodien-1,6(*R)-diol (11) and 2(*Z*),4-Ochtodien-1,6(*R**)-diol (12).** The diols **11** and **12** were eluted in different silica gel column fractions with 25% ethyl acetate in dichloromethane (**11** eluted before **12**), and each was further purified by high-pressure LC with 35% ethyl acetate in isooctane. Diol **11**: $[\alpha]^{20}_D$ +4.3° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3600, 1560 cm^{-1}; UV (MeOH) λ_{max} 238 nm (ϵ 19 400); high-resolution mass measurement of parent peak obsd *m/e* 168.1150, requires *m/e*

Table II. ^{13}C NMR Data for *Ochtodes* Monoterpenoids[a] 1–15

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
C-1	135.1 d	75.4 t	75.3 d	108.0 d	106.9 t	40.5 t	75.5 t	75.2 t	74.6 t	65.5 t	58.6 t	57.7 t	113.1 t	112.6 t	115.1 t
C-2	129.8 d	122.3 d	124.8 d	136.3 d[b]	136.6 d[b]	58.0 d	122.0 d	70.7 d[b]	71.6 d	131.2 d[b]	131.2 d[b]	131.2 d[b]	120.3 d	128.4 d	139.7 d[b]
C-3	135.2 s	137.6 s	138.3 s	134.6 s	132.8 s	135.4 s	none	140.7 s	138.7 s	136.3 s	135.7 s	134.6 s	135.9 s	136.9 s	75.3 s
C-4	106.7 d	80.7 d	82.6 d	66.5 d	65.1 d	67.1 d[b]	81.6 d[b]	76.6 d[b]	75.1 d	126.1 d	128.2 d[b]	124.0 d[b]	38.8 t	33.6 t	124.8 d[b]
C-5	35.9 t	41.7 t	41.4 t	40.0 t	39.0 t	33.1 t	42.0 t	37.1 t	37.0 t	129.0 d[b]	130.2 d[b]	125.9 d	71.7 d[b]	68.2 d[b]	141.1 d[b]
C-6	54.2 d	54.4 d	54.8 d	57.7 d	57.0 d	57.3 d[b]	56.2 d	57.2 d	57.0 d	74.2 d	74.1 d	74.4 d	80.1 d[b]	75.6 d[b]	73.4 d
C-7	39.5 s	41.7 s	43.6 s	38.0 s	38.1 s	37.9 s	none	38.1 s	38.0 s	34.8 s	34.7 s	35.2 s	34.8 s	34.9 s	33.8 s
C-8	63.1 d	63.8 d	55.7 d	138.5 d[b]	140.6 d[b]	136.6 d	74.2 d[b]	129.6 d	131.4 d	36.5 t	36.3 t	43.2 t	138.4 s	139.7 d	46.0 t
C-9$_{ax}$	19.8 q	21.0 q	16.0 q	25.1 q	23.0 q	24.3 q	19.9 q	25.0 q	24.7 q	21.3 q	21.3 q	20.7 q	19.0 q	24.8 q	29.9 q
C-10$_{eq}$	28.0 q	27.6 q	29.1 q	28.7 q	28.2 q	28.3 q	25.7 q	27.8 q	27.7 q	26.8 q	26.7 q	26.5 q	27.8 q	27.2 q	31.8 q

[a] Recorded at 25 MHz in $CDCl_3$ solution. Multiplicities were determined by off-resonance decoupling techniques. [b] Assignments may be reversed.

Table III. Fish Bioassays

compd	fish toxicity (μg/mL)	min concn for feeding inhibition, ppm
1	toxic (10) definite sedation (2.5)	300
4	toxic (10) definite sedation (5)	300
5	toxic (10) definite sedation (2)	300
6	toxic (5) definite sedation (2)	100
7	not toxic sedation (10)	100
8	not toxic or sedative	500
9	not toxic or sedative	600
10	not toxic or sedative	300
11	not toxic or sedative	300
12	not toxic or sedative	100
13	not toxic or sedative	100
14	not toxic or sedative	200
15	not toxic or sedative	1000
control	no toxicity or effect	no inhibition

Table IV

carbon (no. of H's)	δ	Δδ, ppm	r_{measd}, Å	Θ, deg	r_{calcd}, Å	% r
C-2 (2)	5.72	1.43	4.6	40	4.55	1.1
C-4 (1)	4.94	4.5	2.1	50	2.12	0.9
C-5$_{ax}$ (1)	2.05	2.5	3.75	40	3.78	0.8
C-5$_{eq}$ (1)	2.60	1.95	4.25	40	4.11	3.3
C-6 (1)	4.40	1.16	5.75	30	5.75	0.0
C-9 (3)	1.03	0.91	6.8	22	6.75	0.7
C-10 (3)	1.36	0.77	7.0	20	7.24	3.4

168.1150 for $C_{10}H_{15}O_2$. Diol **12**: $[\alpha]^{20}_D$ 0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3500, 1600 cm^{-1}; UV (MeOH) λ_{max} 238 nm (ε 10600); low-resolution mass spectrum (for $C_{10}H_{15}O_2$) *m/e* 168.

Diacetate **26**: ^1H NMR ($CDCl_3$) δ 0.89 (3 H, s), 0.99 (3 H, s), 2.06 (3 H, s), 2.15 (3 H, s), 2.35 (1 H, d, *J* = 15), 2.20 (1 H, d, *J* = 15), 4.65 (2 H, d, *J* = 7), 5.0 (1 H, d, *J* = 3), 5.5 (1 H, d, *J* = 7), 5.6 (1 H, dd, *J* = 10, 3), 6.08 (1 H, d, *J* = 10); IR ($CHCl_3$) 1720, 1710 cm^{-1}.

Diacetate **27**: ^1H NMR ($CDCl_3$) δ 0.90 (3 H, s), 0.93 (3 H, s), 2.05 (3 H, s), 2.09 (3 H, s), 2.25 (2 H, m), 4.70 (2 H, d, *J* = 7), 5.18 (1 H, d, *J* = 3), 5.45 (1 H, t, *J* = 7), 5.73 (1 H, dd, *J* = 10, 3), 6.5 (1 H, d, *J* = 10); IR ($CHCl_3$) 1720, 1710 cm^{-1}.

Keto aldehyde **28**: ^1H NMR ($CDCl_3$) δ 1.15 (3 H, s), 1.20 (3 H, s), 3.07 (2 H, s), 6.13 (1 H, d, *J* = 10), 6.18 (1 H, d, *J* = 6), 7.05 (1 H, d, *J* = 10), 10.11 (1 H, d, *J* = 6); IR ($CHCl_3$) 1690 cm^{-1}; UV (MeOH) λ_{max} 277 nm (ε 10600); low-resolution mass spectrum (for $C_{10}H_{12}O_2$), *m/e* 164.

Keto aldehyde **29**: ^1H NMR 1.1, δ 1.15 (3 H, s), 1.20 (3 H, s), 2.68 (2 H, s), 6.14 (1 H, d, *J* = 10), 6.15 (1 H, d, *J* = 6), 8.0 (1 H, d, *J* = 10), 10.15 (1 H, d, *J* = 6); IR ($CHCl_3$) 1690 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ε 6800); low-resolution mass spectrum (for $C_{10}H_{12}O_2$), *m/e* 164.

1,3(8)-Ochtodien-5(*R), 6(*R**),6(*R**)-diol (13) and 1,3-(8)-Ochtodien-5,6(*S**)-diol (14).** Diols **13** and **14** were eluted in different silica gel column fractions with 25% ethyl acetate in dichloromethane, and each was further purified by high-pressure LC with 35% EtOAc in isooctane.

Diol **13**: $[\alpha]^{20}_D$ 0° (*c* 1.18 $CHCl_3$); IR ($CHCl_3$), 3600, 1600 cm^{-1}; UV (MeOH) λ_{max} 230 nm (ε 12200); low-resolution mass spectrum (for $C_{10}H_{16}O_2$), *m/e* 168.

Diol **14**: $[\alpha]^{20}_D$ 0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3600, 1600 cm^{-1}; UV (MeOH) λ_{max} 230 nm (ε 11800); low-resolution mass spectrum (for $C_{10}H_{16}O_2$), *m/e* 168.

Diacetate **30**: ^1H NMR ($CDCl_3$) δ 1.00 (3 H, s), 1.20 (3 H, s), 2.04 (3 H, s), 2.07 (3 H, s), 2.17 (2 H, s), 5.02 (1 H, d, *J* = 8), 5.10 (1 H, d, *J* = 11), 5.20 (1 H, d, *J* = 18), 5.45 (1 H, d, *J* = 8), 5.53 (1 H, s), 6.36 (1 H, dd, *J* = 18, 11); IR ($CHCl_3$) 1720, 1715 cm^{-1}.

Diacetate **31**: ^1H NMR ($CDCl_3$) δ 1.01 (6 H, s), 2.02 (3 H, s), 2.07 (3 H, s), 2.00 (1 H, d, *J* = 15), 2.16 (1 H, d, *J* = 15), 5.04 (1

H, d, J = 3.0), 5.10 (1 H, d, J = 11), 5.25 (1 H, d, J = 18), 5.49 (1 H, s), 5.63 (1 H, d, J = 3), 6.38 (1 H, dd, J = 18, 11); IR ($CHCl_3$) 1720, 1715 cm^{-1}.

1,3-Ochtodien-3,6(*R)-diol (15).** Silica gel column chromatography (25% EtOAc in CH_2Cl_2) and further purification by high-pressure LC with 35% ethyl acetate in isooctane yielded pure **15**: $[\alpha]^{20}_D$ −14.8° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3600, 1610 cm^{-1}; low-resolution mass spectrum (for $C_{10}H_{16}O_2$), *m/e* 168.

Ketone **32**: ^1H NMR ($CDCl_3$) δ 1.20 (3 H, s), 1.27 (3 H, s), 2.04 (1 H, d, J = 14), 2.15 (1 H, d, J = 14), 5.20 (1 H, d, J = 11), 5.23 (1 H, d, J = 17), 6.01 (1 H, d, J = 10), 6.08 (1 H, dd, J = 11, 17) 6.68 (1 H, dd, J = 10); IR ($CHCl_3$) 3500, 1690, 1600 cm^{-1}; low-resolution mass spectrum (for $C_{10}H_{14}O_2$), *m/e* 166.

Fish Toxicity Bioassay. Compounds **1** and **4–15** were tested for fish toxicity by using the tropical Pacific damselfish *Pomacentrus coeruleus*. *P. coeruleus* is an abundant macroalgal herbivore in many tropical Pacific ecosystems and was locally available in pet stores. Compounds, at the concentrations in Table III, were stirred into seawater by using a small amount of ethanol. A damselfish was placed in water, observed for 1 h, and then placed in fresh seawater. At concentrations effecting sedation, the fish would darken, often stop swimming, and turn over on its side or back. When placed in fresh seawater, the symptoms would disappear, and the fish would return to "normal". At slightly greater concentrations, compounds **1** and **4–6** resulted in the death of *P. coeruleus*. For each compound this bioassay was repeated four times with identical results.

Feeding Inhibition Bioassay. Known concentrations of each compound were made in ether and volumetrically applied to 10 mg of fish food. The ether was evaporated at 60 °C, and the cooled food was dropped into a tank of ten fish. In most cases, the fish would pick the food up in their mouths but immediately reject it, thus indicating a positive avoidance reaction. After several fish rejected the food, it would drop to the bottom of the aquarium and no other fish would indicate interest. At concentrations where no feeding inhibition was observed, the fish would continue to compete for the food source until it was totally comsumed.

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Registry No. **1**, 73872-74-9; **2**, 57461-72-0; **3**, 57496-04-5; **4**, 73872-75-0; **5**, 73872-76-1; **6**, 73872-77-2; **7**, 73872-78-3; **8**, 73872-79-4; **9**, 73872-80-7; **10**, 73872-81-8; **11**, 73891-29-9; **12**, 73872-82-9; **13**, 73872-83-0; **14**, 73872-84-1; **15**, 73872-85-2; **16**, 67237-07-4; **18**, 73872-86-3; **19**, 73872-87-4; **20**, 73872-88-5; **21**, 73872-89-6; **22**, 73872-90-9; **23**, 73872-91-0; **24**, 73872-92-1; **25**, 73872-93-2; **26**, 73872-94-3; **27**, 73872-95-4; **28**, 73872-96-5; **29**, 73872-97-6; **30**, 73872-98-7; **31**, 73872-99-8; **32**, 73873-00-4.

Stereospecific Alkylation of 3,5,5-Trisubstituted-4-hydroxy-1-*p*-tosyl-2-pyrazolines by Trimethylaluminum. An Efficient Synthesis of 3,3,5,5-Tetrasubstituted-1-pyrazolin-4-ones

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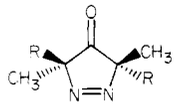
Isomeric *p*-tosylpyrazolines **5** and **6** are obtained in high yield by cyclization of the tosylhydrazones of various β,β-disubstituted-α,β-epoxy ketones **4**. Oxidation of these mixtures to pyrazolones **9** followed by selective reduction affords isomers **5**. Reaction of **5** with 8 equiv of trimethylaluminum in toluene stereospecifically produces the trans, tetrasubstituted 4-hydroxy-1-pyrazolines **7** in high yield. Methylmagnesium bromide and methyllithium are less effective in producing a similar conversion as competing elimination reactions occur. Oxidation of pyrazolols **7** gives the corresponding pyrazolones **1**.

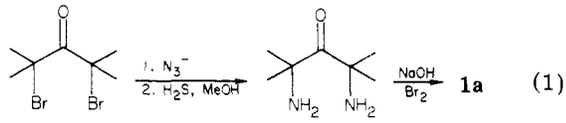
In connection with our current interest in the stereochemistry of several 1-pyrazoline transformations, we required a series of trans, tetrasubstituted pyrazolones **1**



1a, R = CH_3
b, R = C_2H_5
h, R = Ph

containing various alkyl and aryl substituents R. Three members of this series (**1a,b,h**) were reported prior to the present investigation, having served as precursors to allenes[1] and functionalized cyclopropanes.[2]

Although recent interest has also been demonstrated in 4-alkylidene derivatives of **1a**[3] and other bicyclic 4-alkylidene-1-pyrazolines as precursors to trimethylenemethanes,[4] a general approach to compounds **1** has not been described previously. The method described by Mock (eq 1) for the preparation of **1a**[5] is not satisfactory as a



(1)

synthesis of our desired trans targets. This procedure gave a mixture of **1b** and the corresponding cis isomer[6] in ap-

(1) Pirkle, W. H.; Kalish, R. *J. Am. Chem. Soc.* **1967**, *89*, 2781–2.
(2) Convers, R. J. Ph.D. Thesis, University of Illinois, Urbana, IL, 1974.
(3) See: Bushby, R. J.; Pollard, M. D. *Tetrahedron Lett.* **1978**, 3855–60; Bushby, R. J.; Pollard, M. D. *Ibid.* **1977**, 3671–2.
(4) Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446–53 and references therein.
(5) Mock, W. L. Ph.D. Thesis, Harvard University, Cambridge, MA, 1964; *Diss. Abstr.* **1966**, *26*, 6374. A variation of this sequence has been used to prepare **1a**. See: Crawford, R. J.; Tokunaga, H. *Can. J. Chem.* **1974**, *52*, 4033–9.
(6) Thornburg, K. A. Ph.D. Thesis, University of Illinois, Urbana, IL, 1970.

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