3-(o-Fluorophenyl)-3,4-dihydroisocoumarin (5d). The crude product was chromatographed on Florisil and eluted with benzene, providing pure **5d** as a yellowish oil (78% yield) which solidified on standing: UV λ_{max} 247 and 279 nm; IR (nujol) 1730 cm^{-1}; mass spectrum (70 eV), m/z 242 (M^+), 197, 196, 183; NMR (acetone-d_6) 7.08 (5, 1, $J_{3',4'}$ = 8.2 Hz, $J_{3',F}$ = 10.3 Hz, $H_{3'}$), 7.22 (5, 1, $J_{5',6'}$ = 7.3 Hz, $H_{6'}$), 7.32 (d, 1, $J_{5,6}$ = 7.7 Hz, H_5), 7.35 (m, 1, $H_{4'}$), 7.44 (t, 1, $J_{4',5'}$ = 7.7 Hz, $H_{5'}$), 7.57–7.64 (m, 2, $H_{6,7}$), 8.01 ppm (d, 1, $J_{7,8}$ = 7.7 Hz, H_8) and Table II. Anal. Calcd for $C_{15}H_{11}FO_2$: C, 74.37; H, 4.58; O, 13.21. Found: C, 74.34; H, 4.59; O, 13.50.

3-(1-Naphthyl)-3,4-dihydroisocoumarin (5e). Pure **5e** was obtained as colorless needles (87% yield) by crystallization of the crude product from methanol: mp 155–156 °C; UV λ_{max} 233 and 270 nm; IR (nujol) 1710 cm^{-1}; mass spectrum (70 eV), m/z 272 (M^+), 229, 228, 215; NMR (acetone-d_6) 7.44 (d, 1 H), 7.50 (t, 1 H), 7.57 (m, 3 H), 7.66 (t, 1 H), 7.80 (d, 1 H), 7.95 (d, 1 H), 7.90 (dd, 1 H), 8.10 (d, 1 H), 8.26 ppm (d, 1 H) and Table II. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 83.03; H, 5.23.

3-(2-Naphthyl)-3,4-dihydroisocoumarin (5f). Crystallization of the crude product from methanol afforded pure **5f** as colorless plates (68% yield): mp 137–138 °C; UV λ_{max} 238 and 272 nm; IR (nujol) 1710 cm^{-1}; mass spectrum (70 eV), m/z 274 (M^+), 229, 228, 155; NMR spectrum (acetone-d_6) 7.47 (d, 1, $J_{5,6}$ = 7.7 Hz, H_5), 7.50 (t, 1, $J_{6,7} = J_{7,8}$ = 7.6 Hz, H_7), 7.57 (m, 2, $H_{6',7'}$), 7.67 (dt, 1, H_6), 7.74 (dd, 1, $J_{3',4'}$ = 8.5 Hz, $J_{1',3'}$ = 1.8 Hz, $H_{3'}$), 7.97 (m, 2, $H_{5',8'}$), 8.01 (d, 1, $H_{4'}$), 8.08 (d, 1, H_8), 8.09 ppm (d, 1, $H_{1'}$) and Table II. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 82.93; H, 5.10.

3-Methyl-3-(1-naphthyl)-3,4-dihydroisocoumarin (5g). Pure **5g** was obtained by column chromatography of the crude product on Florisil eluted with benzene as a yellowish oil (56% yield): UV λ_{max} 232 and 288 nm; IR (nujol) 1710 cm^{-1}; mass spectrum (70 eV), m/z 298 (M^+), 273 ($M^+ - CH_3$), 270 ($M^+ - CO$), 255, 245; NMR spectrum (acetone-d_6) 2.08 (s, 3, CH_3), 7.28 (m, 2 H), 7.35 (d, 1 H), 7.40 (d, 1 H), 7.52 (m, 4 H), 7.74 (d, 1 H), 7.85 (d, 1 H), 7.88 ppm (d, 1 H) and Table II. Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.60. Found: C, 83.11; H, 5.73.

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Registry No. **1**, 95217-40-6; **2**, 71885-44-4; **3**, 78482-09-4; **4a**, 100-52-7; **4b**, 104-87-0; **4c**, 123-11-5; **4d**, 446-52-6; **4e**, 66-77-3; **4f**, 66-99-9; **4g**, 941-98-0; **5a**, 2674-44-4; **5b**, 95217-41-7; **5c**, 37568-81-3; **5d**, 95217-42-8; **5e**, 83640-59-9; **5f**, 83640-60-2; **5g**, 95217-43-9; *o*-toluoyl chloride, 933-88-0; 2-amino-2-methyl-1-propanal, 124-68-5; *o*-toluic acid, 118-90-1.

New Halogenated Diterpenes from the Red Alga *Laurencia perforata*

Antonio G. González, José F. Ciccio, A. Patricio Rivera, and Julio D. Martin*

Institute of Organic Chemistry, University of La Laguna, and Instituto de Productos Naturales Orgánicos, CSIC, La Laguna, Tenerife, Spain

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The red alga *Laurencia perforata* contains a variety of secondary metabolites, some of which have previously been described from other sources. We report here the isolation and structural determination of three new diterpenoids. The bicarbocyclic diterpene **1** was shown to be related with the also isolated, and previously known, isoaplysin-20 (**2**). The structures of the two more polar diterpenes isolated from the extract were shown to be 3,15-dibromo-7,16-dihydroxyisopimar-9(11)-ene (**5**) and 3,15-dibromo-7,12,16-trihydroxyisopimar-9(11)-ene (**7**). Extensive ^1H NMR decoupling studies and some degradative experiments were used to establish the structures.

The present work is a part of our results on the chemical analysis carried out on different collections of the seaweed *Laurencia perforata* in the Canary and Madeira archipelagos. The diterpenoid components isolated were **1**, **2**, **5**, and **7**, all of which, with the exception of the dihydroxybrominated **2**, known as isoaplysin-20 and isolated from the mollusc *Aplysia kurodai*,[1] are presented for the first time in this work.

The least polar diterpenoid proved to be the bicarbocyclic compound **1**, which was isolated by successive quick chromatographies in silica gel using petroleum ether–ethyl acetate (1%) as eluent. Compound **1** proved identical with one obtained in quantitative yield by heterolytic fragmentation induced on the tosylated **4** by base treatment.[2]

Compound **5**, 3,15-dibromo-7,16-dihydroxyisopimar-9-(11)-ene, was isolated by chromatographic purification from the most polar fractions of the extract. The ^1H and ^{13}C NMR spectra are presented in Tables I and II, together with other derivatives and related compounds.

Treatment of **5** with acetic anhydride–pyridine gave the diacetate **6**, which was isolated as an oil. Compound **6** afforded in quantitative yield the epoxy derivative **9** by treatment with potassium carbonate in methanol, which was further oxidized with pyridinium chlorochromate to give the monoketone **10** as the sole reaction product. The oxidation of the epoxy alcohol **9** with chromic anhydride in acetone gave the enedione **11** (Chart I).

Reduction of **5** with Zn–AcOH afforded a mixture of products from which compound **12** was isolated as a major component, exhibiting an olefinic ABX system in its ^1H NMR spectrum.

The existence of three quaternary carbons, as well as the vinylic carbon, which can be observed in the ^{13}C NMR spectra of the natural product and derivatives (Table II) and the tricarbocyclic nature of same, suggested a pimarane skeleton (**i**) as a basis on which to support the methyl and ethyl appendages observed.[4]

(1) (a) Yamamura, S.; Tereda, Y. *Tetrahedron Lett.* **1977**, 2171. (b) Imamura, P. M.; Rüveda, E. A. *J. Org. Chem.* **1980**, *45*, 510. (c) Nishizawa, M.; Takenaka, H.; Hirotsu, K.; Higuchi, T.; Hayashi, Y. *J. Am. Chem. Soc.* **1984**, *106*, 4290.

(2) The possibility that **1** is an artefact cannot be excluded, despite the fact that it was isolated by extraction from the freshly gathered alga with organic solvents at room temperature. Isoaplysin-20 (**2**) submitted to the extraction conditions of the alga did not undergo transformation to compound **1**.

(3) We thank Prof. S. Yamamura for a small sample of isoaplysin-20 for comparative purposes.

(4) Devon, T. K.; Scott, A. I. "Handbook of Naturally Occurring Compound", Academic Press: New York, 1972; Vol. II.

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Table I. ^{1}H NMR Chemical Shifts[a] and Selected Multiplicities for 5, 6, 9, and 8

	compound 5		compound 6		compound 9		compound 8	
H	δ ($CDCl_3$)	m (J, Hz)	δ ($CDCl_3$)	m (J, Hz)	δ ($CDCl_3$)	m (J, Hz)	δ ($CDCl_3$)	m (J, Hz)
1 ax	1.72	ddd (13, 3, 3)	1.72	ddd (13, 3, 3)	1.70	ddd (13, 3, 3)	1.72	ddd (13, 3, 3)
1 eq	2.25	dd (~13, ~5, ~5)[b]	2.25				2.30	
2 ax	1.48	ddd (13, 13, 5)	1.52	ddd (13, 13, 5)	1.47	ddd (13, 13, 5)	1.53	ddd (13, 13, 6)
2 eq	2.00	ddd (13, 6, 2)	1.99	ddd (13, 5, 2)	1.78	v br dd (13, ~7)[b]	1.85	ddd (13, 6, 2)
3	3.93	dd (13, 6)[b]	3.95	dd (13, 6)	3.95	dd (13, 5)	3.94	dd (13, 6)
5	1.06	dd (14, ~4)[c]	1.12	dd (~13, ~4)[c]				
6 ax	1.60	dd (14, 13)	1.61	dd (13, 13)	1.61	dd (13, 12)		
6 eq	2.25		2.25					
7	3.20	ddd (13, 10, 5)	4.46	ddd (13, 10, 5)	3.21	ddd (15, 12, 5)	4.48	ddd (10, 10, 4)
8	2.20	br s	2.51	br s[d]	2.30	br s	2.59	br s
11	5.30	dt (5, 2, 2)	5.35	dt (5, 2, 2)	5.28	br s	5.39	dd (6, 1)
12 ax	1.82	ddd (18, 4, 2)	1.82	ddd (18, 4, 2)	2.01	ddd (13, 5,3)		
12 eq	2.42	br d (18)	2.46	br d (18)	2.23		5.59	dd (6, 2)
14 ax	1.37	dd (14, 11)	1.34	dd (14, 11)	1.20	dd (13, 10)		
14 eq	2.25		2.05		2.21			
15	4.25	dd (10, 3)	4.50	dd (10, 0.5)	2.49	dd (5, 3)	4.53	dd (10, 4)
16α	3.85	dd (12, 10)	4.26	dd (10, 0.5)	2.62	dd (5, 4)	4.05	dd (9, 4)
16β	3.93	dd (12, 3)[b]	4.28	dd (10, 10)	2.75	dd (4, 3)	4.24	dd (10, 9)
17	1.07	s	1.06	s	1.06	s	1.03	s
18	1.00	s	0.98	s	0.96	s	0.99	s
19	1.07	s	1.05	s	1.07	s	1.06	s
20	1.10	s	1.12	s	1.00	s	1.13	s
OAc			2.10	s			2.06	s
OAc			2.13	s			2.10	s
OAc							2.13	s

[a] 360 MHz. [b] Js obtained from decoupled or decoupling difference spectra. [c] Signal overlapped with CH_3 signal; Js determined by decoupling experiments. [d] Signal overlapped with H-12 eq.

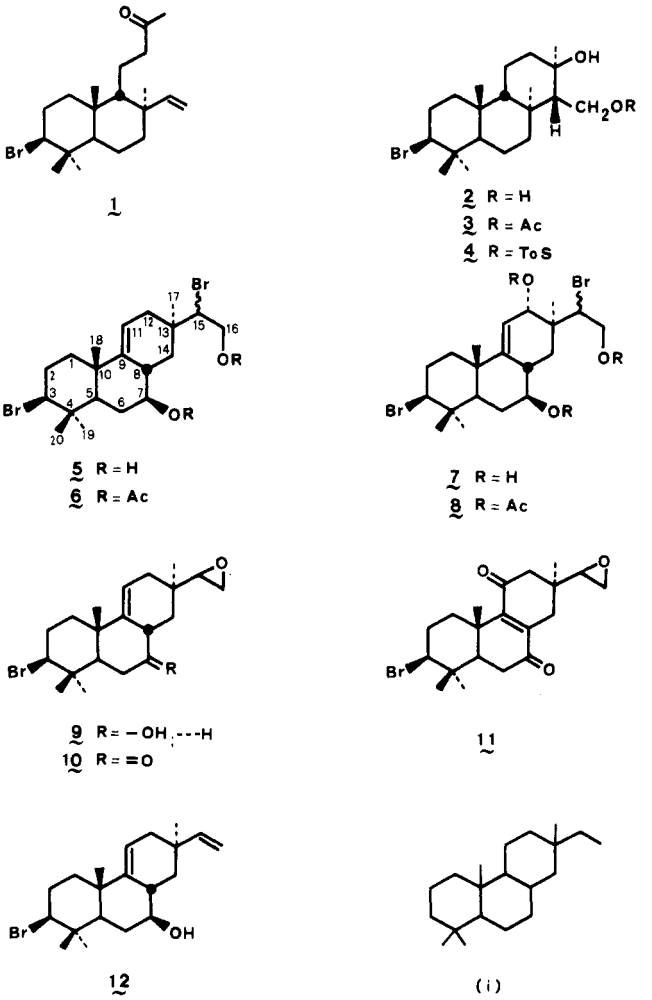
Compound **7**, 3,15-dibromo-7,12,16-trihydroxyisopimar-9(11)-ene, was isolated together with the most polar components of the extract of the alga. Difficulties arising with the purification suggested acetylation of these polar fractions. Chromatographic separation of the acetylated fractions yielded the triacetate **9** which crystallized from *n*-hexane/CH_2Cl_2. The ^{1}H NMR spectrum is presented in Table I, where the chemical shifts and multiplicities, assigned by extensive double resonance studies, are evaluated. The paucity of the amount obtained prevented attempts at chemical correlation.

The relative stereochemistry of the methyl and ethyl substituents for natural products **5** and **7** is proposed on the basis of the spectroscopical similarities to the diterpenoids recently isolated from the marine mollusc *Aplysia dactylomela*[5] and from the red alga *L. obtusa*,[6] which display a similar substitution pattern. Comparisons of the spectroscopic data, particularly of the chemical shift values in the ^{13}C NMR spectra, support the proposed structural correlation.

Experimental Section

Melting points were determined on a Kofler block and are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 237 and Model 681 spectrophotometers and ultraviolet spectra were recorded on a Perkin-Elmer Model 137 or a Unicam SP800. Optical rotations were determined for solutions in chloroform with a Perkin-Elmer Model 141 polarimeter. ^{1}H NMR were recorded on Perkin-Elmer R-32 (90 MHz) and Bruker Model WM 360 spectrometers, chemical shifts are reported relative to Me_4Si (δ 0) and coupling constants are given in hertz. ^{13}C NMR spectra were obtained on a Bruker Model 360 and the chemical shifts are reported relative to Me_4Si (δ 0). Low and high resolution mass spectra were obtained from a VG Micromass ZAB-2F. Column and dry-column chromatography were performed on silica gel G, all Merck products. The TLC plates were developed by spraying with 6 N sulfuric acid and heating. All solvents were purified by standard techniques. Anhydrous sodium sulfate was used for drying solutions.

Chart I



Collection, Extraction, and Chromatographic Separation. *Laurencia perforata* was collected at low tide in Madeira in May 1978, and in Corralejos, Fuerteventura (Canary Islands) in June,

(5) Schmitz, F. J.; Michaud, D. P.; Schmitz, P. G. *J. Am. Chem. Soc.* **1982**, *104*, 6415.
(6) Higgs, M. D.; Faulkner, D. J. *Phytochemistry* **1982**, *21*, 789.

Table II. ^{13}C NMR Chemical Shifts[a] for 5, 6, 9, and 8

no.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20	others
5	38.0	31.1	69.0	39.0	50.2	38.7	77.2	38.1	145.8	39.8	115.6	33.0	35.5	38.0	68.2	64.3	24.7	18.2	30.5	21.1	
6	38.3	31.0	68.1	38.9	49.9	36.0	78.6	29.1	145.1	39.8	116.1	38.3[b]	35.6	37.5[b]	59.1	65.9	24.1	18.2	30.4	21.3	170.6, 170.7, 20.9, 20.9
9	38.6	31.1	68.4	39.0	49.9	38.7	77.6	39.3	146.2	39.8	116.6	32.5	31.4	32.7	56.9	45.5	25.7	18.3	30.5	21.3	
8	38.0	30.8	67.4	39.0	49.3	35.9	78.1	28.9	151.7	39.9	115.2	72.1	39.2	32.3	56.9	65.8	18.3[b]	18.2[b]	30.3	21.2	170.3, 170.5, 170.6, 21.1, 20.8, 21.0

[a] The chemical shifts are reported in ppm with Me_4Si as internal reference. The solvent is $CDCl_3$. [b] The assignments marked with a † are interchangeable on the same line.

July, and September 1982, using SCUBA (−2 to −4 m). The alga was always air-dried and ground in a Wiley mill to a 1-mm particle size. As an example, the dried alga (840 g) was extracted in a Soxhlet apparatus for 24 h each with diethyl ether (2 L) and chloroform (2 L). The combined extracts were evaporated to leave a dark green viscous oil (28 g, 3.3% dry weight). The extracts obtained from the different collections were chromatographed on a column of silica gel (0.2–0.5 mm) mounted on petroleum ether, using petroleum ether and mixtures of increasing polarity obtained with petroleum ether and ethyl acetate as eluents; 500-mL fractions were collected.

Compound 1. The diterpenoid compound 1 was eluted by using mixtures of petroleum ether/AcEt(1%). It was obtained in pure form by successive chromatographies on silica gel (0.05–0.2 mm) using *n*-hexane as solvent. The compound proved non-crystalline: $[\alpha]_D$ −112° (*c* 0.18, $CHCl_3$); IR ν_{max}^{film} 3070, 1710, 1640, 1450, 1150, 905, 860 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.89 (6 H, s), 1.05 (3 H, s), 1.26 (3 H, s), 2.12 (3 H, s), 4.00 (1 H, dd, J = 12.7 Hz), 4.70–5.08 (2 H, m), 5.98 (1 H, dd, J = 17.9 Hz); MS, $C_{20}H_{33}BrO$, M^+ at m/e 370, 368; other fragments at m/e 356, 354, 312, 310; 289, 231, 189, 163, 149. Anal. Calcd. for $C_{20}H_{33}BrO$: C, 65.04; H, 8.94; Br, 21.68. Found: C, 65.08; H, 9.01; Br, 21.83.

Isoaplysin-20 (2). The fractions eluted in the general chromatography in petroleum ether/AcEt (25%) were submitted to successive chromatographies in silica gel 0.05–0.5 mm using mixtures of *n*-hexane–ether (3:7). The compound was purified by recrystallizations in methanol: mp 197–199 °C; IR ν_{max}^{KBr} 3500, 3390, 3250, 1500, 1380, 1140, 970, 910, 870 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.92 (3 H, s), 0.94 (3 H, s), 0.96 (3 H, s), 1.02 (3 H, s), 1.31 (3 H, s), 3.50 (2 H, bs, disappearing when stirred with D_2O), 3.70–4.05 (3 H, m); MS, $C_{20}H_{35}BrO_2$, $M^+ - H_2O$ at m/e 370, 368; other fragments at m/e 355, 353, 312, 310, 289, 230, 228, 203, 191, 189; ^{13}C NMR ($CDCl_3$) δ 18.7, 19.4, 20.5, 21.8, 21.9, 24.1, 31.2, 32.5, 36.0, 36.7, 37.2, 40.1, 40.6, 44.0, 47.6, 54.0, 61.7, 62.2, 69.0, 74.4. Calcd. for $C_{20}H_{35}BrO_2$: C, 62.02; H, 9.04; Br, 20.67. Found: C, 62.12; H, 9.08; Br, 21.00.

Isoaplysin-20 acetate (3) was prepared in pyridine at room temperature and crystallized from petroleum ether as needles: mp 137 °C; IR ν_{max}^{KBr} 3500, 1735, 1250 cm^{-1}; ^1H NMR δ 0.91 (3 H, s), 0.96 (3 H, s), 1.02 (6 H, s), 1.20 (3 H, s), 2.00 (3 H, s), 3.89 (1 H, dd, J = 11.7 Hz), 4.25 (1 H, d, J = Hz), 4.25 (1 H, d, J = 4 Hz); ^{13}C NMR 18.7, 19.2, 20.5, 21.2, 22.0, 21.7, 24.4, 31.2, 32.4, 36.1, 37.1, 37.2, 39.8, 40.1, 43.2, 47.6, 54.1, 60.5, 63.2, 69.0, 72.5, 170.8; MS, $C_{27}H_{37}O_3Br$, M^+ at m/e 430, 428, other fragments at m/e 397, 395, 370, 368, 353, 312, 310. When compared with an authentic sample of isoaplysin-20 monoacetate, the compound proved identical.[3]

Mono-*p*-toluenesulfonate of isoaplysin-20 (4) was prepared from the diol 2 in pyridine and tosyl chloride (1:1) for 6 days. The derivative was purified by chromatography on silica gel (0.05–0.2 mm) using petroleum ether/EtAc (1%) as eluent. The compound crystallized in petroleum ether: mp 110–112 °C; IR ν_{max}^{KBr} 3480, 1600, 1360, 1180, 950, 870 cm^{-1}; ^1H NMR δ 0.91 (3 H, s), 0.97 (6 H, s), 1.02 (3 H, s), 1.07 (3 H, s), 2.45 (3 H, s), 3.98 (1 H, dd, J = 9.8 Hz), 4.30 (2 H, d, J = 7 Hz), 7.48 (2 H, d, J = 9 Hz), 7.86 (2 H, d, J = 9 Hz). The compound 4 dissolved in a minimum amount of *t*-BuOH was treated with a solution of *t*-BuOK/*t*-BuOH at 0 °C for 2 h. The basic extract was extracted with ether and acidified (5% HCl). The concentrate of the organic solvent was purified by chromatography on silica gel, and elution with *n*-hexane afforded a compound that proved identical with the natural compound 1.

3,15-Dibromo-7,16-dihydroxyisopimar-9(11)-ene (5) was obtained from the fractions eluted with mixtures of petroleum ether–EtOAc (25%). The compound crystallized from *n*-hexane/CH_2Cl_2: stabilizing melting point at mp 106–107 °C; $[\alpha]_D$ +12.5° (*c* 0.4, $CHCl_3$); details of the ^1H and ^{13}C NMR spectra are presented in Tables I and II of the general discussion; IR ν_{max}^{KBr} 3350, 1510, 1380, 1061, 1045, 1025, 955 and 800 cm^{-1}; MS; $C_{20}H_{32}Br_2O_2$, M^+ at m/e 448, 446, 444; high-resolution mass measurements, obsd m/e 444.06556, $C_{20}H_{32}{}^{79}Br_2O$ requires 444.0657. Anal. Calcd. for $C_{20}H_{32}Br_2O_2$: C, 51.72; H, 6.90; Br, 34.48. Found: C, 51.77; H, 6.83; Br, 33.90.

3,15-Dibromo-7,16-diacetoxyisopimar-9(11)-ene (6) was prepared from **5** by dissolving in pyridine to which acetic anhydride was added, at room tempature and for 24 h. The reaction

mixture was poured onto ice and extracted with ether in the usual way, to yield a noncrystalline solid: $[\alpha]_D$ +6.7° (c 1.3, $CHCl_3$); Details of the ^1H and ^{13}C NMR spectra are given in Tables I and II; IR ν_{max}^{KBr} 1730, 1450, 1370, 1020, 950 and 910 cm^{-1}; MS, $C_{24}H_{36}Br_2O_4$, M^+ - 18 at m/e 490, 488, 486, further important peaks are found at m/e 423, 421, 381, 379, 337, 335, 241.

3-Bromo-7-hydroxy-15,16-epoxyisopimar-9(11)-ene (9). The diacetate 6 was dissolved in methanol–acetone and an excess of potassium carbonate was added. The suspension was stirred at room temperature for 2 h, and the reaction mixture was poured onto ice, neutralized with (5% HCl), and extracted with ether in the usual manner. The solid residue obtained by elimination of the solvent crystallized from n-hexane/methylene chloride: mp 166–167 °C; $[\alpha]_D$ -24° (c 0.64 $CHCl_3$); the ^1H and ^{13}C NMR spectra are described in Tables I and II; IR ν_{max}^{KBr} 3500, 1460, 1370, 1285, 1070, 920 and 875 cm^{-1}; MS, $C_{20}H_{31}BrO_2$, M^+ at m/e 384, 382, further important peaks are found at m/e 366, 364, 335, 333, 267, 253, 251. Anal. Calcd for $C_{20}H_{31}BrO_2$: C, 62.66; H, 8.09; Br, 20.89. Found: C, 62.70; H, 9.03; Br, 21.

3-Bromo-7-keto-15,16-epoxyisopimar-9(11)-ene (10). Pyridinium chlorochromate (431 mg, 2 mmol) was added with stirring to a solution of the epoxy alcohol 9 (386 mg, 1.0 mmol) dissolved in dry methylene chloride (15 mL). After 2 h dry ether (100 mL) was added and the supernatant was decanted from the blackish, gummy residue obtained. The ether-insoluble residue was washed three consecutive times with ether portions (10-mL each). The combined ether extracts were concentrated and chromatographed on a short column of silica gel with a mixture of n-hexane–ether (2:1) as eluent. A crystalline residue (294 mg) was obtained, which was homogeneous in TLC and crystallized from n-hexane: mp 158–160 °C; IR ν_{max}^{KBr} 3080, 1710, 1600, 1480, 1220, 1020, 860, 840 and 810 cm^{-1}; ^1H NMR (60 MHz) δ 0.93 (3 H, s), 0.98 (3 H, s), 1.03 (3 H, s), 1.05 (3 H, s), 2.60 (3 H, m), 3.98 (1 H, dd, J = 11.4 Hz), 5.40 (1 H, bs); MS, $C_{20}H_{29}BrO_2$, M^+ at m/e 382, 380, further important peaks are found at m/e 506, 504, 502, 446, 444, 442, 407, 405, 365, 363, 347, 345.

3-Bromo-7,11-diketo-15,16-epoxyisopimar-8-ene (11). Compound 10 (386 mg, 1.0 mmol) in acetone (35 mL) was treated at room temperature with Jones reagent (0.23 mol). After 15 min, the solution was poured into crushed ice and the product was extracted with ether. The ether solution was washed with water, aqueous solution of sodium bicarbonate, and water and dried over sodium sulfate, and the solvent was evaporated to give a bright yellow residue that was chromatographed on silica gel (0.05–0.2 mm). Elution with n-hexane afforded a yellow, noncrystalline solid that proved homogeneous on TLC (210 mg): UV λ_{max}^{EtOH} 271 nm (ε 18 200); IR ν_{max}^{KBr} 3040, 1670, 1600, 1250, 1220, 860, 830, 805 cm^{-1}; ^1H NMR (60 MHz) δ 0.95 (6 H, s), 1.08 (3 H, s), 1.10 (3 H, s), 2.60 (2 H, m), 3.94 (1 H, dd, J = 11.5 Hz); MS, $C_{20}H_{27}BrO_3$, M^+ at m/e 396, 394, other significant fragments appear at m/e 316, 314, 263, 249.

3-Bromo-7-hydroxyisopimar-9(11),5-diene (12). Powdered zinc (120 mg) and glacial acetic acid (10 mL) were added to compound 5 (80 mg) dissolved in tetrahydrofuran (25 mL). The mixture was stirred at room temperature for 6 h and later heated under reflux for half an hour under a stream of argon. The reaction mixture was poured onto ice and the product extracted in ether. The residue (53 mg) was filtered off in a short column of silica gel (0.05–0.2 mm) and the compound was eluted in n-hexane–ether (2:1). The compound was crystallized from n-hexane–methylene chloride: mp 110–112 °C; IR ν_{max}^{KBr} 3500, 3080, 1640, 1240, 1210, 920, 890, 860 cm^{-1}; ^1H NMR (90 MHz) 0.98 (3 H, s), 1.01 (3 H, s), 1.07 (6 H, s), 3.92 (1 H, dd, J = 12.8 Hz), 4.88 (1 H, d, J = 18 Hz), 4.88 (1 H, d, J = 13 Hz), 5.28 (1 H, t, J = 4 Hz), 5.84 (1 H, dd, J = 18.13 Hz); MS, $C_{20}H_{31}Br_2O$, M^+ at m/e 368, 366, other important fragments are found at m/e 350, 348, 300, 298, 288, 252, 198.

3,15-Dibromo-7,12,16-triacetoxyisopimar-9(11)-ene (7). The triol was obtained by elution from the general chromatography of the petroleum ether/AcEt (1:1). The combined fractions (2.48 g) were dissolved in pyridine (10 mL) and acetic anhydride (10 mL) was added, leaving the solution with shaking at room temperature overnight. The mixture was poured into ice and the soluble residue extracted in organic solvents in the usual way. The residue obtained (2.33 g) was submitted to further chromatography on silica gel (0.05–0.2 mm), using mixtures of n-hexane–ether as eluents. The triacetate 8 was separated from the n-hexane–ether (2:1) fractions as a crystalline solid. Recrystallization from n-hexane gave 8: mp 166–168 °C; $[\alpha]_D$ -159.5° (c 0.68, $CHCl_3$); IR ν_{max}^{KBr} 3040, 1735, 1730, 1620, 1250, 1230, 980, 860 cm^{-1}; details of the ^1H NMR and ^{13}C NMR spectra are given in Tables I and II; MS, $C_{26}H_{38}Br_2O_6$, M^+ at m/e 608, 606, 604, other important fragments at m/e 506, 504, 502, 446, 444, 442, 407, 405, 365, 363, 347, 345.

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Total Synthesis of (+)-Sparsomycin. Approaches Using Cysteine and Serine Inversion[1]

Dah-Ren Hwang, Paul Helquist,*[2] and Mohammed Saleh Shekhani

Department of Chemistry, State University of New York, Stony Brook, New York 11794-3400

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The antitumor antibiotic (+)-sparsomycin and its epimeric sulfoxide isomer have been synthesized in optically active form starting with either L-cysteine or L-serine. The former route involves a racemization and resolution sequence whereas the latter approach, which proceeds in much higher overall yield, involves a formal "inversion" of configuration of L-serine by selective manipulation of the functional groups surrounding the central asymmetric carbon atom.

Introduction

Sparsomycin 1, a metabolite of *Streptomyces sparsogenes*[3] and *S. cuspidosporus*,[4] has been the subject of intensive biomedical investigations due to its activity against several tumor systems[5,6] bacteria,[4,6] fungi,[7] and viruses.[8]

(1) (a) Taken from the Ph.D. Dissertations of M. S. Shekhani, State University of New York at Stony Brook, 1979, and D.-R. Hwang, State University of New York at Stony Brook, 1982. (b) For a preliminary account of a portion of this work see: Helquist, P.; Shekhani, M. S. *J. Am. Chem. Soc.* **1979**, *101*, 1057.

(2) Address correspondence to this author at the Department of Chemistry, University of Notre Dame, Notre Dame, IN 46556.

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