the basis of the coincidence of the wine-red color and the product 1,1-diphenylpropene (3), we speculated that carbanion v must be an intermediate (Scheme I). This was established by quenching the reaction mixture with trimethylchlorosilane, which gave 1,1-diphenyl-3-(trimethylsilyl)propene (6, Scheme I). The mechanism is a matter for speculation since it remains to be established whether addition of organocuprates to olefins (especially unsaturated ketones) occurs by an electron-transfer mechanism[10] or by a nucleophilic addition mechanism,[11] or whether a Cu(III) adduct such as i is an intermediate. If i were an intermediate, the observed results could be readily explained. Transfer of a phenyl group from Cu to C-3 of the 1,1-difluoropropene moiety would give 1 while transfer to C-1 would give 3,3-difluoro-3-phenylpropene (ii). As an allylic fluoride ii would be susceptible to coupling with $Ph_2CuMgBr$ to give iii, which in analogy to i could transfer a phenyl group to either of two carbons, leading to a mixture of 4 and 5 or 3-fluoro-3,3-diphenylpropene (iv). The mechanism by which iv is transformed to v is unknown but must involve a reduction, possibly coupled with simultaneous Cu(I)-catalyzed linkage of PhMgBr to give biphenyl.

Obviously the copper-catalyzed coupling reaction of Grignard reagents with 3,3,3-trifluoropropene is not a very synthetically useful reaction, but these studies do establish the nature of the coupling and point to the feasibility of related reactions between other allylic fluorides for which regioselectivity may be less of a problem.

Experimental Section

3,3,3-Trifluoropropene was purchased from PCR Research Chemicals, Inc., and used without further purification. Tetrahydrofuran was dried and purified immediately prior to use by distillation over sodium metal. ^1H NMR spectra were obtained on a Model PS100 100-MHz FT NMR spectrometer. Tetramethylsilane was used as the internal standard. High-resolution electron-impact mass spectra were obtained on a modified Kratos/AEI MS90 mass spectrometer, operating at a dynamic resolution of M/ΔM 10 000. Low-resolution mass spectra were obtained with a consolidated 12-1108 mass spectrometer.

GC analysis and preparative GC were performed with a Hewlett-Packard 5710A gas chromatograph and a 12 ft × 0.25 in. 10% SE-30 on Gas-Chrom Q column.

Reaction of PhMgBr with CH_2=$CHCF_3$. A solution of phenylmagnesium bromide in THF (50 mL) was prepared by combining bromobenzene (4.26 mL, 0.0404 mol) and magnesium turnings (0.936 g, 0.0385 mol). The solution was cooled to −6 °C and dry CuBr (0.276 g, 1.93 mmol) added. A solution of CH_2=$CHCF_3$ (3.7 g, 0.0385 mol) in 50 mL of THF was slowly added over a period of 45 min. The reaction mixture was then allowed to warm to room temperature and after 5.5 h worked up by quenching with saturated aqueous NH_4Cl and extracting with pentane. The pentane extracts were dried over $MgSO_4$, filtered, and the product mixture (2.6 g) obtained by evaporation of the solvent. A typical GLC analysis on the SE-30 column programmed from 100–270 °C at 8°/min gave the following retention times: 1, 5.4 min; 2, 13.6 min; 3, 17.0 min; 4, 18.3; and 5, 19.3 min. The structure of 1 was confirmed by GLC comparison of a sample of 1,1-difluoro-3-phenylpropene prepared by the method of Fontanelli and Sianesi, and 2 by comparison to an authentic sample of biphenyl. Structures of all of the products were confirmed by ^1H NMR and mass spectrometry.

1,1-Difluoro-3-phenylpropene (1): ^1H NMR (CCl_4) δ 3.10 (d, 2 H, J = 8 Hz), 4.15 (m, 1 H), 7.00 (br s, 5 H); mass spectrum (high resolution) calcd m/e for $C_9H_8F_2$, 154.0594; found m/e, 154.0594; mass spectrum (low resolution), m/e (rel intensity) 154 (100), 153 (45), 134 (35), 133 (61), 127 (16), 104 (28), 103 (13), 91 (14), 78 (12), 77 (26), 51 (29).

1,1-Diphenylpropene (3): ^1H NMR (CCl_4) δ 1.72 (d, 3 H, J = 8 Hz), 6.12 (t, 1 H, J = 8 Hz), 7.18 (m, 10 H); mass spectrum (high resolution) calcd m/e for $C_{15}H_{14}$, 194.1096, found m/e, 194.1087; mass spectrum (low resolution), m/e (rel intensity) 195 (16), 194 (100), 193 (58), 192 (11), 191 (10), 179 (35), 178 (37), 165 (32), 152 (11), 147 (10), 117 (21), 116 (32), 115 (67), 105 (20), 103 (10), 91 (25), 89 (11), 77 (19), 51 (12).

(*E*)-1-Fluoro-1,3-diphenylpropene (4): ^1H NMR (CCl_4) δ 3.55 (d, 2 H, J = 8 Hz), 5.6 (dt, 1 H, $J_{H-F_{cis}}$ = 22 Hz, J_{H-H} = 8 Hz), 7.20 (m, 10 H); mass spectrum (high resolution) calcd m/e for $C_{15}H_{13}F$, 212.1002, found m/e, 212.1002; mass spectrum (low resolution), m/e (rel intensity) 213 (17), 212 (100), 211 (37), 197 (23), 196 (12), 192 (24), 191 (25), 189 (10), 165 (11), 135 (20), 134 (34), 133 (68), 115 (27), 109 (22), 103 (11), 91 (14), 77 (11).

(*Z*)-1-Fluoro-1,3-diphenylpropene (5): ^1H NMR (CCl_4) δ 3.55 (d, 2 H, J = 8 Hz), 5.45 (dt, 1 H, $J_{H-F_{trans}}$ = 36 Hz, J_{H-H} = 8 Hz), 7.18 (m, 10 H); mass spectrum (high resolution) calcd m/e for $C_{15}H_{13}F$, 212.1002, found m/e, 212.0997; mass spectrum (low resolution) was essentially identical to that of 4.

1,1-Diphenyl-3-(trimethylsilyl)propene (6): ^1H NMR (CCl_4) δ 0.08 (s, 9 H), 170 (d, 2 H, J = 8 Hz), 6.10 (t, 1 H, J = 8 Hz), 7.15 (m, 10 H); mass spectrum (high resolution) calcd m/e for $C_{18}H_{22}Si$, 266.1492, found m/e, 266.1491; mass spectrum (low resolution), m/e (rel intensity) 266 (32), 115 (13), 74 (15), 73 (100), 45 (15).

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Registry No. 1, 4980-68-1; 3, 778-66-5; 4, 85371-02-4; 5, 85371-03-5; 6, 83438-57-7; CuBr, 7787-70-4; phenyl bromide, 108-86-1; 3,3,3-trifluoropropene, 677-21-4.

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Acetoxycrenulide, a New Bicyclic Cyclopropane-Containing Diterpenoid from the Brown Seaweed *Dictyota crenulata*

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The small brown seaweeds (Phaeophyta) of the family Dictyotaceae are conspicuous members of most highly competitive tropical and subtropical habitats. Chemical studies have shown that these algae produce a variety of unique secondary metabolites that perhaps function as defensive compounds in the natural habitat.[1] In our studies of this algal group from the Gulf of California, Mexico, we have encountered several *Dictyota* species that produce new diterpenoid ring systems.[2,3] In this note we amplify upon our earlier work by reporting, in full, the structure of a new diterpenoid, acetoxycrenulide (1), which is a major metabolite, along with pachydictyol A,[4] of *D. crenulata* J. Agardh.[5] Acetoxycrenulide possesses a reg-

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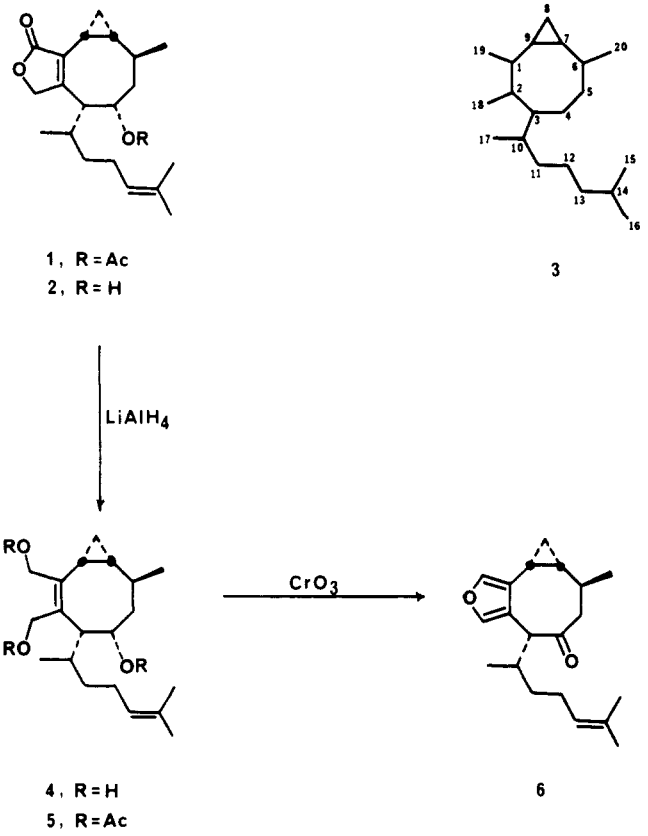
(2) K. J. Robertson and W. Fenical, *Phytochemistry*, **16**, 1071 (1977).
(3) J. Finer, J. Clardy, W. Fenical, L. Minale, R. Riccio, J. Battaile, M. Kirkup, and R. E. Moore, *J. Org. Chem.*, **44**, 2044 (1979).
(4) D. R. Hirschfeld, W. Fenical, G. H. Y. Lin, R. M. Wing, P. Radlick, and J. J. Sims, *J. Am. Chem. Soc.*, **95**, 4049 (1973).
(5) Specimens of *D. crenulata* J. Agardh. have been deposited in the National Herbarium, National Museum of Natural History, Smithsonian Institution, Washington, DC.

0022-3263/83/1948-1903$01.50/0

ular diterpenoid but unprecedented bicyclo[6.1.0]nonane skeleton with acetoxy and α,β-unsaturated γ-lactone functionalities.[6] In fish toxicity testing, acetoxycrenulide was severely debilitating and ultimately toxic at levels of 10 μg/mL toward the herbivorous reef-dwelling fish *Eupomacentrus leucostictus*.[7]

Dictyota crenulata was collected near Cabo San Lucas, Baja California, Mexico, in March, 1976, as part of an expedition on board the research vessel Dolphin. The alga was air-dried and ground and repetitively extracted with chloroform–methanol (2:1) to yield a viscous green gum after removal of extraction solvents. Open-column chromatography (silica gel) of the extract, followed by further purification by silica HPLC, yielded acetoxycrenulide (1)



as a viscous oil that repeatedly failed to crystallize. Acetoxycrenulide showed $[\alpha]^{26}_D$ +13° (*c* 0.67, $CHCl_3$) and analyzed for $C_{22}H_{32}O_4$ by high-resolution mass measurement of its parent ion at 360 amu. The four oxygen atoms in acetoxycrenulide were readily assigned to an acetate ester and an unsaturated γ-lactone by interpretation of various spectral features. Specifically, infrared absorption at 1735 cm^{-1}, a three-proton singlet at δ 2.03 in the ^1H NMR spectrum of **1**, and fragmentations illustrating the loss of acetate ($M^+ - 59$) were in strong support of the acetate ester assignment. Further infrared absorption at 1760 cm^{-1}, coupled with UV absorption at 227 nm (ϵ 11 500), suggested the presence of the unsaturated γ-lactone functionality.

The ^{13}C NMR features of acetoxycrenulide reinforced the acetate and lactone assignments suggested above and provided significant additional structural information. A lactone singlet carbonyl was observed at δ 174.2 along with the two singlet carbons at δ 128.8 and 166.5, which were assigned to the α and β carbons of the polarized lactone olefinic bond. That these latter carbons were off-resonance singlets illustrated that the lactone olefin was fully substituted. An off-resonance triplet carbon at δ 71.2 was assigned to the unsubstituted γ-carbon of the lactone, and a δ 72.2 doublet was assigned as the acetate-bearing carbon. Other ^{13}C NMR features showed acetoxycrenulide to possess an additional trisubstituted double bond [δ 123.5 (d), 132.4 (s)] and a di- or trisubstituted cyclopropane ring [δ 8.4 (t), 10.3 (d)]. The unsaturation inherent in acetate, unsaturated lactone, and olefins accounted for five of the seven degrees of unsaturation indicated in the formula for **1**. Since acetoxycrenulide was confirmed to contain a cyclopropane ring, the molecule was concluded to be bicarbocyclic.

The ^1H NMR spectrum of **1** illustrated several additional structural features. Two olefin-substituted methyl groups were observed at δ 1.59 (s) and 1.70 (s), and two doublet methyls were observed at δ 0.99 (J = 5 Hz) and 1.02 (J = 7.5 Hz). Two cyclopropane protons were found as one-proton multiplets at δ 0.39 and 0.89. The complexities of these bonds indicated each was coupled to at least three other protons, hence, suggesting that the cyclopropane ring was disubstituted. A midfield ABX pattern was also observed with the A component at δ 4.85 (dd, J = 16 and 2.5 Hz) and the B component at δ 4.74 (dd, J = 16 and 2.5 Hz). These protons were assigned to the lactone methylene protons at C-18. By analysis of J_R values, these bands were found to correlate with the ^{13}C NMR off-resonance triplet at δ 71.5. The additional 2.5-Hz coupling in these signals was assigned as homoallylic coupling with the requisite transoid proton at C-9.[8]

Treatment of **1** with sodium carbonate in methanol resulted in the selective saponification of the acetate ester to yield the corresponding alcohol, hydroxycrenulide (**2**). The conversion of **1** to **2** was accompanied by a ^1H NMR shift of the ester methine proton (C-4) at δ 5.48 (br t, J = 4 Hz) to δ 4.35 (br t, J = 4 Hz) in the corresponding alcohol, thus illustrating the ester to be secondary. Reduction of acetoxycrenulide with $LiAlH_4$ in ether provided a moderate yield of the corresponding triol **4**, which when treated with acetic anhydride in pyridine was converted to the triacetate **5**. The ^1H NMR features of **4**, particularly the presence of two AB patterns, one centered at δ 3.91 (2 H, dd, J = 12 and 12 Hz) and the other at δ 4.46 (1 H, d, J = 10 Hz) and 3.02 (1 H, d, J = 10 Hz), were in strong support of the prior assignment of the lactone as an α,β-disubstituted α,β-unsaturated γ-lactone.

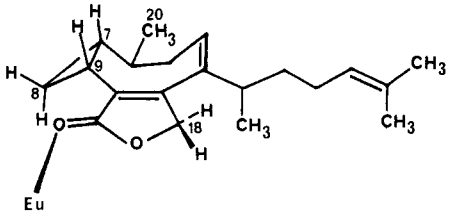
Oxidation of the triol **4** with CrO_3/pyridine yielded the ketofuran **6**, along with equivalent amounts of 4-ketocrenulide. The production of this β,β'-dialkylfuran not only substantiated the lactone assignment, but it also yielded important information to fix both the size and location of the side chain at C-3. Unlike the other derivatives, ketofuran **6** exhibited mass spectral fragmentation of the side chain ($M^+ - C_8H_{15}$). In retrospect, the C_8 terpenoid side chain, which is extremely common in *Dictyota* metabolites,[1] was also clearly represented in the ^1H NMR spectral features of **1**. The observed fragmentation at C-3 in **6** as well as the presence of a deshielded one-proton bond at δ 3.74 (d, J = 11 Hz) in the ^1H NMR

(6) A brief account of this compound under the name "acetoxycrenulatin" was published earlier: see W. Fenical in "Marine Natural Products Chemistry", D. J. Faulkner and W. Fenical, Eds., Plenum Press, New York, 1977, p 179. This nomenclature was subsequently abandoned, since the name "crenulatin" had been eariler coined for a coumarin derivative: see S. C. Basa, *Aust. J. Chem.*, **28**, 1159 (1975).

(7) A complete report of the fish toxicity assay we used has appeared: see V. J. Paul, O. J. McConnell, and W. Fenical, *J. Org. Chem.*, **45**, 3401 (1980).

(8) For a discussion of the magnitude and stereochemistry of homoallylic coupling, see L. M. Jackman and S. Sternhall, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon Press, Elmsford, NY, 1969, pp 316–328.

Chart I. Results of the ^1H NMR Lanthanide-Induced Shift [Eu(fod)$_3$] Experiment with the Diene Lactone 7

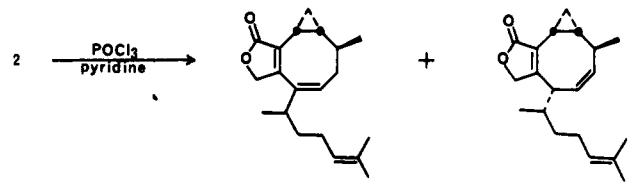


7

C no.	Δδ	Θ	r (meas), Å	r (calcd), Å	% error
6α	0.68	25	7.3	7.0	4.1
6β	0.68	15	7.5	7.5	0
7	0.52	21	7.7	7.9	2.6
8α	1.46	27	5.4	5.3	1.9
9	1.39	16	5.9	5.9	0
18α	1.08	40	4.8	4.8	0
18β	1.10	40	4.8	4.8	0
20α	0.21	35	7.8	9.1	16.7
20β	0.21	20	9.5	10.7	12.6

spectrum of this compound illustrated that the ketone must be placed at C-4. The facile cleavage of the side chain in this position is accommodated by the pseudobenzylic nature of the C-3–C-10 bond, as well as its predictable β-scission behavior activated by the C-4 ketone.

Based upon the data defined above, acetoxycrenulide could be assigned as a bicyclo[6.1.0]nonane derivative, obviously biogenetically related to dictyodial and dictyolactone.[3] The position of the lactone carbonyl and the ring methyl groups, as well as the relative stereochemistry at C-3, C-4, C-6, C-7, and C-9, remained to be defined. Dehydration of hydroxycrenulide (2) with $POCl_3$/pyridine



7 8

yielded a mixture of the cyclooctadiene lactone derivatives 7 and 8, which were extensively analyzed by ^1H NMR. Decoupling experiments with diene 7 allowed the interrelation of all protons at C-4 through C-9, thus establishing the locations of the ring methyl and cyclopropane groups. Using the conformation of 1,3,5-cyclooctatriene[9] as a model to predict the preferred conformation of 7, we undertook a ^1H NMR lanthanide-induced shift study to fix numerous elements of stereochemistry. Chart I illustrates the parameters involved in the shift study and the data obtained. These experiments clearly established the location of the lactone carbonyl at C-19 in close proximity to the cyclopropane ring, and it also illustrated the relative stereochemistries at these centers. The stereochemistry at C-6, which involves the C-20 methyl, could not be confidently established by this experiment, since calculated and observed shift values for both configurations were within the experimental limits of this method. Fortunately, acetoxycrenulide has been recently chemically interrelated with a closely related compound, which itself was fully defined by X-ray crystallographic methods. Based upon this finding, the C-20 methyl group must be positioned in the "up" or β position as illustrated in Chart I.[10]

In an analogous way, the ^1H NMR features of the diene lactone 8 were considered. A ring conformation analogous to 1,3,6-cyclooctatriene[3] was assumed for 8, and decoupling experiments were performed to relate several key spin-coupled protons (Experimental Section). Analysis of the molecular model of 8, and considering the dihedral angles and coupling constants measured, led to the assignment of the side chain at C-3 as an α substituent. In the β position, severe transannular crowding would be realized with the cyclopropane ring.

The final assignment of the structure of acetoxycrenulide required an assessment of the stereochemistry of the acetoxy functionality at C-4. The flexibility of the eight-membered ring in 1 precluded the use of dihedral angle-coupling constant analysis. However, the proximity of the C-18 methylene to C-4 substituents in the α position was clearly visible in molecular models. Since these protons shift markedly from δ 4.71 and 5.00 in 1 to δ ~4.6 in both 7 and 8 illustrating the deshielding effects in 1, the acetoxy was assigned to the α position.

Experimental Section

IR spectra were recorded on a Perkin-Elmer 137 instrument. UV spectra were recorded on a Perkin-Elmer Coleman 124 spectrophotometer. ^1H NMR and decoupling experiments were performed on a Varian HR-220 spectrometer in $CDCl_3$, with and without Me_4Si as internal reference, with δ 0. ^{13}C NMR spectra were determined on a Varian CFT-20 spectrometer in $CDCl_3$ with Me_4Si as internal reference. The off-resonance multiplicities are shown in parentheses. Low-resolution mass spectra were recorded at 70 eV on a Hewlett-Packard Model 5930A mass spectrometer. High-resolution mass spectra were obtained at the UCLA Chemistry Department. Silica gel, Grade 62, 60–200 mesh (W. R. Grace), was used for column chromatography, and Brinkman precoated TLC plates (silica gel 60 F-254, 2 mm) were used for preparative TLC. High-pressure liquid chromatographic separations were performed on a Waters Associates HPLC Model 6000A, with two 30 cm × 4 mm μ-Porasil columns connected in series or a 50 cm × 16 mm home-built Lichrosorb column.

Isolation of Acetoxycrenulide (1). Air-dried and ground *Dictyota crenulata* (1 kg) collected in the Gulf of California at Cabo San Lucas, Mexico (March, 1976), was exhaustively extracted with 20% methanol in chloroform, and the extract was concentrated under reduced pressure. A portion of the extract (35 g) was chromatographed on a 90 × 5 cm silica gel column (700 g), eluting initially with benzene. After elution with 7 L of benzene, the solvent was changed to 1% diethyl ether in benzene, and acetoxycrenulide was eluted as a mixture. Final purification was achieved by HPLC, to yield 137 mg (0.004% of extract) of acetoxycrenulide (1) as a colorless oil: $[\alpha]^{26}_D$ +13° (*c* 0.67, $CHCl_3$); UV (MeOH) λ_{max} 227 nm (ε 11 500); IR (CCl_4) ν_{max} 2920, 1760, 1735, 1450, 1375, 1225, 1040, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.39 (1 H, m), 0.89 (1 H, m), 0.99 (3 H, d, *J* = 5 Hz), 1.02 (3 H, d, *J* = 7.5 Hz), 1.59 (3 H, s), 1.70 (3 H, s), 2.03 (3 H, s), 3.23 (1 H, d, *J* = 7.5 Hz), 4.74 (1 H, dd, *J* = −16 and 2.5 Hz), 4.85 (1 H, dd, *J* = −16 and 2.5 Hz), 5.07 (1 H, t, *J* = 7.5 Hz), 5.48 (1 H, br t, *J* = 4 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 8.4 (t), 10.3 (d), 17.1, 17.7, 21.3, 23.4, 25.5, 25.7, 25.9, 29.3, 32.8, 35.7, 43.9 (t), 47.4 (d), 71.5 (t), 72.2 (d), 123.5 (d), 128.8 (s), 132.4 (s), 166.5 (s), 169.7 (s), 174.2 (s); MS, *m/e* 360, 318, 301, 289, 230, 215, 201, 188, 173, 133, 109, 107, 105, 95, 93, 91, 81, 79, 69, 67, 59, 57, 55, 43, 41. High-resolution mass measurement calcd for $C_{22}H_{32}O_4$, 360.2300; found, 360.2308.

Selective Saponification of Acetoxycrenulide (1) to Hydroxycrenulide (2). Two milliliters of an aqueous saturated

(9) F. A. L. Anet, and I. Yavari, *Tetrahedron Lett.*, 4221 (1975).

(10) During the progress of this research we learned that acetoxycrenulide and several derivatives had been isolated from the sea hare *Aplysia vaccaria* by Sims and associates at the University of California, Riverside. Their structure elucidation of 1 involved the reduction of the corresponding C-18 hydroxy compound to yield acetoxycrenulide. The structure of their derivative was fully confirmed by X-ray crystallographic methods. Please refer to the accompanying paper.

Na_2CO_3 solution was introduced into a solution of 1 (64 mg, 0.18 mmol) in 5 mL of methanol, and the solution was stirred at room temperature for 16 h. The mixture was diluted with water and extracted with 3 × 10 mL portions of diethyl ether. The combined ether extracts were dried over $MgSO_4$ and concentrated in vacuo to give a yellow oil. HPLC separation (Lichrosorb, 15% EtOAc–CH_2Cl_2) of this oil gave 49 mg (86%) of hydroxycrenulide (2) as a colorless oil: IR (neat) ν_{max} 3550, 2960, 1760, 1660, 1450, 1380, 1105, 1060, 1025, and 785 cm^{-1}; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.33 (1 H, m), 0.93 (1 H, m), 1.00 (1 H, d, J = 7 Hz), 1.03 (1 H, d, J = 7 Hz), 1.1–1.5 (m), 1.59 (3 H, s), 1.69 (3 H, s), 1.7–2.1 (m), 3.09 (1 H, d, J = 8 Hz), 4.35 (1 H, br t, J = 4 Hz), 4.71 (1 H, dd, J = –17 and 3 Hz), 5.00 (1 H, dd, J = –17 and 2 Hz), 5.07 (1 H, br t, J = 7 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 8.2 (t), 10.1 (d), 17.4 (q), 17.6 (q), 23.7 (q), 25.6, 25.7, 26.2, 28.4 (t), 32.7 (t), 35.8 (t), 48.4 (t), 49.2 (d), 69.6 (d), 72.6 (t), 123.9 (d), 127.8 (s), 132.1 (s), 169.7 (s), 175.3 (s); MS, m/e 318 (M^+), 300, 275, 149, 123, 121, 119, 109, 95, 86, 71, 69, 57, 41.

Reduction of Acetoxycrenulide (1) to the Triol 4. To a cooled slurry (ca. 10 °C) of $LiAlH_4$ (200 mg) in diethyl ether under N_2 was added a 5-mL ethereal solution of acetoxycrenulide (40 mg) via syringe over a 10-min period. After 2 h the reaction was quenched with careful dropwise addition of H_2O. The mixture was partitioned between 100 mL of Et_2O and 50 mL of H_2O, and the Et_2O layer was dried over $MgSO_4$ and concentrated to yield 4 homogeneous by TLC as a colorless oil: IR (CCl_4) ν_{O-H} 3600–3200 cm^{-1}; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.50 (1 H, m), 0.64–0.96 (2 H, complex m), 0.99 (6 H, d, J = 7 Hz), 1.56 (3 H, s), 1.66 (3 H, s), 3.02 (1 H, d, J = 10 Hz), 3.66 (2 H, br s, D_2O exch), 3.91 (2 H, dd, J = 12 and 12 Hz, superimposed on a 1 H, broad signal that disappears with D_2O), 4.28 (2 H, m), 4.46 (1 H, d, J = 10 Hz), 5.02 (1 H, t, J = 7.5 Hz); MS, m/e 322 (M^+), 304, 286, 272, 243, 215, 189, 145, 133, 119, 109, 107, 105, 95, 93, 91, 81, 79, 77, 64, 55, 43, 42.

Triacetate 5. A solution of triol 4 in 5 mL of pyridine and 2 mL of acetic anhydride was allowed to stir at room temperature for 65 h. The mixture was then partitioned between Et_2O and H_2O. The Et_2O layers were dried over $MgSO_4$, concentrated, and purified by HPLC on μ-Porasil; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.89 (3 H, m), 0.98 (3 H, d, J = 6 Hz), 1.05 (3 H, d, J = 6 Hz), 1.59 (3 H, s), 1.68 (3 H, s), 1.98 (3 H, s), 2.02 (3 H, s), 2.03 (3 H, s), 3.22 (1 H, d, J = 10 Hz), 4.55 (2 H, s), 4.68 (2 H, s), 5.08 (1 H, t, J = 7.5 Hz), 5.36 (1 H, t, J = 4 Hz); MS, m/e 328 (M^+ – $2CH_3COOH$), 286, 268, 253, 243, 225, 213, 199, 185, 175, 159, 157, 145, 133, 131, 119, 109, 107, 105, 95, 93, 91, 81, 69, 57, 55, 43, 41.

Oxidation of Triol 4 to Ketofuran 6. A solution of triol 4 (85 mg) in 1 mL of pyridine was slowly added to a cool (10 °C) solution of CrO_3 (500 mg) in pyridine (5 mL). The resultant brown solution was stirred overnight and subsequently partitioned between H_2O and ether. The ether phase was collected, the water was reextracted with ether, the combined ether extracts were dried over anhydrous $MgSO_4$ and filtered, and the filtrate was reduced in vacuo. HPLC separation (μ-Porasil, 30% Et_2O in petroleum ether) yielded 4-ketocrenulide (43%) and the ketofuran 6 (34%). 4-Ketocrenulide was identified based upon the following spectral characteristics: IR (film) ν_{max} 1765, 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.51 (1 H, m), 0.94 (3 H, d, J = 7 Hz), 1.18 (3 H, d, J = 6 Hz), 1.60 (3 H, s), 1.70 (3 H, s), 2.07 (3 H, br m), 2.46 (1 H, d, J = 11 Hz), 2.67 (1 H, d of d, J = 11 and 11 Hz), 4.18 (1 H, d, J = 11 Hz), 4.65 (1 H, d of d, J = –16 and 2.3 Hz), 4.72 (1 H, d of d, J = –16 and 2.3 Hz), 5.05 (1 H, t, J = 7.5 Hz); MS, m/e (relative intensity) 316 (M^+, <1), 301 (<1), 274 (<1), 167 (4), 149 (18), 109 (35), 95 (26), 81 (55), 69 (100), 57 (49), 55 (66), 43 (50). Ketofuran 6 illustrated the following spectral features: IR (film) ν_{max} 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 220 MHz) δ 0.32 (1 H, m), 0.97 (3 H, d, J = 5 Hz), 1.10 (3 H, d, J = 7.5 Hz), 1.56 (3 H, s), 1.66 (3 H, s), 2.00 (2 H, m), 2.36 (1 H, d, J = 11 Hz), 2.55 (1 H, dd, J = 11 and 11 Hz), 3.74 (1 H, d, J = 11 Hz), 5.05 (1 H, t, J = 7.5 Hz), 7.15 (1 H, s), 7.21 (1 H, s); MS, m/e (relative intensity) 300 (M^+, 10), 285 (2), 258 (4), 245 (4), 229 (4), 215 (3), 201 (4), 189 (7), 175 (7), 161 (16), 147 (19), 133 (26), 119 (33), 109 (48), 107 (24), 105 (45), 100 (45), 95 (37), 91 (48), 81 (44), 69 (100), 57 (41), 55 (70), 43 (48), 41 (70).

Dehydration of Crenulide 4 to the Diene Lactones and 8. A solution of hydroxycrenulide 2 (30 mg, 0.094 mmol) and an excess amount of $POCl_3$ in 4 mL of anhydrous pyridine was stirred under nitrogen atmosphere at 0 °C for 0.5 h. The reaction was quenched by the cautious addition of distilled water, and the aqueous phase was extracted with 3 × 10 mL of diethyl ether. The combined ether extracts were then dried over $MgSO_4$ and reduced in vacuo. Purification by TLC with 5:5:1 hexanes–dichloromethane–ethyl acetate yielded the diene lactone 7 (11 mg, 39%) and diene lactone 8 (8 mg, 28%) as colorless oils. Diene lactone 7: UV (MeOH) λ_{max} 231 nm (ϵ 4600), 274 (ϵ 5400); IR (CCl_4) ν_{max} 2940, 1760, 1640, 1440, 1040, 1020 cm^{-1}; ^1H NMR (CCl_4, 220 MHz) δ 0.55 (1 H, m, C-8α), 0.80 (1 H, m, C-7), 0.95 (1 H, m, C-8β), 1.06 (3 H, d, J = 7 Hz, C-20), 1.07 (3 H, d, J = 7 Hz, C-17), 1.34 (1 H, ddt, J = –14, 7, and 7 Hz, C-11), 1.45 (1 H, ddt, J = –14, 7, and 7 Hz, C-11), 1.47 (1 H, m, C-6), 1.57 (3 H, s, C-16), 1.62 (1 H, m, C-9), 1.67 (3 H, s, C-15), 1.94 (2 H, q, J = 7 Hz, C-12), 2.04 (1 H, ddd, J = –17, 11, and 7 Hz, C-5α), 2.19 (1 H, sextet, J = 7 Hz, C-10), 2.35 (1 H, ddd, J = –17, 4, and 4 Hz, C-5β), 4.56 (1 H, dd, J = 16 and 2 Hz, C-18), 4.72 (1 H, dd, J = 16 and 2 Hz, C-18), 5.00 (1 H, t, J = 7 Hz, C-13), 5.54 (1 H, dd, J = 7 and 4 Hz, C-4); MS, m/e 300 (M^+), 285, 271, 257, 245, 219, 189, 173, 161, 145, 129, 115, 105, 91, 83, 69, 55, 41. Diene lactone 8: UV (MeOH) λ_{max} 321 nm (ϵ 7200); IR (CCl_4) ν_{max} 2940, 1760, 1640, 1440, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.43 (1 H, m), 0.86 (1 H, m), 0.93 (3 H, d, J = 7 Hz), 1.11 (3 H, d, J = 7 Hz), 1.2–1.5 (m), 1.58 (3 H, s), 1.66 (3 H, s), 1.98 (3 H, m), 3.63 (1 H, br m), 4.52 (2 H, d, J = 2.5 Hz), 5.01 (1 H, t,J = 7 Hz), 5.27 (1 H, ddd, J = 12, 5, 2 Hz), 5.48 (1 H, ddd, J = 12, 5, and 2 Hz); MS, m/e 300 (M^+), 285, 271, 257, 245, 217, 215, 201, 189, 173, 157, 145, 129, 115, 105, 91, 77, 69, 55, 41.

Lanthanide-Induced ^1H NMR Shift Study of Diene 1. Aliquots of $Eu(fod)_3$ in $CDCl_3$ were added to compound 7 in $CDCl_3$, and sequential 220-MHz ^1H NMR spectra were recorded. Calculations were performed as previously described,[11] and the refined data are presented in Chart I, along with the predicted molecular conformation of diene lactone 7. A best fit situation was found to exist with the europium atom anti to the cyclopropane ring, 2.7 Å from oxygen with a C–O–Eu angle of ca. 105°.

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New Crenulides from the Sea Hare *Aplysia vaccaria*

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The scarcity of natural predators for sea hares has spurred interest in these opisthobranch molluscs as sources of toxins or chemical defense substances.[1] We became interested in *Aplysia vaccaria* because it is reported to eat brown algae, in contrast to *A. californica*, which eats almost exclusively red algae.[2] It is now generally accepted that sea hares concentrate metabolites produced by their dietary algae.[1] In many cases the compounds concentrated

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