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DEFENSE ALLOMONES OF SOME MARINE MOLLUSKS

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Abstract—Certain marine mollusks that lack obvious physical protection have evolved various biological and chemical defense strategies. One type of chemical defense involves accumulation of small organic molecules, largely from the diet, which afford protection from common predators. Our work and research by others has shown that the animals can utilize different structural types. Interestingly several of the defense allomones which have been defined are structurally related to the drimane sesquiterpenoids which have been shown to be antifeedants against terrestrial insects.

INTRODUCTION

Mollusks comprise the second largest phylum of invertebrate animals. More than 80,000 living species have been described. Mollusks are also among the most familiar invertebrates, as they include such culinary delicacies as oysters, squids, and octopods, as well as animals with exquisitely beautiful shells, long popular with collectors. Among the lesser known mollusks is the order Nudibranchia (subclass Opisthobranchia, class Gastropoda). Many nudibranchs are brightly colored and delicately shaped; all lack an external shell. Yet despite this lack of protective armor, it had long been observed by marine biologists that nudibranchs are rarely eaten by predatory fish.[1] Early explanations for this remarkable survival ability cited their cryptic coloration or their habit of hiding under stones.[2] Thompson[1] in his review of opisthobranch defense mechanisms presented examples and evidence of biological (e.g. stinging cells) and chemical (e.g. acidic secretions), rather than the physical defense strategies mentioned above. By pH measurements Thompson[1] documented the strongly acidic character of the skin secretion of some of the animals. He also observed by human gustatory tests, carried out by himself and by a courageous assistant, that the non-acidic skin secretions of some animals tasted bitter, bitter-sour, or were tasteless. Thompson[1] did not speculate on the chemical nature of these non-acidic secretions, which might well exemplify an additional and distinct defensive weapon.

In 1963 Johannes[3] reported the observation that mucus from the nudibranch *Phyllidia varicosa* Lamarck, 1801 killed several species of crustaceans and a molly within 0.5 to 5 hr after the assay animal was placed in an aquarium containing either *P. varicosa* or an approximately 2% solution of mucus in seawater. He saw his experiments as evidence for a third type of defense mechanism, already foreshadowed by Thompson's work.[1] Johannes[3] characterized the mucus as a volatile, relatively heat-stable, tasteless material of neutral pH, possessing a strong unusual smell. He further linked these results to an early observation by Risbec[4] that a voluminous, strong-smelling mucus is emitted by most *Phyllidia* spp. when disturbed.

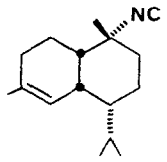
In this paper we will describe some of our work dealing with this third mode of molluscan defensive strategy, as well as some pertinent recent work by others.

Our early work. Johannes's report prompted us to probe the chemical nature of the *Phyllidia varicosa* mucus. Gentle squeezing of a freshly netted animal yielded about 5 mL of mucus, which contained about 1 mg of active principle. We maintained the animals in an aquarium, but soon realized that a second milking produced but little, and subsequent milkings, no additional active material. Serendipitously, during a dive we discovered the animal's diet when *P. varicosa* was observed while feeding on an off-white sponge, *Hymeniacidon* sp. We readily established that an ethanolic sponge extract yielded a rich mixture of lipids, of which the nudibranch defense allomone was a prominent component. Although biologists had been aware that nudibranchs feed on highly specific diets, most often coelenterates, but also sponges and bryozoans,[5] ours was the first evidence that nudibranchs selectively accumulate chemical defensive agents from their food.

The volatile character of the *P. varicosa* allomone led us to attempt purification by GLC, which however destroyed the characteristic odor of the active principle. We succeeded in isolating the pure metabolite as a mobile oil by vacuum distillation, followed by methylene chloride extraction, and tlc on alumina. A single diagnostic IR band at 2120 cm^{-1} suggested an isocyano function, which we confirmed by thermal isomerization to nitrile (2250 cm^{-1}) and acid hydrolysis to formamide (1685 cm^{-1}). Initially, we believed the compound to be identical with 10-isocyano-zizanane (≡(+)-amorphane) (**1**), which we had in hand from a deep-water sponge, *Halichondria* sp.[6] Once we were able to obtain sufficient quantities of the *P. varicosa* allomone from its food source (*vide supra*), it became obvious that the new isonitrile possessed a different, *viz* tricyclic sesquiterpene skeleton. We first suspected an *ent*-ylangane (**2**) skeleton because of its obvious structural relationship to **1**. Extensive chemical degradation of the *P. varicosa* allomone proved this to be erroneous. X-ray diffraction of a derivative revealed a new carbon skeleton, functionalized at C-9, 9-isocyanopupukeanane (**3**).[7,8] Interestingly, the sponge, but apparently not the mollusk, contains varying amounts of the isomeric 2-isocyanopupukeanane,[9] along with other sesquiterpenoids.[10] The new carbon skeleton of the pupukeananes has been the target of a number of total syntheses.[11-14]

RELATED RESEARCH

Subsequent work by us and by others has shown that nudibranchs are capable of sequestering from their prey a wide spectrum of metabolites and of using them as defense allomones. In fact, no other isocyanosesquiter-



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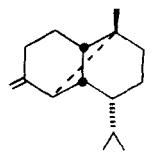

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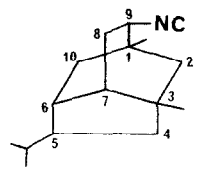

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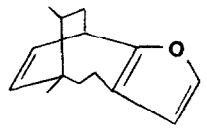

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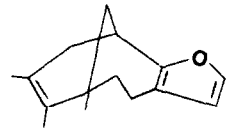

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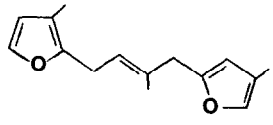

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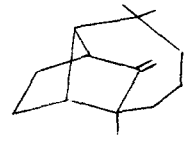

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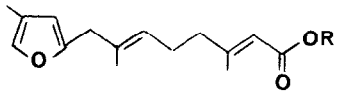


8 R = 

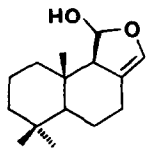
9 R = 

penes have so far been implicated, although it must be remembered that no further work on *Phyllidia* spp. has as yet been reported.

From two dorid nudibranchs, *Hypselodoris godeffroyana* and *Chromodoris maridadilus*, and from their common prey, the sponge *Dysidea fragilis*, we isolated two furanosesquiterpenoids, nakafuran-8 (**4**) and nakafuran-9 (**5**).[15] Both compounds possess antifeedant properties in a laboratory assay against common reef fishes, *Chaetodon* spp.

Other investigators have isolated sesquiterpenoids from nudibranchs, but a predator-prey relationship has not been firmly established in all cases. Of the four structural types isolated so far, three are furanosesquiterpenes. The simplest of these longifolin (**6**),—not to be confused with the well-known longifolene (**7**)—was reported by Cimino *et al.* from *Glossodoris gracilis*,[16] and previously from the sponge *Pleraplysilla spinifera* by the same workers.[17] The compound was already known from a lauraceous terrestrial plant. From another dorid, *Chromodoris marislae*, Hochlowski and Faulkner[18] isolated as the major constituent marislin (**8**), which is a furanosesquiterpenoid acid esterified with the hemiacetal of methylenesuccindialdehyde. The authors failed to detect marislin (**8**) in any of some twenty common Gulf of California sponges. Nor did they find the previously known Mediterranean sponge metabolite pleraplysillin-2 (**9**),[19] to which marislin is related by a simple allylic proton shift. Transformation of **8** to **9** takes place slowly during routine handling and rapidly in boron trifluoride etherate.[18] The third compound in this group was isolated by the Italian workers[20] from the digestive glands of *Dendrodoris limbata*. Compound **10**[21] is a drimane hemiacetal, which is esterified with a number of long chain saturated and unsaturated fatty acids. The authors[20] point to the intriguing structural relationship between **10** and the terrestrial sesquiterpenoid polygodial (**11**), which was isolated by Nakanishi *et al.*[22] from the East African *Warburgia stuhlmanni* and recognized as an antifeedant (*vide infra*).

Andersen and Sum[23] studied a dorid, *Archidoris odhneri*, from British Columbia waters and isolated from the organic extract of the whole animal 2,3-dihydroxypropyl (all *E*)-farnesate (**12**) and its two monoacetates. A defensive role of these compounds is implied.



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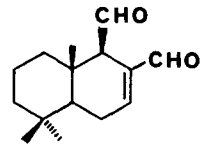

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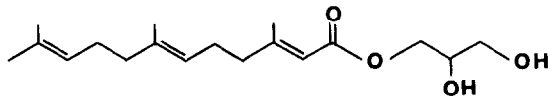

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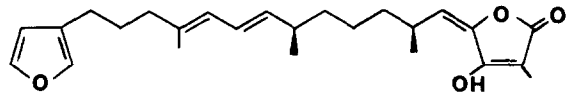

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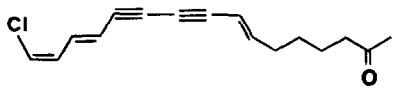

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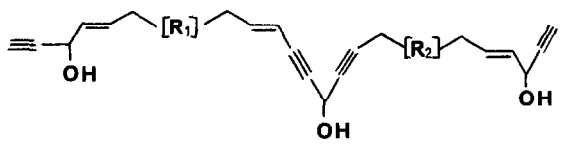


15

$R_1 + R_2 = C_nH_{2n-6}$ $n = 25$

The only sesterterpenoid so far, fasciculatin (**13**), was isolated by Cimino *et al.*[16] from the digestive glands of *Dendrodoris grandiflora*. Italian workers had previously isolated this compound from the sponge *Ircinia fasciculata*,[24] although no *I. fasciculata* was seen near the collection site of *D. grandiflora*.

Walker and Faulkner[25] isolated from the dorid nudibranch *Diaulula sandiegensis* a series of nine linear C_{16} secondary alcohols or ketones by leeching the animals in methanol at low temperature. These compounds are characterized by multiple olefinic and acetylenic unsaturation and by a chloromethylene terminus of which (1*Z*, 3*E*, 9*Z*) - 1 - chlorohexadeca - 5,7 - diyne - 1,3,9 - triene - 15 - one (**14**) is an example. Although the dorids were observed while feeding on sponges, none of these or related compounds were found in these sponges nor in sponges that were identified from an examination of the gut contents of *D. sandiegensis*. No evidence was cited for a defensive role of the metabolites.

The Mediterranean nudibranch *Peltodoris atromaculata* and its prey, the sponge *Petrosia ficiformis*, have in common a series of large linear triols containing multiple double and triple bonds. Castiello *et al.*[26] isolated the compounds from the gut of the dorid and from the sponge. The chain length of the compounds ranges from C_{46} to C_{55} and compound **15** illustrates their chemical make-up.

A group at Stanford studied *Anisodoris nobilis*, initially the aqueous extract of the whole animal, subsequently of the digestive glands. Fractionation was monitored by mammalian bioassay, which resulted in the isolation of 1-methylisoguanisine (**16**),[27–29] which caused reduced arterial pressure and reduced heart rate in the rat. The same compound had been independently isolated and identified from an Australian sponge *Tedania digitata* by Quinn *et al.*[30] The Stanford workers also refer to the compound under the alias doridosine. The role if any of this compound in the marine ecosystem is unknown.

The Onchidiacea are not invariably classified as nudibranchs. However, they are intertidal marine slugs with glands that secrete noxious fluids at the side of their bodies.[31] Ireland and Faulkner isolated the sesquiterpene onchidal (**17**) from *Onchidella binneyi*,[32] but no direct evidence for a defensive role of this compound was adduced.

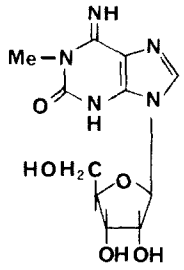
Although members of the order Nudibranchia have been the prime objective of recent research, other naked

gastropods have not been neglected. From *Aplysia brasiliana* (order Anaspidea or sea hares) Meinwald *et al.*[33] isolated a fish antifeedant panacene (**18**), which is an interesting variant of the linear C_{15} enynes common to sea hares and to their diet, red algae of the genus *Laurencia*.[34] The same animal yielded several additional compounds with antifeedant properties, these possessing more familiar C_{15} enyne structures.[35] Brasilenyne (**19**) will serve as an example.

Although pheromones are outside the scope of this discussion, one interesting piece of research should be cited. The opisthobranch order Cephalaspidea also includes some families without shells. Fenical *et al.*[36–38] investigated the alarm pheromone of *Navanax* (syn. *Chelidonura*) *inermis*, which proved to be a mixture of 10-(3-pyridyl)-, 10-phenyl-, and 10 - (4 - hydroxyphenyl) - 3,5,7,9 - decatetraen - 2 - one (navenones A–C) (**20**). The navenones are secreted by the mollusks as a yellow liquid which becomes part of the animal's slime trail when molested or threatened and causes abrupt termination of trail-following behavior. Fenical *et al.*[38] further showed that the navenones—unlike nudibranch defense allomones—are not diet-derived, but are biosynthesized by *N. inermis*.

OUR RECENT WORK[39]

As a beginning of a more systematic investigation of nudibranchs and their specific prey in Hawaiian waters we have studied the relatively rare *Chromodoris albonotato* collected at −5 m off Shark's Cove, Oahu. The live animals were briefly extracted with methanol/dichloromethane. The resulting organic residue was triturated with acetonitrile. The soluble portion yielded a white crystalline solid, m.p. 97–99°, which we named pu'ulenal (**21**).[40] A formula of $C_{17}H_{24}O_3$ and salient spectral data suggested a bicyclic sesquiterpene possessing three Me groups on quaternary carbons (δ 0.99, 0.94, 0.88). Four elements of unsaturation and all three O atoms were accounted for by an α,β-unsaturated aldehyde [δ 9.63; 6.74 (1H, br dd, $J = 4.8$, 3.4 Hz); ν_{max} 1695 cm^{-1}; λ_{max} 227 nm] and a vinyl acetate [δ 2.10; 7.14 (1H br s); ν_{max} 1755 cm^{-1}; λ_{max} 262 nm]. Addition of base destroyed the long wavelength chromophore irreversibly, thereby confirming presence of an enolacetate. Spectral data for both chromophores are strongly reminiscent of those reported for onchidal (**17**).[32] Double resonance experiments succeeded in extending the enal chromophore by $-CH_2-CH<$, leading to two possible part



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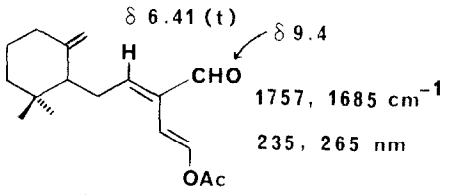

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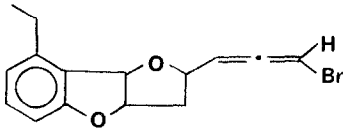

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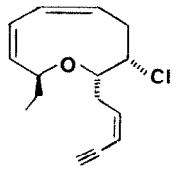

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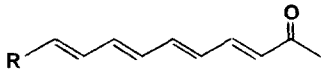

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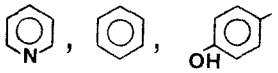
R = 

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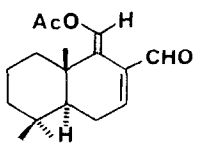

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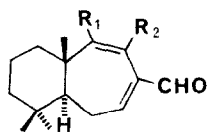


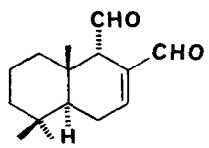
22 R_1 = OAc, R_2 = H
23 R_1 = H, R_2 = OAc

structures, -CH-CH_2-CH=C(CHO)-C=CHOAc (*a*) or -CH-CH_2-CH=C(CHO)-CH=COAc (*b*). This moiety plus three Me's on quaternary carbons add up to the partial formula $C_{14}H_{28}O_3$, which differs from **17** by C_3H_6, or three methylene groups. Four isoprenoid structures readily accommodate these data: **21** and its *Z*-isomer, and two isomeric compounds based on a widdrane skeleton, **22** and **23**. The two pairs may be readily distinguished by hydrolysis of the enol acetate, which leads to a dialdehyde for **21** and to a ketoaldehyde for **22** and **23**. Mild hydrolysis of pu'ulenal by chromatography on QAE Sephadex A-25 in the hydroxide form led to a 5:2 mixture of dialdehydes, which was separated by hplc. The epimeric nature of the two aldehydes [δ 9.86 (1H, d, $J = 2.5$ Hz), 9.42 1H, s) and 9.58 (1H, d, $J = 4$ Hz), 9.50 (1H, s)] was suggested by nearly identical UV, IR, and MS spectra. Both **21** and its *Z*-isomer would be expected to be transformed to mixtures of **11** and **24**. Compound **11** is the previously known plant metabolite polygodial,[41] first isolated from *Polygonum hydropiper* by Barnes and Loder[42] and by Ohsuka[43] because of the hot spicy taste of the plant. Nakanishi and Kubo[41] isolated polygodial (**11**) from *Warburgia stuhlmanni* and recognized its potent antifeedant activity against the African army worm. In fact, Nakanishi and Kubo found that hot taste to the human palate is associated with antifeedant activity. Base-catalyzed epimerization of the C-9 proton is known to produce 9-*epi*polygodial.[44] Spectral comparison of our major hydrolysis product with an authentic sample of (-)-polygodial (**11**)[45] proved their identity. When authentic **11** was subjected to the QAE-Sephadex treatment, a 5:2 mixture of C-9 epimers also resulted.

Since these results were equally explicable by **21** or its *Z*-isomer, pu'ulenal was reduced by sodium borohydride in ethanol to a single product, $C_{15}H_{26}O_2$, in addition to two uncharacterized acetates. The formula, coupled with the spectral data, established the gross structure of pu'ulenadiol (**25**), but failed to distinguish between **21** and its *Z*-isomer. A qualitative LIS study of pu'ulenal (**21**) and ^{1}H NMR comparison with values of pertinent model compounds confirmed the *E*-geometry of the enol acetate. Although aldehydes chelate only weakly, it has been shown that they do so preferentially in presence of acetate.[46] Addition of Eu(fod)$_3$ to pu'ulenal (**21**) caused large shifts of the acetate methyl and of the exocyclic olefinic proton, but the proton shifted at a faster rate than did the methyl, thus providing unequivocal evidence for *E*-geometry of the exocyclic olefin. Synthetic model compounds **26** and **27**[47] and their proton chemical shifts further confirmed the stereochemical assignments.

The work by Cimino *et al.*[20] (*vide supra*) on *Dendrodoris limbata*, this work on *Chromodoris albonotata* and work in progress in our laboratory by Roy Okuda on *Dendrodoris nigra* strongly implicate drimane sesquiterpenes as prominent defense allomones.

From another dorid nudibranch, *Hypselodoris daniellae*, collected at the Ala Wai Canal, Honolulu, we were able to isolate a single metabolite. Two animals were processed in the same way as *C. albonotata* yielding a colorless fragrant oil of composition $C_{15}H_{16}O$. Interpretation of spectral data, including some double resonance experiments, pointed to a structure resembling spiniferin-2 (**28**), first isolated by Cimino *et al.* from the sponge *Pleraplysilla spinifera*.[48] Comparison with the published data confirmed identity. We have not so far observed *H. daniellae* while feeding.



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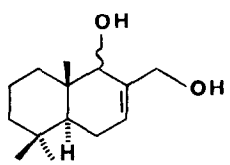

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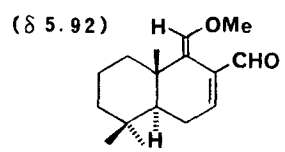

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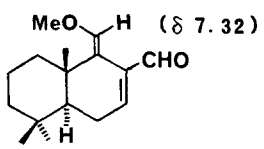
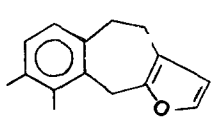


27



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CONCLUSION

Research reported so far indicates that marine mollusks that lack physical protection have evolved chemical defensive strategies that include accumulation of a variety of organic structural types, most frequently from dietary sources. In many cases the origin of the defense allomones has not been fully established. Nor has it been demonstrated by laboratory assay in a majority of studies that these presumed allomones are effective repellents or antifeedants against the common predators of a particular mollusk. Among the most intriguing molluscan defense allomones which have been discovered are the drimane-based sesquiterpenes that are related to the terrestrial plant-derived insect antifeedants.

EXPERIMENTAL

Chromodoris albonotata. Three specimens were collected at Pupukea, Oahu in June 1980. All specimens were collected at −15 m with SCUBA and identified by S. Johnson. The live specimens (0.183 g) were soaked in MeOH/CH_2Cl_2, 1:1, for 30 min. The extract was evaporated to a yellow powder (15.9 mg). Trituration of the crude extract with MeCN and evaporation of the soln yielded 11.1 mg of white crystalline pu'ulenal (**21**), m.p. 97–99°.

Pu'ulenal (**21**). $[\alpha]_D^{25} = -14.67°$ (*c* 0.15, $CHCl_3$); UV (MeOH) 227 nm (ϵ 5560), 262 nm (ϵ 2341), (MeOH + OH^-) 227 nm (ϵ 5070); IR (CH_2Cl_2) 2930, 2850, 1755, 1685, 1605, 1370, 1225, 1210, 1091, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.62 (1H, s), 7.14 (1H, br s), 6.76 (1H, br dd, *J* = 4.8, 3.4), 2.50 (1H, ddd, J = 21, 4.8, 4.8), 2.26 (1H, ddd, J = 21, 11.4, 4.8), 2.10 (3H, s), 1.82 (1H, br d, *J* = 13), 1.7–1.4 (4H, complex), 1.49 (1H, dd, *J* = 11.4, 4.8), 1.21 (1H, ddd, *J* = 13, 13, 4.4), 0.99 (3H, s), 0.94 (3H, s), and 0.88 (3H, s); EIMS (*m/z*) 276.16966 (M^+, $C_{17}H_{24}O_3$, calc. 276.17255, 34%), 234 (M^+–C_2H_2O, *base*), 219 (M^+–C_2H_2O–CH_3, 27%), 205 (10%), 201 (10%), 173 (8%), 149 (11%), 105 ($C_8H_9^+$, 14%), 91 ($C_7H_7^+$, 18%), and 77 ($C_6H_5^+$, 9%).

^1H NMR Double resonance (360 MHz). Saturation of 1H signal at δ 6.76 (1H, br dd *J* = 4.8, 3.4) caused collapse of signals 2.50 (1H, ddd *J* = 21, 4.8, 4.8) and 2.26 (1H, ddd *J* = 21, 11.4, 3.4) to doublets of doublets and sharpened signals 7.14 (1H, br s). Irradiation of signal δ 2.26 collapsed a 21 Hz geminal coupling to signal at δ 2.50 and simplified signal at δ 1.49 (1H, dd *J* = 114., 4.8) to a doublet.

LIS study. Consecutive 0.01 M aliquots of $Eu(fod)_3$, in chloroform-d, were added to pu'ulenal (**21**) in an NMR tube dissolved in chloroform-d, until 1M equivalent was reached. After each addition ^1H NMR spectra were recorded. The induced shifts ($\Delta\delta$) were determined by plotting the chemical shift of each proton signal against the molar quantities of $Eu(fod)_3$ added. Distances and angles were measured on a Dreiding model of **21** assuming the europium-oxygen bond distance to be 2.9 Å and the carbon-oxygen-europium bond angle to be about 120°. Me protons were treated as a single proton with bond length of 1.94 Å from the ring carbons.

Polygodial (**11**) *and 9 epipolygodial* (**24**). Pu'ulenal (**21**, 1.5 mg) was chromatographed on 3 g of QAE-Sephadex A-25, washed and prepared in the hydroxide form, with MeOH/CH_2Cl_2, 1:1. Collected of the eluant, and evaporation yielded 1.39 mg (quantitative) of a 5:2 mixture of **11** and **24**. Likewise, a sample of (-)polygodial (4.8 mg) was treated with QAE-Sephadex A-25. Again a 5:2 mixture of **11** and **24** was obtained in quantitative yield. Separation of **11** and **24** was accomplished by hplc using LiChrosorb Si-60 with dichloromethane as the mobile phase. Spectral characteristics of **11**: $[\alpha]_D^{25} = -9.17$ (*c* 0.24, $CHCl_3$); UV (MeOH 227 nm (ϵ 9800); IR (CH_2Cl_2) 1720, 1680, 1632, 1385, 1365, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.86 (1H, d, *J* = 2.5), 9.42 (1H, s), 7.10 (1H, dd, *J* = 5, 2.6), 3.26 (1H, br s), 2.57 (1H, ddd, *J* = 21, 5.5), 2.22 (1H, br ddd, *J* = 21, 11.5, 3), 1.79 (1H, br d, J = 12), 1.65–1.35 (5H, complex), 1.18 (1H, ddd, *J* = 12, 11, 5), 0.97 (3H, s), 0.94 (3H, s), and 0.92 (3H, s); EIMS (*m/z*) 234 (M^+, $C_{15}H_{22}O_2$, 8%), 232 (M^+-2H, 7%), 206 (M^+-CO, base), 191 (M^+–CO–CH_3, 50%), 177 (22%), 163 (26%), 121 ($C_9H_{13}^+$, 68%), 110 (64%), 109 ($C_8H_{13}^+$, 78%), 107 ($C_8H_{11}^+$, 54%), 105 ($C_8H_9^+$, 42%), 95 ($C_7H_{11}^+$, 54%), 93 ($C_7H_9^+$, 45%), 91 ($C_7H_7^+$, 65%), 81 ($C_6H_9^+$, 43%), 79 ($C_6H_7^+$, 46%), and 77 ($C_6H_5^+$, 50%). Spectral characteristics for 9-*epi*polygodial (24): UV (MeOH) 227 nm (ϵ 10,100); IR (CH_2Cl_2) 1725, 1685, 1635, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.58 (1H, d, *J* = 4), 9.50 (1H, s), 7.12 (1H, br dd, *J* = 5.2), 2.76 (1H, d, *J* = 4), 2.35 (1H, m), 2.23 (1H, m), 2.0–1.1 (7H, complex), 0.85 (3H, s), 0.83 (3H, s), and 0.82 (3H, s); EIMS (*m/z*) 234 (M^+, $C_{15}H_{22}O_2$, 12%), 232 (M^+–2H, 10%), 206 (M^+–CO, base), 191 (M^+–CO–CH_3, 65%), and 77 ($C_6H_5^+$, 59%).

Pu'ulenadiol (**25**). Excess NaH_4, dissolved in 1 mL EtOH, was slowly added to a stirring ethanolic soln of **21** (1.2 mg) maintained at 0°. After 1 hr the reaction was quenched with acetone and filtered through a disposable pipette containing silica gel. Evaporation of the solvent yielded a 3-component mixture (1.1 mg). Separation by hplc using LiChrosorb Si-60 with EtOAc as the mobile phase provided 2 fractions, one containing pure **25** (600 μg) and the other fraction was a mixture of two acetates. Spectral data: ^1H NMR ($CDCl_3$) δ 5.81 (1H, br dd, *J* = 6, 4), AB system 4.34 (1H, br d, *J* = 13.5), and 4.01 (1H, d, *J* = 13.5), AB system 3.92 (1H, dd, *J* = 12.5, 3.5) and 3.68 (1H, dd, J = 12.5, 7.5), 2.3–1.0 (10H, complex), 0.88 (6H, s), and 0.76 (3H, s); EIMS (*m/z*) 238 (M^+, $C_{15}H_{26}O_2$, 4%), 220 (M^+–H_2O, 4%), 190 (23%), 175 (10%), 109 ($C_8H_{13}^+$, base).

Hypselodoris daniellae. Two specimens of *Hypselodoris daniellae* were collected at the Ala Wai Canal, Oahu, directly across from the yacht harbor, in April 1980. *H. daniellae* is common throughout the year. Population decreases only occur when fresh rain water enters the canal from mountain streams.

Both specimens (489 mg, wet wt) were steeped in 25 mL of MeOH/dichloromethane, 1:1, for 30 min. Evaporation of the solvent left 43 mg of a yellow oil which had a sweet odor.

Spiniferin-2 (**28**). *The ^1H NMR spectrum of the crude material* from *H. daniellae* showed a furanosesquiterpene and fatty acid derivative mixture. Trituration with 10 mL of MeCN solubilized the furanosesquiterpene and caused the fatty acid derivatives to precipitate. Evaporation of solvent provided 27 mg of furanosesquiterpene which proved to be identical with **28**.[48]

UV (hexanes) 223 nm (ϵ 9200), 229 nm (ϵ 10,500), 265 nm (ϵ 550); IR (CH_2Cl_2) 3030, 2940, 2870, 1470, 1220, 1085, and 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19 (1H, d, J = 2), 6.96 (2H, s), 6.13 (1H, br d, *J* = 2), 4.08 (2H, br s), 3.18 (2H, m), 2.65 (2H, m), and 2.35 (6H, s); EIMS (*m/z*) 212 (M^+, $C_{15}H_{16}O$, 21%), 133 ($C_{10}H_{13}^+$, 15%), 119 ($C_9H_{11}^+$, base), 105 ($C_8H_9^+$), 84%), and 94 ($C_6H_6O^+$, 77%).

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