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MODIFIED LABDANE DITERPENES FROM *AMPHIACHYRIS AMOENA*[1]

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ABSTRACT.—Two new modified labdane diterpenes, amoenolide L [**1**] and amoenolide M [**2**] with a 3-(*p*-hydroxyphenyl)propionate ester unit, were isolated from the above-ground parts of *Amphiachyris amoena*. Their stereochemical structures were assigned by spectral methods including uv, ir, fabms, and one- and two-dimensional high field ^{1}H- and ^{13}C-nmr. Properties of their acetate derivatives are also recorded.

The presence of normal labdane diterpenes and related glycosides in the above-ground parts of *Amphiachyris amoena* (Shinners) Solbrig (Compositae), have been reported (1–3). Described herein are the isolation, structure elucidation by spectral means, and complete assignment of ^{1}H- and ^{13}C-nmr spectra for two new modified labdanes, amoenolides L [**1**] and M [**2**]. These compounds have a diterpenoid skeleton intermediate between a labdane and a clerodane, where Me-20 has migrated from C-10 of the labdane to C-9, but Me-18 remains at C-4 rather than being present at C-5 as in clerodanes. These compounds sometimes have been called chettaphanes (4) and more recently the name halimanes has been proposed (5); at least 12 are recorded in the literature (6–11).

RESULTS AND DISCUSSION

A major diterpene of *A. amoena*, amoenolide A [**3**], has the established ring system of (−)-labdane with the β-ethyl α,β-unsaturated γ-lactone side-chain (1). Amoenolide M [**2**] likewise showed spectral characteristics (^{1}H-, ^{13}C-nmr, ms, and ir) of the same side-chain unit, and the molecular formula $C_{29}H_{36}O_7$ as established by hrms. The additional nine carbons above those for a diterpene were shown to be from a 3-(*p*-hydroxyphenyl)propionyl ester unit (ms peak at *m/z* 166) for which a very intense carbonyl absorption at 1732 cm^{-1} was observed in the ir spectrum. A contribution to this absorption was also a ketonic carbonyl (^{13}C-nmr peak at 212.55 ppm). A bathochromic shift in the uv spectrum with dilute base supported the presence of a phenolic group. The lactonic and ester carbonyls were observed at 174.42 and 172.75 ppm, respectively. The nature of six of the seven oxygens was thus established and the seventh was identified as a hydroxyl from the preparation of diacetate **4**. The carbinyl proton was identified by its shift from 4.07 to 5.32 ppm upon acetylation. The ^{1}H- and ^{13}C-nmr spectra are found in Tables 1 and 2, respectively, with assignments made as described below.

Detailed 1D and 2D nmr studies were performed for **2**, but only those results pertinent for structure elucidation are given here. The ^{1}H-^{1}H COSY experiment (12) at 500 MHz revealed five coupled units: the ethyl α,β-unsaturated γ-lactone, the AA′BB′ aromatic system, two dimethylene groups, one of which was shown to be the methylenes of C-1 and C-2, and the other was the propionyl side-chain, and a seven-proton system consisting of C-6 to C-8 and including Me-17. The ethyl unit attached to the lactone group was identified by allylic (H-12 to H-14) and long-range coupling (H-12 to H-16). Inasmuch as from the molecular formula, amoenolide M [**2**] has twelve degrees of unsaturation, of which eight are associated with the two "side-chains," the central core

[1]Taken in part from the Ph.D. Dissertations of Dónal P. O'Mathúna and Michael J. Pcolinski as were accepted by the Graduate School, The Ohio State University, in August 1988 and June 1992, respectively.

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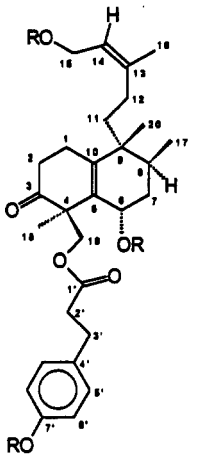
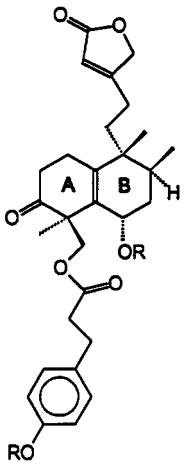
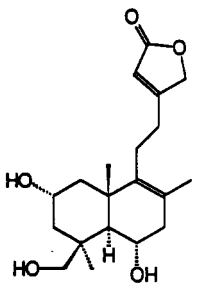


1 R=H
5 R=CH_3CO



2 R=H
4 R=CH_3CO



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must have four. A ketone (212.55 ppm) and an olefin (136.53 and 139.87 ppm) account for two of these, thus the core must be bicyclic, and apparently supportive of a labdane skeleton for the diterpene unit.

The proton-coupled units along with the two additional methyls and the oxymethylene could not be accommodated on a normal labdane skeleton, but were easily positioned if one ring (ring A) was of the labdane type and the other (ring B) was of the clerodane type. The proton-coupled unit (C-6 to C-17) containing the secondary methyl group in **2** was then located in ring B with the tetrasubstituted olefin forming the ring junction, and the dimethylene unit and the ketone placed in ring A. The two methyls and the oxymethylene could then be placed at C-4 and C-9, with specific designation determined by the long-range CH-correlation experiment (COLOC) at 6.35 Tesla (13). This, plus the one-bond CH-correlation results (14–16), gave the spectral assignments for the ^{13}C-nmr data listed in Table 2. The nmr experiments were performed in both $CDCl_3$ and pyridine-d_5 to clarify overlapping patterns. 1D and 2D nmr experiments with methyl 3-(*p*-hydroxyphenyl)propionate were conducted to aid in making assignments for that part of the structure.

The methyl singlet at 1.39 ppm (Me-18) in the COLOC study of **2** showed 2-bond coupling to the quaternary carbon at 51.42 ppm (C-4) and 3-bond couplings to the ketone carbonyl at 212.55 ppm (C-3), the oxymethylene carbon at 66.73 ppm (C-19), and the quaternary olefinic carbon at 136.53 ppm (C-5), thereby establishing the groups at C-3 through C-5. Also, the methylene proton (4.46 ppm) of the oxymethylene carbon at 66.73 ppm (C-19) showed 3-bond coupling to the ester carbonyl at 172.75 ppm, which was also 2-bond coupled to the methylene proton at 2.46 ppm (H-2′) of the propionyl unit. This required that the *p*-hydroxyphenylpropionyl group be positioned on the methylene at C-4. Long-range coupling from the aromatic protons at 6.73 and 6.92 ppm identified the benzylic carbon (C-3′) at 30.32 ppm, as well as the quaternary aromatic carbons (C-4′ and C-7′) at 132.09 and 155.07 ppm, respectively. The other singlet methyl group at 0.99 ppm (H_3-20) was 2-bond coupled to the aliphatic quaternary carbon at 42.36 ppm (C-9) and 3-bond coupled to the methylene carbon at 33.51 ppm (C-11), to the methine carbon at 31.22 ppm (C-8), and to the quaternary olefinic carbon at 139.87 ppm (C-10). Furthermore, the methyl doublet protons (0.90 ppm, H_3-17) showed 2-bond coupling to the methine carbon at 31.22 ppm (C-8) and 3-bond couplings to the quaternary carbon at 42.36 ppm and the methylene carbon at

TABLE 1. ^{1}H-Nmr Assignments for Compounds **1**, **2**, and **4**[a].

Proton	Compound				
	1	**1**[b]	**2**	**2**[b]	**4**
H-1	2.28α hm	2.43α m	2.12α hm	2.23α dddd (16.4,8.5,8.5,2.6)	2.22α m
	2.43β hm	2.40β m	2.50α dddd (16.4,6.1,6.1,1.0)	2.50β dddd (16.5,6.2,6.2,1.6)	2.52α hm
H-2	2.70α hm	2.80α ddd (13.9,7.0,7.0)	2.72α hm (ddd) (13.9,9.5,6.2)	2.82α hm (ddd) (14.0,9.6,6.0)	2.65α ddd (14.8,8.7,6.0)
	2.30β hm	2.47β m	2.27β hm	2.43β ddd (13.9,5.7,5.7)	2.29β hm
H-6	3.98 hm	4.44 hdd (7.7,7.7)	4.07 br dd (6.9,6.9)	4.48 br dd (7.6,7.6)	5.32 dd (6.8,6.8)
H-7	1.76α ddd (12.0,6.0,2.3)	2.00α ddd (12.0,6.0,2.2)	1.81α hm	2.01α hm (ddd) (12.2,6.1,2.2)	2.04α hm
	1.53β m	1.88β ddd (12.2,12.2,9.6)	1.58β hm	1.90β ddd (12.2,12.2,9.8)	1.55 β ddd (13.2,10.9,7.5)
H-8	1.64 ddq (11.8,6.9,2.3)	1.79 hddq (12,6.7,2)	1.57 hm	1.73 ddq (12.2,6.7,2.8)	1.67 hm
H-11	1.41 (2H) m	1.49 hm 1.47 hm	1.63 (2H) hm	1.60–1.70 (2H) hm	1.66 (2H) m
H-12	1.90 m	2.15 ddd (12.3,12.3,6.4)	2.15 hm	2.31 ddd (16.8,11.4,5.8)	2.16 m
	1.51 hm	1.78 hm	1.85 hm	2.01 hm	1.91 m
H-14	5.34 dd (6.7,6.7)	5.68 ddd (6.6,6.6,1.0)	5.71 m (5 pk) (1.4)	5.99 m (5 pk) (1.4)	5.77 m (5 pk) (1.4)
H-15	4.03 dd (12.0,7.7)	4.46 hm			
	3.99 dd (12.0,7.5)	4.43 hm			

TABLE 1. Continued.

Proton	Compound				
	1	**1**[b]	**2**	**2**[b]	**4**
H-16	1.68 (3H) s	1.70 (3H) s	4.47 (2H) d (1.4)	4.664 dd (18.3,1.8) 4.661 dd (17.2,1.5)	4.55 (2H) s
H-17	0.90 (3H) d (6.8)	0.86 (3H) d (6.7)	0.90 (3H) d (6.0)	0.90 (3H) d (6.8)	0.91 (3H) d (6.8)
H-18	1.37 (3H) s	1.64 (3H) s	1.39 (3H) s	1.68 (3H) s	1.27 (3H) s
H-19	4.52 d (10.7) 4.44 d (10.7)	5.12 d (10.3) 4.88 d (10.3)	4.51 d (10.7) 4.46 d (10.8)	5.09 d (10.3) 4.93 d (10.3)	4.51 d (11.0) 3.88 d (11.0)
H-20	0.92 (3H) s	0.89 (3H) s	0.99 (3H) s	0.99 (3H) s	1.04 (3H) s
H-2′	2.48 ddd (15.5, 7.2, 6.4) 2.36 ddd (15.5,7.8,7.8)	2.59 m 2.58 m	2.46 ddd (14.8,8.4,6.0) 2.31 hm ddd (15.2,8.0,8.0)	2.64 ddd (15.1,8.3,6.1) 2.56 ddd (15.8,7.9,7.9)	2.49 ddd (16.1,8.1,6.8) 2.41 ddd (16.1,7.8,7.8)
H-3′	2.80 ddd (14.2,7.8,7.8) 2.72 ddd (13.9,6.9,6.9)	2.92 ddd (14.0,7.8,7.8) 2.77 hm	2.80 ddd (14.1,8.1,8.1) 2.73 ddd (14.5,8.1,6.8)	2.97 ddd (14.0,7.9,7.9) 2.85 ddd (14.3,8.2,6.1)	2.92 ddd (14.7,7.4,7.4) 2.85 ddd (14.7,7.3,7.3)
H-5′, H-9′[c]	6.92 (2H) dm (8.4)	7.13 (2H) dm (8.6)	6.92 (2H) dm (8.4)	7.12 (2H) dm (8.5)	7.13 (2H) dm (8.5)
H-6′, H-8′[c]	6.73 (2H) dm	7.09 (2H) dm (8.6)	6.73 (2H) dm (8.4)	7.06 (2H) dm (8.5)	7.00 (2H) dm (8.5)

[a]Taken at 500 MHz in $CDCl_3$ with data-point resolution of 0.3 Hz and chemical shifts (δ) in ppm as referenced to TMS with residual solvent peaks taken as internal standard: $CHCl_3$ at 7.26 ppm and the upfield peak of pyridine-d_4 at 7.19 ppm. Stereochemical designations α and β following the chemical shift refer to the proton below and above the plane, respectively, of the illustrated drawing. Spin-coupled patterns are designated as follows: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broadened, and h=hidden or overlapped. The spin coupling (*J*) is given in parentheses in Hz; it refers to separation values solely for characterization and may not be the true *J* as in non-first-order patterns.

[b]In pyridine-d_5.

[c]The H-5′, H-6′, H-8′, and H-9′ protons form a typical AA′BB′ pattern.

TABLE 2. ^{13}C-Nmr Data for Compounds **1**, **2**, and **4**[a].

Carbon	Compound					
	1	Multiplicity	**1**[b]	**2**	**2**[b]	**4**[d]
1	24.70	t	24.60	25.09	25.06	24.58
2	36.97	t	37.74	36.64	36.96[c]	36.84
3	213.52	s	212.74	212.55	212.17	211.04
4	51.32	s	51.66	51.42	51.78	51.11
5	135.29	s	136.65	136.53	137.89	132.09[c]
6	69.13	d	68.79	69.11	68.86	70.46
7	38.41	t	38.85	38.19	38.79	33.16
8	31.05	d	31.33	31.22	31.47	30.94
9	42.48	s	42.53	42.36	42.46	42.04
10	141.13	s	140.05	139.87	139.14	144.09[c]
11	35.28	t	35.22	33.51	33.35	34.10
12	27.00	t	27.32	23.74	23.89	23.61
13	140.22	s	137.50	170.61	171.40	170.21
14	123.83	d	126.51	115.35	115.07	115.68
15	58.90	t	58.59	174.42 s	174.14 s	173.68 s
16	23.73[c]	q	23.58	73.15 t	73.26 t	72.94 t
17	16.06	q	16.02	16.01	16.06	16.07
18	23.75[c]	q	23.62	23.78	23.92	22.51
19	66.49	t	67.05	66.23	66.74	66.42
20	20.89	q	20.81	20.73	20.63	20.68
1′	173.27	s	172.82	172.75	172.68	172.05
2′	36.57	t	36.58	36.88	36.91[c]	36.17
3′	30.34	t	30.52	30.32	30.54	30.36
4′	132.22	s	131.32	132.09	131.35	138.19[c]
5′,9′	129.44	d	129.63	129.30	129.74	129.29
6′,8′	115.56	d	116.11	115.73	116.25	121.98
7′	154.82	s	157.14	155.07	157.46	149.47
*Me*CO						21.80 q
*Me*CO						21.28 q
Me*C*O						169.71 s
Me*C*O						169.66 s

[a]Taken at 67.9 MHz in $CDCl_3$ unless stated otherwise with multiplicities determined by SFORD. Multiplicities when different from those in the column are given after the chemical shift (δ) in ppm and are referenced to TMS with reference peak of solvent taken at 77.2 ppm (center) for $CDCl_3$. Abbreviations are: s=singlet, d=doublet, t=triplet, and q=quartet.

[b]In pyridine-d_5 with reference taken at 123.5 ppm (center) for the upfield carbon.

[c]May be interchanged within the same column.

[d]Multiplicities determined by a DEPT experiment at 125 MHz.

38.19 ppm (C-7). These data supported the structural units from C-7 to C-10. Finally, the COLOC experiment identified the quaternary carbons of the lactone group, since the olefinic proton at 5.71 ppm (H-14) showed 2-bond couplings to the carbons at 170.61 (C-13) and 174.42 ppm (C-15), as well as the methylene carbon at 73.15 ppm (C-16). Similarly, the methylene protons at 4.47 ppm (H-16) were 2-bond coupled to the carbon at 170.61 ppm and 3-bond coupled to the carbons at 174.42 (C-15) and 115.73 ppm (C-14). C-13 and C-16 were assigned by comparison with those reported for amoenolide A [**3**] as established from their T_1 relaxation times[4] (1).

[4]Previous results (1–3) showed that the downfield peak in the region 170–175 ppm was the lactone carbonyl and the upfield peak was the quaternary olefinic carbon for all of the lactone-containing terpenes from this plant.

Long-range CH-coupling located all but one proton-coupled dimethylene unit, which was placed at C-1 and C-2 by elimination, with the exact assignment established by homonuclear decoupling at 270 MHz. Irradiation of the carbinyl proton at 4.07 ppm (H-6) removed not only the large coupling to H_2-7, but also a small homoallylic coupling from the patterns of the methylene protons at 2.50 and 2.12 ppm, thereby locating the H-1 protons.

Specific stereochemical designations for the four asymmetric centers of amoenolide M [**2**] were made by nOe experiments using the difference method (17,18). Because the absolute stereochemistry of amoenolide A [**3**] was established (1), Me-20 as reference point was located on the β-face of the molecule in accordance with the biogenetic *syn* 1,2-migration. Irradiation of Me-20 (0.99 ppm) in $CDCl_3$ showed nOe enhancement of Me-17 (0.90 ppm) by 4%, of H-1β (2.50 ppm) by 5%, of H-7β (1.58 ppm) by 6%, and of H_2-12 (1.85 and 2.15 ppm) by 3%. This located Me-17 on the β-face and identified the β-side protons of the methylenes at C-1 and C-7. Irradiation of the carbinyl proton H-6 (4.07 ppm) showed relaxation to one of the oxymethylene protons at H-19 (4.46 ppm) by a 3% enhancement, to the two methylene protons of C-7 (1.58 and 1.81 ppm) by 4 and 6%, respectively, and to the aromatic proton H-5′ by 1%, but not to the Me-18. All of these interacting protons are likewise β-oriented. However, irradiation of Me-18 showed a 4% enhancement for one C-2 methylene (2.72 ppm), thus designating it to the α-position, as well as enhancing each H-19 (4.46 and 4.51 ppm) by 3%. Similar results were obtained in pyridine-d_5 as solvent but are not recorded here. The configurations of the four asymmetric centers were thus determined to be 4*R*, 6*S*, 8*S*, and 9*R*. Nmr assignments for amoenolide M diacetate [**4**] were made from 2D experiments (COSY and CH-correlation) and by comparison with the data for the parent alcohol **2**.

Amoenolide L [**1**], mp 154–155°, has the formula $C_{29}H_{40}O_6$ from fabms, with the MNa^+ peak at *m/z* 507. The hrms showed only the $M-H_2O$ ion. Thus, amoenolide L [**1**] has one less oxygen and four additional hydrogens when compared with amoenolide M [**2**], and the number of double-bond equivalents is reduced by two. The ^{1}H-nmr spectrum had patterns readily recognizable for the 3-(*p*-hydroxyphenyl)propionyl ester unit, the carbinyl pattern and the three methyl groups of amoenolide M [**2**]. Conspicuously absent was the α,β-unsaturated γ-lactone pattern (confirmed by the ^{13}C-nmr spectrum), and in its place was a methyl (1.68 ppm), a hydroxymethyl (4.03 and 3.99 ppm), and an olefin with one proton (5.34 ppm). Acetylation of amoenolide L [**1**] to a triacetate **4** confirmed the presence of the third hydroxyl. The four-carbon lactone unit is thus replaced by a hydroxybutylene for which the stereochemical disposition was established as follows.

The ^{1}H,^{1}H-COSY experiment revealed coupling between the olefinic methyl (1.68 ppm), the hydroxymethyl (4.03 and 3.99 ppm), and the olefinic proton (5.34 ppm). The ^{1}H-nmr spectrum showed the olefinic proton and the hydroxymethyl protons forming an ABX system with a J_{AX} of 7.5 Hz (3-bond coupled); while the olefinic methyl was a slightly broadened singlet ($J<1$ Hz, $\omega_{1/2}$ 3.3 Hz, whereas Me-18 and Me-20 had $\omega_{1/2}$ 1.4 and 2.0 Hz, respectively). Thus, the olefinic proton and the hydroxymethyl must be geminally disposed. Orientation of the olefinic methyl as cis (*Z*) or trans (*E*) to the olefinic proton was determined by nOe studies. Irradiation of the olefinic proton (H-14) at 5.34 ppm enhanced both the methyl (H-16) at 1.70 ppm and the hydroxymethyl protons (H-15) at 4.46 and 4.43 ppm by 6 and 3% (both), respectively. Irradiation of the methyl enhanced only the olefinic proton by 8%. This result also excluded the possibility of an isoprene irregular substitution about the double bond (i.e., the methyl and hydroxymethyl on the same olefinic carbon).

Amoenolide L [**1**] was subjected to extensive 2D nmr studies (COSY, CH-

correlation and COLOC), as well as nOe studies in both $CDCl_3$ and pyridine-d_5. The results demonstrated that amoenolides L [**1**] and M [**2**] have the same stereochemical structure except for the terminal four carbons of the side-chain. Details of these studies are not given here but the data are reported in Tables 1 and 2.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps are uncorrected and were taken on a Fisher-Johns hot stage apparatus. Nmr spectra were determined in the stated solvent with reference to TMS using the residual solvent peak ($CHCl_3$ taken as 7.26 ppm and pyridine-d_5 as 7.19 ppm for the middle peak of the upfield triplet for ^1H, and 77.2 ppm and 123.5 ppm for ^{13}C, respectively) on Bruker AM-500 and IBM AF-270 instruments equipped with Aspect 3000 data systems, with chemical shifts (δ) in ppm and coupling constants (J) in Hz. Uv spectra were taken on a Beckman UV-5260 spectrophotometer. Ir spectra were recorded on a Beckman 4320 or a Laser Precision RFX-40 (Fourier transfer) spectrophotometer on AgCI plates or in $CHCl_3$. Ei mass spectra were obtained using a Kratos MS-30 or a VG70-50 instrument by direct inlet at 70 eV or by fab. Optical rotations were measured on a Perkin-Elmer photoelectric polarimeter. Si gel, G, Si gel, and RP-8 material for tlc and cc were from E. Merck. Solvents were reagent grade and distilled before use.

The pulse programs for the nmr experiments were from the Bruker collection: COSY.AU for ^1H shift correlation, XHCORRD.AU for CH-correlation with homonuclear ^1H decoupling, COLOC.AU for long-range (2- to 4-bond) CH-correlation with polarization delay (D2=0.06 sec) set for 8 Hz coupling, and NOEMULT.AU for nOe difference.

Tlc plates (0.25 mm) were sprayed with *p*-anisaldehyde-H_2SO_4-95% EtOH (1:1:18) and heated at 110–120° until the desired color intensity developed.

PLANT MATERIAL.—As previously described by O'Mathúna and Doskotch (1).

CHROMATOGRAPHIC SEPARATION OF MeOH SOLUBLES.—A terpene-containing fraction (26.9 g from 91.5 g of crude EtOH extract from 4 kg of powdered above-ground plant material) from a Sephadex LH-20 column separation of the 90% MeOH partition fraction (1), showing a red zone on tlc analysis (other zones gave blue-purple shades), was chromatographed on 600 g of Si gel 60 (70–220 mesh). Elution with $CHCl_3$ and MeOH-$CHCl_3$ mixtures (0.5, 1, 2, 5, 10, 20, and 30%) and on collecting 15 ml effluent fractions gave one fraction of 4.6 g which on tlc with hexane-Me_2CO (3:2) showed four red spots. Chromatography on 100 g of Si gel 60 with hexane-Me_2CO (2, 5, 10, 20, and 30%) and collecting 5 ml effluent fractions, gave 1.6 g of residue from the 30% solvent mixture that showed two zones (red and blue) on tlc. This material was adsorbed on 2 g of Si gel, added to a 55-g column of Si gel 60 packed with EtOAc-PhMe (5%), and eluted with 5, 10, 20, and 33% solvent mixtures. The red zone material (250 mg) on RP-8 tlc plates with MeOH-H_2O (7:3) separated into two red zones. Chromatography on a RP-8 column (0.5 cm×24 cm) starting with MeOH-H_2O (20%) and incrementally increasing the MeOH to 50% eluted first amoenolide M [**2**] (33 mg) followed by amoenolide L [**1**] (18 mg), in a yield of 3.6×10^{-3}% and 2.0×10^{-3}%, respectively, from the crude extract. These compounds slowly decomposed on handling. Amoenolides L [**1**] and M [**2**] gave R_f values of 0.21 and 0.19 with MeOH-$CHCl_3$ (1:19) on Si gel tlc plates and 0.18 and 0.60 with MeOH-H_2O (4:6) on RP-8 plates, respectively.

Amoenolide L [**1**].—The column fraction in $CHCl_3$ was treated with 1 drop of H_2O and formed crystals of amoenolide L: mp 54–55°; $[\alpha]^{23.5}D$ −27° (c=0.5, MeOH); ir ($CHCl_3$) ν max 3400 (OH), 1730 (ester C=O), 1670 (C=C), 1450, 1380, 1220, and 830 (Ph); uv (MeOH) λ max (log ϵ) 267 (3.22), 220 (3.97), and 204 nm (end abs. 4.16); fabms, glycerol, *m/z* 507 (MNa^+, 5), 485 (MH^+, 0.4); eims *m/z* 466.2663 (M−H_2O, $C_{29}H_{38}O_5$ requires 466.2720, 0.2), 448 (M−$2H_2O$, 0.7), 366 (3), 299 (11), 219 (24), 201 (32), 189 (43), 159 (37), 120 (20), 107 (100), 91 (13); ^1H- and ^{13}C-nmr data are given in Tables 1 and 2, respectively.

Amoenolide L triacetate [**5**].—Acetylation of compound **1** (12 mg) with Ac_2O/pyridine (10 drops each) for 4 h, then evaporation at reduced pressure followed by partitioning between $CHCl_3$ and H_2O gave from the $CHCl_3$ layer on removal of solvent, triacetate **5** (14 mg) as a heavy oil: $[\alpha]^{23.5}D$ −8° (c=0.7, MeOH); ir ($CHCl_3$) ν max 1740 (ester C=O), 1370, 1220 (C-O of Ac), 1020 (C-O) cm^{-1}; fabms, dithiothreitol-dithioerythritol (5:1) (19), *m/z* 633.4576 (MNa^+, $C_{35}H_{46}O_9Na$ requires 633.3039, 4), 551 (MH−Ac, 1), 491 (MH−2Ac, 4); eims *m/z* 403.2530 (M−$C_{11}H_{11}O_4$, Ar ester cleavage, $C_{24}H_{35}O_5$ requires 403.2486, 0.7); ^1H nmr ($CDCl_3$, 270 MHz) AA'BB' pattern for H-6', H-8', and H-5', H-9' at 7.12 (dm, J=9 Hz) and 6.97 (dm, J=9 Hz), respectively, 5.32 (hm, H-6), 4.46 (d, J=6, Hz, H-15), 4.46 (d of ABq, J=11 Hz, H-19A), 3.90 (d of ABq, J=11 Hz, H-19B), 2.27 (s, Ac), 2.04 (s, Ac), 2.02 (s, Ac), 1.69 (d, J=1 Hz, Me-16), 1.25 (s, Me), 1.24 (s, Me), 0.92 (d, 7, Me-17).

Amoenolide M [**2**].—The isolated homogeneous heavy colorless oil gave: $[\alpha]^{23.5}D$ −1.8° (*c*=0.16, MeOH); ir (film) ν max 3405 (OH), 1708 (lactone C=O), 1732 (very intense and broad, ester C=O and C=O), 1635, 1614, 1575, 1300–1150 cm^{-1}; uv (MeOH) λ max 278 nm (log ε 2.42), (0.01 N NaOH) 296 nm (log ε 3.98); eims *m/z* 496.2454 (M^+, $C_{29}H_{36}O_7$ requires 496.2460, 1), 478 ($M-H_2O$, 1), 466 ($M-CH_2O$, 0.2), 331 ($M-HOC_6H_4(CH_2)_2CO_2$, 3), 330 ($M-HOC_6H_4(CH_2)_2CO_2H$, 7), 220 ($C_{14}H_{20}O_2$, 10), 166 ($HOC_6H_4(CH_2)_2CO_2H$, 22), 120 (C_8H_8O, 40), 111 ($CH_2CH_2C_4H_3O_2$, 11), 107 ($HOC_6H_4CH_2$, 100), 97 (4), ^1H- and ^{13}C-nmr data are given in Tables 1 and 2, respectively.

Amoenolide M diacetate [**4**].—Amoenolide M (10 mg) was treated with 1 ml each of Ac_2O and pyridine for 20 h, and then the mixture was handled as described for amoenolide L triacetate to give diacetate **4** as a clear heavy oil: $[\alpha]^{23.5}D$ +6.5° (*c*=0.21, MeOH); ir (film) ν max 1778, 1745, 1637, 1452, 1371, 1238, 852 cm^{-1}; fabms, 3-nitrobenzyl alcohol (20), *m/z* 603 (MNa^+, $C_{33}H_{40}O_9Na$, 21), 521 ($M-AcO$, 22), 107 ($HOC_6H_4CH_2$, 59), and 69 (100), ^1H- and ^{13}C-nmr data are given in Tables 1 and 2, respectively.

Methyl 3-(p-hydroxyphenyl)propionate.—The Fischer-Speier esterification of 3-(*p*-hydroxyphenyl)propionic acid (1.1 g, Aldrich) in MeOH (100 ml) with concentrated H_2SO_4 (5 ml) at reflux for 4 h gave the methyl ester (0.9 g) after workup by pouring into cold $CHCl_3$ (200 ml) and mixing with 300 ml (3×) of 5% aqueous $NaHCO_3$ and H_2O (2×), followed by evaporation of the $CDCl_3$ phase at reduced pressure. The nmr spectral assignments[5] were made from 1D (nOe) and 2D (CH-correlation and COLOC) experiments: ^1H nmr ($CDCl_3$) δ 2.61 (2H, t, *J*=7.7 Hz, H-2), 2.88 (2H, t, *J*=7.7 Hz, H-3), 7.03 (2H, dm, *J*=8.5 Hz, H-5 and H-9), 6.76 (2H, dm, *J*=8.5 Hz, H-6 and H-8), 6.50 ppm (OH); (pyridine-d_5) δ 2.65 (2H, t, *J*=7.6 Hz, H-2), 2.94 (2H, t, *J*=7.6 Hz, H-3), 7.20 (2H, dm, *J*=8.6 Hz, H-5 and H-9), 7.12 (2H, dm, *J*=8.6 Hz, H-6 and H-8); ^{13}C nmr ($CDCl_3$) δ 174.40 (s, C-1), 36.21 (t, C-2), 30.20 (t, C-3), 132.25 (s, C-4), 129.46 (d, C-5 and C-9), 115.55 (d, C-6 and C-8), 154.47 (s, C-7), 51.95 (s, MeO); (pyridine-d_5) δ 174.06 (s, C-1), 37.11 (t, C-2), 31.29 (t, C-3), 132.29 (s, C-4), 130.66 (d, C-5 and C-9), 117.10 (d, C-6 and C-8), 158.17 (s, C-7), 52.10 (MeO).

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[5]Numbering, for ease of comparison, is the same as in the terpenes for the ester side-chain with the prime removed.