system. First diastereoisomer eluted: mass spectrum, m/e 354 ($M^{+\cdot}$, 2), 392 (2), 363 (1), 320 (8), 217 (65), 203 (48), 139 (100), 77 (80). Second diastereoisomer: mass spectrum, m/e 354 ($M^{+\cdot}$, 1), 392 (6), 321 (10), 320 (14), 217 (78), 203 (62), 139 (82), 77 (100).

Competitive Rate Determination. The amount of isopropyl iodide and methyl vinyl ketone reported in Table II was added to acetic acid (30 mL) at 5 °C under stirring, the solution of $TiCl_3$ (20 mL, 1.02 M) was added, and the mixture was cooled to 5 °C. 4-Chlorobenzenediazonium tetrafluoroborate was dissolved in $CH_3COOH-H_2O$ (8:2, 3 mL) at 5 °C and this was added in one portion to the solution. The reaction was run for 2 h. Diethyl ether was added (100 mL), and the aqueous solution was separated and extracted twice with ether (10 mL); the combined extracts were basified at 0 °C with NaOH until the value pH was 8, washed with saturated NaCl solution, dried, and analyzed by GLC on columns A and B after addition of 1-phenyl-2-propanone as internal standard. The results are reported in Table II and plotted in Figure 1.

Competitive Experiments. The amounts of α,β-unsaturated carbonyl compound reported in Table III were dissolved in acetic acid (40 mL), and $TiCl_3$ solution (20 mL, 21 mmol) was added. The diazonium salt (0.043 g, 0.19 mmol) dissolved in $CH_3COO-H-H_2O$ (2:1, 3 mL) was added to the resulting solution cooled to 5 °C. Te reaction was run for 2 h. Following the separation procedure used above, the extracts were distilled to 20 mL and analyzed for the β attack by GLC on the same columns at 200–240 °C. The results of these competitive experiments are reported in Table III.

Registry No. **1a**, 78-94-4; *trans*-**1b**, 3102-33-8; **1c**, 5166-53-0; **1d**, 26465-92-9; **1e**, 141-79-7; **1f**, 122-57-6; **4a**, 3506-75-0; **4b**, 74395-07-6; **4c**, 79083-88-8; **4d**, 79083-89-9; **4e**, 6269-30-3; **4f**, 29869-86-1; **5b**, 79083-90-2; **5c**, 79083-91-3; **5d**, 79083-92-4; **5f**, 79083-93-5; **6e**, 75478-75-0; **8**, 79083-94-6; **10**, 24254-65-7; **11**, 79083-95-7; **12**, 79083-96-8; 4-chlorobenzenediazonium tetrafluoroborate, 673-41-6; methyl crotonate, 18707-60-3.

Metabolites of Four Nudibranchs of the Genus *Hypselodoris*

Jill E. Hochlowski, Roger P. Walker, Chris Ireland, and D. John Faulkner*

Scripps Institution of Oceanography, La Jolla, California 92093

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The nudibranchs *Hypselodoris agassizi*, *H. ghiselini*, *H. californiensis*, and *H. porterae* contain selected metabolites of dietary origin. A new sesquiterpene furan, agassizin (**1**), was isolated from *H. agassizi* collected in Mexico. *H. ghiselini* from the Gulf of California contained a diterpene epoxide, ghiselinin (**4**), dendrolasin (**6**), nakafuran 9 (**3**), and a related methoxy butenolide (**5**). *H. californiensis* from the Gulf of California contained dendrolasin (**6**) and nakafuran 8 (**7**), while specimens from San Diego, CA, contained furodysinin (**8**), euryfuran (**9**), and pallescensin A (**10**). Furodysinin (**8**) and euryfuran (**9**) were also isolated from *H. porterae*. The sponge *Euryspongia* sp. was found to be the source of euryfuran (**9**). The structures of the new natural products **1**, **4**, **5**, and **9** were determined by interpretation of spectral data.

As part of a study of the chemical defense mechanisms of opisthobranch molluscs,[1] we have recently investigated the metabolites of a number of dorid nudibranchs. Although adult dorid nudibranchs are among the most brightly colored of marine animals and have no obvious physical defense mechanisms, they have few predators. In order to deter predators, many dorid nudibranchs concentrate selected metabolites from their sponge diet in nonmucous skin glands located in the dorsum and employ these metabolites in a defensive secretion.[2] We have shown that the biologically active metabolites of *Cadlina luteomarginata* were easily extracted by soaking the nudibranchs in an appropriate solvent.[3] We therefore proposed that the major metabolites obtained in this fashion from nudibranchs constitute the major components of a defensive secretion. In this paper, we report the structural elucidation of the major metabolites of the dorid nudibranchs *Hypselodoris agassizii*, *H. ghiselini*, *H. californiensis*, and *H. porterae*.

Specimens of the nudibranch *Hypselodoris agassizi* (Bergh, 1894)[4] were collected intertidally at Cruz de Juanacaxtle, Nayarit, Mexico. Seventy animals were soaked in methanol for 8 days, after which the methanol was decanted. Evaporation of the solvent under vacuum gave an aqueous suspension that was extracted with dichloromethane. Examination of the crude extract by TLC and ^1H NMR revealed three components, steroids, fats, and a furanoid sesquiterpene, agassizin (**1**, 0.76 mg/animal; see Chart I).

Agassizin (**1**), $[\alpha]_D$ −94° (c 1.2 MeOH), had the molecular formula $C_{15}H_{18}O$. The UV spectrum [266 nm (ϵ 3500), 220 (9250)] was consistent with the furan and homocyclic diene moieties although the intensities of the peaks were low compared with those of pallescensin G (**2**) [lit.[5] 266 nm (ϵ 18 000), 220 (16 000)]. The ^{13}C NMR spectrum contained four furan carbon signals at δ 112.2 (d), 117.6 (s), 139.4 (d), and 142.5 (s) and four olefinic signals at δ 120.4 (d), 123.1 (d), 132.1 (d), and 149.3 (s); the disubstituted furan agassizin (**1**) must therefore be tricyclic. The ^1H NMR spectrum (C_6D_6) contained two furan proton signals at δ 7.06 (d, 1 H, J = 1.5 Hz) and 5.99 (d, 1 H, J = 1.5 Hz), and AB quartet at δ 3.47 (d, 1 H, J = 15 Hz) and 3.27 (d, 1 H, J = 15 Hz) due to the bis allylic methylene protons, an isolated CH_2CH_2 system at δ 2.45 (m, 1 H), 2.26 (m, 1 H), and 1.63 (m, 2 H), and a methyl signal at δ 0.77 (s, 3 H). Irradiation at δ 1.63 reduced the signals at δ 2.26 and 2.45 to an AB quartet (J = 16 Hz). The protons on the six-membered ring gave signals at δ 5.51 (d, 1 H, J = 5 Hz, C-1), 5.74 (br dd, 1 H, J = 9, 5 Hz, C-2), 5.40 (dd, 1 H, J = 9, 2.5 Hz, C-3), and 2.59 (m, 1 H, J = 7, 7, 7, 2.5 Hz, C-4), the latter signal being coupled to a methyl signal at δ 0.82 (d, 3 H, J = 7 Hz). Irradiation of the signal at δ 2.59 caused

(1) Walker, R. P.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1475. Hochlowski, J. E.; Faulkner, D. J. *Tetrahedron Lett.* **1981**, *22*, 271. Ireland, C.; Faulkner, D. J. *Tetrahedron, Suppl.* **1981**, 233. Ireland, C.; Faulkner, D. J. *Bioorg. Chem.* **1978**, *7*, 125. Faulkner, D. J.; Ireland, C. In "Marine Natural Products Chemistry"; Faulkner, D. J., Fenical, W. H., Eds.; Plenum Press: New York, 1977; pp 23–34 and references cited therein.

(2) Thompson, T. E. *J. Mar. Biol. Assoc. U.K.* **1960**, *39*, 123.

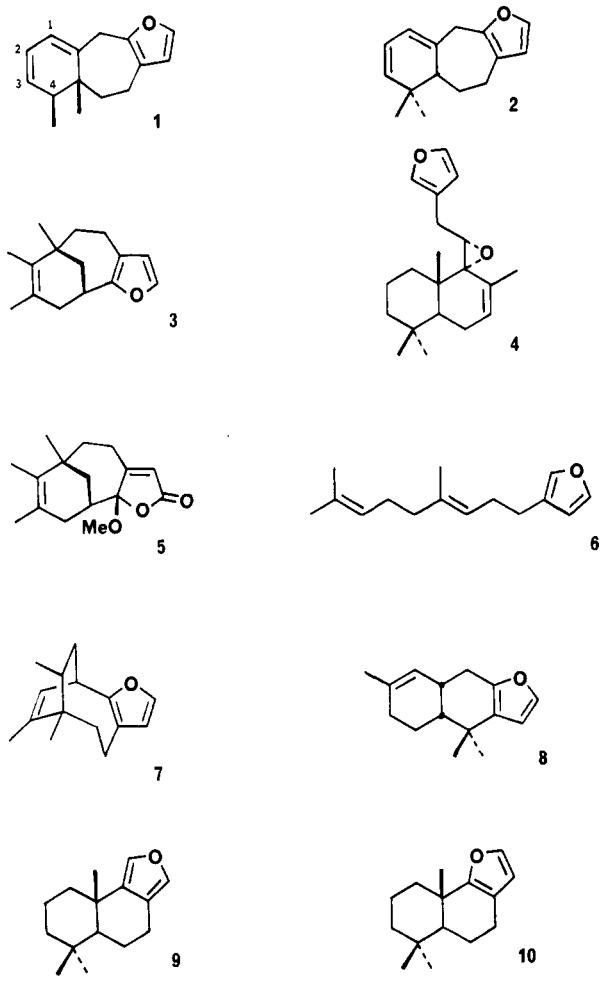
(3) Thompson, J. E.; Walker, R. P.; Wratten, S. J.; Faulkner, D. J. submitted for publication in *Tetrahedron*.

(4) Bergh, L. S. R. *Bull. Mus. Comp. Zool.* **1894**, *25*, 125.

(5) Cimino, G.; De Stefano, S.; Guerriero, A.; Minale, L. *Tetrahedron Lett.* **1975**, 1421.

0022-3263/82/1947-0088$01.25/0

Chart I

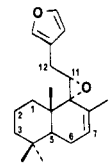


sharpening of the signal at δ 5.74. The small coupling constant between the signals at δ 2.59 and 5.40 and the presence of allylic coupling between the signals at δ 2.59 and 5.74 both suggested that the proton at C-4 was orthogonal to the diene system and that the two methyl groups were therefore cis to one another. Comparison of the ^{1}H NMR data with those of pallescensin G (**2**),[5] particularly the chemical shifts of the bis allylic methylene protons, required the oxygen of the furan ring to be adjacent to that methylene group.

Specimens of the nudibranch *Hypselodoris ghiselini* Bertsch, 1978[6] were collected by hand by using SCUBA at Isla Danzante, Gulf of California. Thirty animals were soaked in methanol for 20 days. The dichloromethane-soluble material from the methanol extract contained nakafuran 9 (**3**, 1.6 mg/animal),[7] ghiselinin (**4**, 0.2 mg/animal), the butenolide **5** (0.1 mg/animal) related to nakafuran 9 (**3**), and dendrolasin (**6**, 0.04 mg/animal).[8]

Ghiselinin (**4**), $[\alpha]_D$ +7.5° (*c* 0.27 MeOH), had the molecular formula $C_{20}H_{28}O_2$. The ^{1}H NMR spectrum (see Table I) was particularly informative since almost every signal could be observed and assigned by careful decoupling experiments. The signals at δ 7.31 (br s, 1 H), 7.23 (br s, 1 H), and 6.24 (br s, 1 H) were due to protons on a β-substituted furan. The methylene protons at δ 2.86 (dd, 1 H, J = 14, 8 Hz) and 2.55 (dd, 1 H, J = 14, 6 Hz) were coupled to an α-epoxy proton at δ 3.98 (dd, 1 H, J = 8, 6 Hz). The ^{13}C NMR signals at δ 70.0 and 58.4 provided additional evidence for the presence of an epoxide ring. The olefinic signal at δ 5.50 was broadened by allylic coupling to a vinyl methyl group at δ 1.87 and was vicinally coupled to a two-proton signal that was obscured by the vinyl methyl group. The methylene protons at δ 1.87 were also coupled to a bridgehead proton at δ 1.10 so that irradiation at δ 1.87 gave rise to sharp singlets at δ 5.50 and 1.10. The spectrum contained three methyl signals at δ 0.86 (s, 3 H), 0.89 (s, 3 H), and 0.92 (s, 3 H) and six signals assigned to protons on ring A. The signal at δ 0.69 (td, 1 H, J = 13, 13, 3 Hz), assigned to the 1α proton, is of particular interest since it must lie in the ring current of the 9α,11-epoxide ring. A NOEDS[9] experiment revealed a strong nuclear Overhauser enhancement of the signal at δ 3.98 on irradiation of the methyl signals at δ 1.87, allowing assignment of the geometry about the epoxide ring. The ^{13}C NMR spectrum was in good agreement with chemical shift values expected for a drimane ring system.[10]

Table I. Selected ^{1}H NMR Signals for Ghiselinin 4



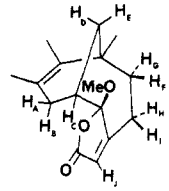
assignment	shift, δ	mult	J, Hz
1α	0.69	td	13, 13, 3
1β	1.74	dt	13, 3, 3
2α	1.45	m	
2β	1.52	m	
3α	1.11	td	13, 13, 3
3β	1.38	dt	13, 3, 3
5α	1.10	m[a]	
6α	~1.87	m[a]	
6β	~1.87	m[a]	
7	5.50	br s	
11	3.98	dd	8, 6
12	2.55	dd	14, 6
12	2.86	dd	14, 8

[a] Couplings are not first order.

The butenolide **5**, $[\alpha]_D$ +38° (*c* 0.47, MeOH), had the molecular formula $C_{16}H_{22}O_3$. The infrared band at 1770 cm^{-1}, together with the ^{1}H NMR signals at δ 3.19 (s, 3 H) and 5.62 (br s, 1 H), suggested the presence of a γ-methoxy α,β-unsaturated γ-lactone with additional substituents at the β- and γ-positions. Having previously encountered at γ-methoxy α,β-unsaturated γ-lactone accompanying the corresponding furan in a sponge,[11] we examined the possibility that the butenolide **5** might have the nakafuran 9 (**3**) carbon skeleton. The ^{1}H NMR spectrum of the butenolide **5**, assigned as in Table II, was in excellent accord with the proposed structure. Allylic coupling between the olefinic signal at δ 5.62 and the two-proton signal at δ 2.36 (H_H, H_I) and homoallylic coupling between the methyl signal(s) at δ 1.50 and the proton signal at δ 2.17 (H_A) fixed the position of three allylic protons. Decoupling experiments showed that the fourth allylic proton signal was at δ 1.54. The observation of W couplings between H_B (1.54 Hz) and H_E (1.98 Hz) and between H_D (1.62 Hz) and H_G (1.69 Hz) was particularly useful in assigning the remaining signals. The observation of an allylic proton signal at δ 1.54 (H_B) implied that the proton must lie in

(6) Bertsch, H. *Veliger* **1978**, *21*, 236.
(7) Schulte, G.; Scheuer, P. J.; McConnell, O. J. *Helv. Chim. Acta* **1980**, *63*, 2159.
(8) Vanderah, D. J.; Schmitz, F. J. *Lloydia* **1975**, *38*, 271 and references cited therein.
(9) Hall, L. D.; Saunders, J. K. W. *J. Am. Chem. Soc.* **1980**, *102*, 5703.
(10) Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden: London, 1976; p 44.
(11) Walker, R. P.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1098.

Table II. ^{1}H NMR Data for Methoxy Butenolide 5



assignment	shift, δ	J, Hz
H_A	2.17	18, 2
H_B	1.54	18, 2
H_C	2.46	6, 4, 2
H_D	1.62	13, 4, 2
H_E	1.98	13, 3, 2
H_F	1.79	14, 9, 8[a]
H_G	1.69	14, 5, 3, 2[a]
H_H	2.36	b
H_I	2.36	b
H_J	5.62	c
4 CH_3	1.04, 1.50, 1.50, 3.19	

[a] Couplings to H_H and H_I are not first order. [b] Multiplet. [c] Broad singlet.

the shielding cone of the trisubstituted olefinic bond and indicated the geometry shown.

Specimens of *Hypselodoris californiensis* (Bergh, 1879)[12] were collected by hand in the intertidal regions at Isla San Jose, Gulf of California. Forty animals were soaked in acetone for 1 month. The ether-soluble material from the acetone extract was chromatographed on silica gel to yield two known metabolites, dendrolasin (**6**, 1.5 mg/animal) and nakafuran 8 (**7**, 1.0 mg/animal). Both compounds were identified by direct comparison with authentic samples. Two individuals of *H. californiensis* collected at Point Loma, CA (−15 m), contained furodysinin (**8**, 2 mg/animal), euryfuran (**9**, 0.75 mg/animal), and pallescensin A (**10**, 0.6 mg/animal).

Specimens of *Hypselodoris porterae* (Cockerell, 1902)[13] (≡*Chromodoris porterae*) were collected at Point Loma, CA (−15 m). Six animals, found exclusively on *Dysidea amblia*, were stored in methanol at −20 °C for 1 year. The dichloromethane-soluble material from the methanol extract was chromatographed by LC on Partisil to yield furodysinin (**8**, 0.5 mg/animal) and euryfuran (**9**, 0.5 mg/animal).

Euryfuran (**9**) was found in *Eurispongia* sp., a sponge collected intertidally at Casa Cove, La Jolla, CA. The dichloromethane-soluble material from a methanol extract was chromatographed on silica. The resulting nonpolar material was purified by LC on Partisil to yield pallescensin A (**10**, 0.07% dry weight), identical in all respects with an authentic sample,[14] and euryfuran (**9**, 0.4% dry weight). Euryfuran (**9**), $[\alpha]_D$ −24° (*c* 0.5, $CHCl_3$), had the molecular formula $C_{15}H_{22}O$. The ^{1}H NMR spectrum ($CDCl_3$) contained signals at δ 7.07 (d, 1 H, *J* = 1.4 Hz) and 7.04 (dd, 1 H, *J* = 2.5, 1.4 Hz) (δ 6.95 and 6.93 in CCl_4 solution), assigned to two α-protons on a β,β′-disubstituted furan ring, at δ 2.76 (dd, 1 H, *J* = 16.5, 6.5 Hz) and 2.48 (m, 1 H, *J* = 16.5, 12, 7.5, 2.5 Hz) due to methylene protons adjacent to the furan ring, and at δ 1.20 (s, 3 H), 0.99 (s, 3 H), and 0.90 (s, 3 H) due to three methyl groups. These data were similar to those reported for a furan that had been synthesized on several occasions.[15] Comparison of our ^{1}H NMR spectrum with that of a synthetic sample[16] left no doubt that the materials were identical. Euryfuran (**9**) is relatively unstable and decomposed during the measurement of the ^{13}C NMR spectrum.

Both nakafuran 8 (**7**) and nakafuran 9 (**3**) had been previously isolated from the Hawaiian sponge *Dysidea fragilis* and were also found in two nudibranchs, *H. godeffroyana* and *Chromodoris maridadilus*, that were eating the sponge at the time of collection.[7] The isolation of nakafuran 9 (**3**) from *H. ghiselini* and nakafuran 8 (**7**) from *H. californiensis* suggests either selective storage of metabolites from the same sponge or selective feeding on two sponge species each containing only one of the metabolites. In previous studies on nudibranchs we have encountered both selective feeding and selective storage of metabolites. Since nakafuran 8 (**7**), nakafuran 9 (**3**), furodysinin (**8**), and pallescensin A (**10**) are all known to possess antifeedant properties, it seems reasonable to suggest that agassizin (**1**), ghiselinin (**4**), the butenolide **5**, dendrolasin (**6**), and euryfuran (**9**) might also repel predators.[17]

Experimental Section[18]

Collection, Extraction, and Chromatography. Seventy-one specimens of *Hypselodoris agassizi* were collected intertidally at Cruz de Juanacaxtle, Nayarit, Mexico, in Feb 1981 and stored in methanol (200 mL) for 10 days. The methanol was decanted and evaporated to yield an aqueous suspension that was extracted with dichloromethane. The dichloromethane extract was dried over sodium sulfate and the solvent evaporated to yield an oil. The oil was chromatographed by LC on a "Magnum-9" silica gel column with ether as the eluant to yield agassizin (**1**; 54 mg, 0.76 mg/animal) as the major product.

Eighty specimens of *Hypselodoris ghiselini* were collected by hand by using SCUBA (−2 to −5 m) at Isla Danzante, Gulf of California, in July 1980. The nudibranchs were stored in methanol (200 mL) for approximately 20 days after which time the solvent was evaporated and the resulting suspension extracted with dichloromethane. The dichloromethane extract was dried over sodium sulfate and the solvent evaporated to yield an oil. The oil was chromatographed by LC on a Partisil column with 1:1 ether–hexane as the eluant to yield nakafuran 9 (**3**; 125 mg, 1.6 mg/animal), ghiselinin (**4**; 16 mg, 0.2 mg/animal), dendrolasin (**6**; 3 mg, 0.04 mg/animal), and the methoxy butenolide **5** (8 mg, 0.1 mg/animal). The samples of nakafuran 9 (**3**) and dendrolasin (**6**) were identical in all respects with authentic samples.

Forty specimens of *Hypselodoris californiensis* were collected by hand from a lagoon on Isla San Jose, Gulf of California, in Apr 1977. The animals were soaked in acetone (250 mL) for several months; the acetone was then removed under reduced pressure and the aqueous residue extracted with ether (3 × 50 mL). The combined ether extracts were dried over sodium sulfate and the solvent evaporated to yield an oil (400 mg). The oil was chromatographed on silica gel to yield nakafuran 8 (**7**; 40 mg, 1.0 mg/animal) and dendrolasin (**6**; 60 mg, 1.5 mg/animal), both identical in all respects with authentic samples.

Two specimens of *Hypselodoris californiensis* were found on the sponge *Dysidea amblia* at Point Loma, San Diego, CA (−15 m), in Aug 1980. The animals were stored in methanol (50 mL) at −20 °C for 8 months. The methanol was removed, and the animals were steeped in methanol (50 mL) at 10 °C for 2 days. The combined extracts were evaporated, and the residue was partitioned between dichloromethane (4 × 50 mL) and water (50 mL). The dichloromethane extract was dried over sodium sulfate and the solvent evaporated to give an oil (97 mg). The oil was

(12) Bergh, L. S. R. *Proc. Acad. Nat. Sci. Philadelphia* **1879**, *10*, 71.
(13) Cockerell, T. D. A. *Nautilus* **1902**, *16*, 29 (≡*Chromodoris porterae*).
(14) Cimino, G.; De Stefano, S.; Guerriero, A.; Minale, L. *Tetrahedron Lett.* **1975**, 1417.
(15) Henderson, J. S.; McCrindle, R.; McMaster, D. *Can. J. Chem.* **1973**, *51*, 1346. Asakawa, Y.; Takemoto, T. *Experientia* **1979**, *35*, 1420. Akita, H.; Naito, T.; Oishi, T. *Chem. Lett.* **1979**, 1365.
(16) We thank Dr. Steven V. Ley and Michael Mahon for a ^{1}H NMR spectrum of a synthetic sample of the furan **9**.
(17) In general, the quantities of metabolites obtained from the nudibranchs were insufficient to perform quantitative antifreedant tests.
(18) For general procedures see: Walker, R. P.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1475.

dissolved in dichloromethane and passed through a silica gel plug. The nonpolar material was purified by LC on a Partisil column with hexane as the eluant to yield furodysinin (8; 4 mg, 0.6% dry weight) and a mixture of euryfuran (9; 1.5 mg, 0.2% dry weight) and pallescensin A (10; 1.2 mg, 0.2% dry weight). Furodysinin (8) and pallescensin A (10) were identified primarily by their ^{1}H NMR spectra and mass spectra.

Six specimens of *Hypselodoris porterae* were found on *Dysidea amblia* at Point Loma, San Diego, CA (-15 m), in June and Aug 1980. They were extracted in exactly the same manner as *H. californiensis*. The dichloromethane-soluble material was purified by LC on a Partisil column with hexane as the eluant to yield furodysinin (8; 3 mg, 4.9% dry weight) and euryfuran (9; 3 mg, 4.9% dry weight).

Euryspongia sp. was collected intertidally at Casa Cove, La Jolla, CA, on July 3, 1981. The sponge was steeped in methanol (2 L) at 5 °C for 2 days, the methanol was decanted, and the extraction was repeated for 2 days and finally for 2 weeks. The combined extracts were evaporated, and the aqueous residue (~200 mL) was extracted with dichloromethane (4 × 250 mL). The dichloromethane extracts were dried over sodium sulfate, and the solvent was evaporated to give an oil (1.54 g, 11.9% dry weight). The oil was chromatographed on silica gel, and the nonpolar fraction was purified by LC on a Partisil column with hexane as the eluant to yield euryfuran (9; 77 mg, 0.4% dry weight) and pallescensin A (10; 12 mg, 0.07% dry weight). Both materials are exceptionally volatile.

Agassizin (1): $[\alpha]_D$ -94° (*c* 1.2, MeOH); UV (MeOH) 225 nm (ϵ 9250) 266 (3470); ^{1}H NMR ($CDCl_3$) δ 0.87 (s, 3 H), 1.02 (d, 3 H, J = 7 Hz), 1.87 (m, 2 H), 2.4-2.7 (m, 3 H), 3.26 (d, 1 H, J = 15 Hz), 3.62 (d, 1 H, J = 15 Hz), 5.47 (d, 1 H, J = 9 Hz), 5.68 (d, 1 H, J = 5 Hz), 5.82 (m, 1 H), 6.19 (br s, 1 H), 7.16 (br s, 1 H); ^{1}H NMR (C_6D_6) δ 0.77 (s, 3 H), 0.82 (d, 3 H, J = 7 Hz), 1.63 (m, 2 H), 2.26 (m, 1 H), 2.45 (m, 1 H), 2.59 (m, 1 H, J = 7, 7, 7, 2.5 Hz), 3.27 (d, 1 H, J = 15 Hz), 3.47 (d, 1 H, J = 15 Hz), 5.40 (dd, 1 H, J = 9, 2.5 Hz), 5.51 (d, 1 H, J = 5 Hz), 5.74 (dd, 1 H, J = 9, 5 Hz), 5.99 (d, 1 H, J = 1.5 Hz), 7.06 (d, 1 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 149.3 (s), 142.5 (s), 139.4 (d), 132.1 (d), 123.1 (d), 120.4 (d), 117.6 (s), 112.2 (d), 38.5 (s), 34.3 (d), 34.2 (t), 32.7 (t), 19.7 (t), 17.1 (q), 14.1 (q); high-resolution mass measurement, obsd m/z 214.1356, $C_{15}H_{18}O$ requires 214.1358.

Ghiselinin (4): $[\alpha]_D$ +7.5° (*c* 0.27, MeOH); IR (CCl_4) 3010, 1545, 1245, 1200, 1100 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.69 (td, 1 H, J = 13, 13, 3 Hz), 0.86 (s, 3 H), 0.89 (s, 3 H), 0.92 (s, 3 H), 1.10 (m, 1 H), 1.11 (td, 1 H, J = 13, 13, 3 Hz), 1.38 (dt, 1 H, J = 13, 3, 3 Hz), 1.87 (br s, 3 H), 1.87 (m, 2 H), 2.55 (dd, 1 H, J = 14, 6 Hz), 2.86 (dd, 1 H, J = 14, 8 Hz), 3.86 (dd, 1 H, J = 8, 6 Hz), 5.50 (br s, 1 H), 6.24 (br s, 1 H), 7.23 (br s, 1 H), 7.31 (br s, 1 H); ^{13}C NMR (C_6D_6) 143.1, 140.4, 122.7, 111.7, 70.0, 58.4, 50.2, 42.4, 40.2, 38.1, 35.1, 33.5, 32.1, 25.2, 23.8, 22.4, 19.1, 14.6 (2 signals obscured by solvent); mass spectrum, m/z 300 (trace), 220 (M - C_5H_4O); high-resolution mass measurement, obsd m/z 300.2094, $C_{20}H_{28}O_2$ requires 300.2089.

Methoxy butenolide 5: $[\alpha]_D$ +38° (*c* 0.47, MeOH); IR (CCl_4) 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$) see Table II; high-resolution mass measurement, obsd. m/z 262.1569, $C_{16}H_{22}O_3$ requires 262.1569.

Euryfuran (9): $[\alpha]_D$ -24° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 0.99 (s, 3 H), 1.20 (s, 3 H), 2.48 (m, 1 H, J = 16.5, 12, 7.5, 2.5 Hz), 2.76 (dd, 1 H, J = 16.5, 6.5 Hz), 7.04 (dd, 1 H, J = 2.5, 1.4 Hz), 7.07 (d, 1 H, J = 1.4 Hz); mass spectrum, m/z, 218, 203 (base peak); high-resolution mass measurement, obsd m/z 218.1686, $C_{15}H_{22}O$ requires 218.1671.

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Asymmetric Synthesis of Five- and Six-Membered Lactones from Chiral Sulfoxides: Application to the Asymmetric Synthesis of Insect Pheromones, (*R*)-(+)-δ-*n*-Hexadecanolactone and (*R*)-(+)-γ-*n*-Dodecanolactone

Guy Solladié* and Firouz Matloubi-Moghadam

Laboratoire de Chimie Organique de l'Ecole Nationale Supérieure de Chimie, ERA du CNRS No. 687, Université Louis Pasteur, 67008 Strasbourg, France

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Two synthetic schemes, starting from the condensation of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate and dodecanal and pelargonaldehyde, were elaborated to prepare respectively (*R*)-(+)-δ-*n*-hexadecanolactone and (*R*)-(+)-γ-*n*-dodecanolactone. The observed enantiomeric excesses were higher than 80%. The absolute configuration of (+)-γ-*n*-dodecanolactone was assigned by circular dichroism.

Lactonic functionality is fairly common among natural products and in a variety of biologically active molecules. For this reason, the synthesis of chiral lactonic systems is still a challenging problem in a very active area of organic synthesis.

Until now the most general way to prepare optically active lactones has been the optical resolution of a chiral precursor as shown by Pirkle,[1] who proposed an elegant chromatographic resolution of hydroxy nitriles, or by Coke,[2] who used the classical crystallization process to resolve β-amino alcohols.

Chiral five-membered lactones were also prepared by microbial reduction of keto acids[15] and recently[3] from optically active α-acetylenic alcohols readily obtained by asymmetric reduction.

During the last few years, we developed an asymmetic aldol-type condensation from (*R*)-(+)-*tert*-butyl (*p*-tolyl-

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