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BIOACTIVE TERPENOIDS FROM CARIBBEAN MARINE ALGAE OF THE GENERA *PENICILLUS* AND *UDOTEA* (CHLOROPHYTA)

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Abstract—Chemical examinations of the Caribbean green algal genera *Penicillus* Lamarck and *Udotea* Lamouroux (Family Udoteaceae, Order Caulerpales, Phylum Chlorophyta) have resulted in the isolation of six new linear terpenoid compounds from two major species of *Penicillus*, and six terpenoid metabolites from three species of *Udotea*. These new metabolites possess a wide range of antibiotic activity, some produce inhibition of cell division in the fertilized urchin egg bioassay, and several show toxicity toward herbivorous damselfish.

Marine algae of the Order Caulerpales (Chlorophyta) are conspicuous members of tropical reef habitats, and it has been shown that marine algae of the families Udoteaceae and Caulerpaceae are of very low preference in the diets of tropical herbivores.[1,2] Several previous chemical investigations have provided evidence that algae from this group produce biologically-active terpenoid[3-12] and non-terpenoid aromatic[13] compounds, and we have proposed[3,4,11] that these metabolites function as the basis of a chemical defense adaptation. In this report we wish to describe the results of more detailed chemical studies of two genera, *Udotea* and *Penicillus* (Udoteaceae), which are common within the Caribbean Sea. Several metabolites have already been reported from the pantropical *Udotea* species.[4,5] This is the first report on the natural products chemistry of *Penicillus* species, which are unique algae endemic to the tropical Atlantic Ocean.

Collections of various *Penicillus* and *Udotea* species were made in at least two Caribbean locales, the Florida Keys and Bahama Islands, and the metabolites isolated from these algae are listed in Table 1 and illustrated in Fig. 1. In all, six new linear terpenoids were isolated from two major Caribbean *Penicillus* species and four new metabolites were isolated, along with two known compounds, from three distinct *Udotea* species. The majority of the new metabolites possess multiple enol-acetate functionalities (*E*, *E*-1,4-diacetoxybutadiene moieties), or closely related aldehyde functional groups, which appear to contribute strongly to their biological activities. In this regard, metabolites **1**–**9** have been shown to possess biological activities which include antimicrobial, cytotoxic and ichthyotoxic properties.

From *Penicillus capitatus*, a widely-distributed and abundant Caribbean species, we isolated the highly bioactive sesquiterpenoids **1** and **2** as 10 and 3% of the chloroform extracts, respectively. Curiously, both **1** and **2** were also isolated from the morphologically unrelated alga *Udotea cyathiformis* in approximately the same relative amounts. Triacetate **1** analyzed for $C_{21}H_{30}O_6$ by high-resolution mass spectrometry in combination with consideration of ^{13}C NMR spectral features. The presence of the *E*, *E*-1, 4-diacetoxybutadiene functional group was evident based upon UV absorption at λ_{max} 248 nm (ϵ = 13,000), ^1H NMR bands at δ 7.60 (d, J = 12 Hz), δ 7.18 (s) and δ 5.76 (d, J = 12 Hz), and ^{13}C NMR ester carbonyl bands at 167.7 and 167.0 ppm, which are characteristic features of this functional group (Tables 2 and 3).[3,4,6,8] In addition to the bis enol-acetate functionality, **1** was clearly recognized to possess an additional secondary acetate group as deduced by further ^1H and ^{13}C NMR resonances [^1H δ 2.08 (3H, s), δ 5.78 (1H, t, J = 7 Hz), ^{13}C: 169.9 (s), 69.4 (d) ppm]. Both the ^1H and ^{13}C NMR spectra of **1** also showed the presence of two additional trisubstituted double bonds, one of which was a typical gem-dimethyl terpenoid olefin and the other a Me

Table 1. Metabolites isolated from Caribbean *Penicillus* and *Udotea* species

Species	Collecting Site	Compounds
Penicillus capitatus Lamarck	Grand Bahama Island	**1**, **2**
Penicillus dumetosus (Lamouroux) Blainville	Florida Keys Gun Cay, Bahamas	**3**-**6**
Udotea conglutinata (Ellis and Solander) Lamouroux	Highborn Key, Bahamas	**7**
Udotea flabellum (Ellis and Solander) Lamouroux	Chub Cay, Bahamas	**8**, **9**
Udotea cyathiformis Decaisne	Grand Bahama Island	**1**, **2**

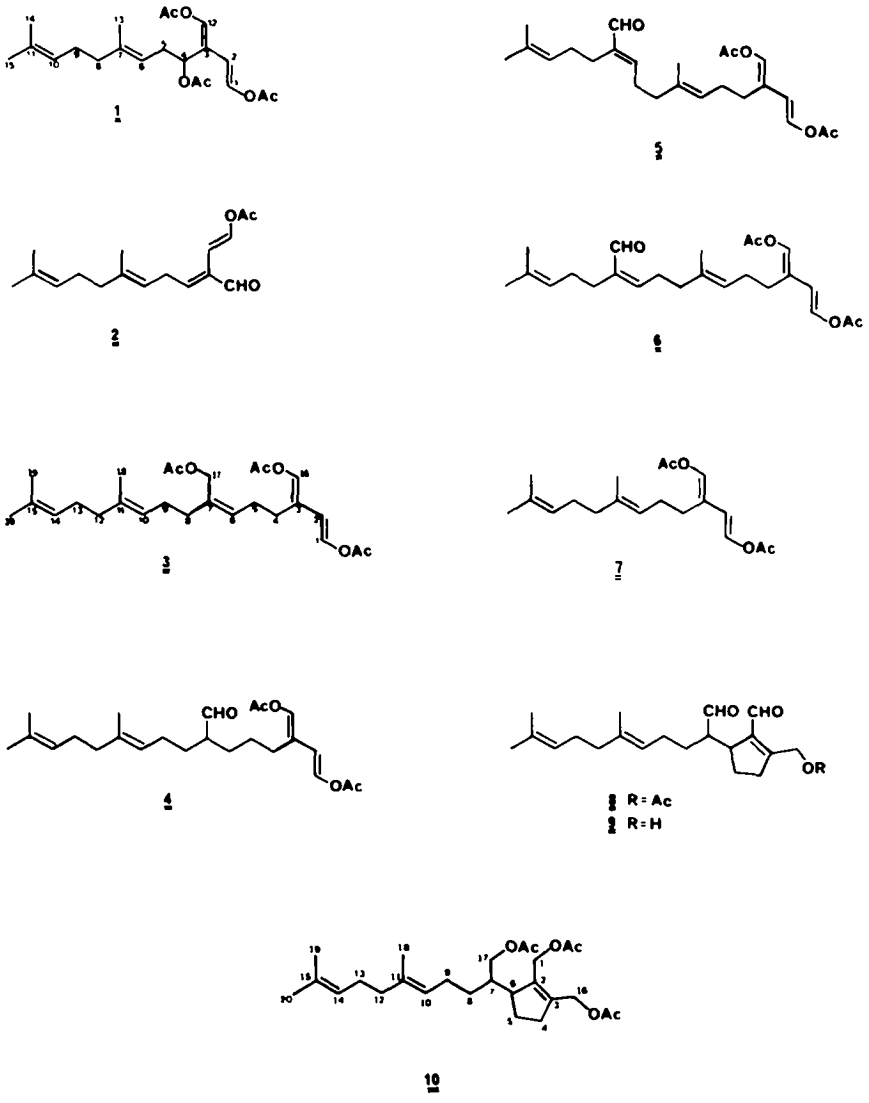

Fig. 1.

substituted *E* double bond, as deduced by its shielded ^{13}C methyl resonance of approximately 17 ppm (Table 3).[14]

The seven degrees of unsaturation in the molecular formula for **1** were accounted for by three acetate carbonyls and four olefinic bonds, hence **1** must be a linear sesquiterpenoid. The spectral features of **1** were almost identical to the known compounds caulerpenyne[7] and rhipocephalin.[3] This comparison, an intense mass spectral fragmentation yielding $C_{10}H_{15}$ (cleavage of the C4–C5 bond), and ^1H NMR decoupling studies allowed a confident assignment of all protons in **1** and therefore the structure to be fully assigned. Nuclear Overhauser enhancement, as measured using NOE difference spectroscopic techniques, of the C12 proton was observed upon irradiation of the C2 proton signal. This confirmed **1** to possess the *E*, *E*, transoid and co-planar arrangement of the diacetoxybutadiene group as already shown in caulerpenyne.[7] Attempts were not made to define the absolute stereochemistry at the asymmetric carbon C4.

The more minor metabolite, the aldehyde **2**, analyzed for $C_{17}H_{24}O_3$ again by a combination of high-resolution mass spectral and ^{13}C NMR methods. The presence of an α,β-unsaturated aldehyde in conjugation with an enol-acetate was indicated by UV absorption at 229 nm (ϵ = 2800) and by IR bands at 1705 and 1685 cm^{-1}. The ^1H NMR spectrum of **2** showed the presence of an aldehyde proton at δ 9.22 which readily correlated with a ^{13}C aldehyde doublet carbon observed at 193.3 ppm. The α,β-unsaturated aldehyde olefin geometry could be assigned as *E* from a comparison with prior model compounds (*E* ^1H NMR δ 9.2–9.4, Z δ 10.0–10.1).[15,16] Comparison of these latter spectral features with those of the related terpenoid onchidal[17] showed that they possessed identical functional groups.

Evaluation of the degree of unsaturation inherent in the molecular formula of **2**, and considering the total unsaturation recognized for olefin and CO bonds, showed that compound **2** was also acylic. As with **1**, a complete assignment of all protons in the molecule was accomplished by spin-decoupling.

Table 2. ^{1}H NMR values for *Udotea* and *Penicillus* metabolites

C#	1	2	3	4	5 (in $CDCl_3$)	6 (in $CDCl_3$)	8	9 (in $CDCl_3$)
1	7.6,d J=12 Hz	8.10,d J=12 Hz	7.40,d J=12 Hz	7.34,d J=12.5 Hz	7.43,d J=12.5 Hz	7.43,d J=12.5 Hz	10.07s	10.1s
2	5.76,d J=12 Hz	6.05,dd J=12,2 Hz	5.85,d J=12.5 Hz	5.85,d J=12.5 Hz	5.93,d J=12.5 Hz	5.94,d	--	
4	5.78,t J=7 Hz	6.28,t J=7 Hz	2.28 mult	[a]2.30 mult	[a]2.40 mult	[a]2.31 mult	2.56 mult	2.63,t J=7 Hz
5	2.45,ddd J=14,8,7 2.28,ddd J=14,8,7	3.10,t J=7 Hz	[c]2.00 mult	1.40 mult	[a]2.30 mult	[a]2.30 mult	1.45 mult	1.45 mult
6	5.00 mult	5.14,t J=7 Hz	[a]5.30,t J=7 Hz	1.40 mult	[b]5.21,t J=7 Hz	[b]5.38 mult	3.31 mult	3.43 mult
7	--	--	--	2.30 mult	--	--	2.85 mult	2.80 mult
8	1.99 mult	2.00 mult	[c]2.15 mult	[a]1.99 mult	[a]2.00 mult	[a]2.00 mult	1.70 mult	1.75 mult
9	1.99 mult	2.00 mult	[c]2.1[illegible]t	[a]2.10 mult	[a]2.10 mult	[a]2.10 mult	[a]1.99 mult	[a]2.05 mulg
10	5.00 mult	5.00 mult	[a]5.18,t J=7 Hz	[b]5.03,t J=6 Hz	6.43,t J=7 Hz	6.44,t J=8 Hz	5.00 mult	5.09 mult
12	7.18,s	9.22,d J=2 Hz	[c]2.20 mult	[a]2.00 mult	[a]2.20 mult	[a]2.10 mult	[a]1.99 mult	[a]2.05 mult
13	[a]1.63,3H,s	[a]1.74,3H,s	[c]2.20 mult	[a]2.00 mult	[a]2.00 mult	[a]2.00 mult	[a]1.85 mult	[a]1.75 mult
14	[a]1.62,3H,s	[a]1.74,3H,s	[a]5.02,t J=7 Hz	[b]5.13,t J=7 Hz	[b]5.10,t J=7 Hz	[b]5.08 mult	5.00 mult	5.09 mult
15	[a]1.59,3H,s	[a]1.60,3H,s	--	--	--	--	--	--
16	--	--	7.15,s	7.11,s	7.18,s	7.18,s	4.85,bs	4.63,bs
17	--	--	4.50,2H,s	9.47,d J=2.7 Hz	[c]1.67,3H,s	[c]1.66,3H,s	9.51,d J=1 Hz	9.63,d J=2 Hz
18	--	--	[b]1.63,3H,s	[c]1.67,3H,s	9.35,s	10.09,s	[b]1.65,3H,s	[b]1.67,3H,s
19	--	--	[b]1.57,3H,s	[c]1.57,3H,s	[c]1.67,3H,s	[c]1.63,3H,s	[b]1.58,3H,s	[b]1.60,3Hs,
20	--	--	[b]1.56,3H,s	[c]1.57,3H,s	[c]1.57,3H,s	[c]1.57,3H,s	[b]1.58,3H,s	[b]1.58,3H,s
OAc	2.20,3H,s 2.17,3H,s 2.08,3H,s	2.18,s,3H	2.17,3H,s 2.15,3H,s 2.03,3H,s	2.13,3H,s 2.11,3H,s	2.17,3H,s 2.15,3H,s	2.18,3H,s 2.16,3H,s	2.06,3H,s	

a,b,c - Values may be switched
d - All spectra were recorded in CCl_4 solution at 360 MHz relative to internal TMS unless otherwise noted.

These data and consideration of the characteristic ^{13}C NMR bands for linear terpenoids[14,15] allowed structure **2** to be fully assigned.

In contrast to the sesquiterpenoids (**1** and **2**) isolated from *P. capitatus*, another abundant *Penicillus* species, *P. dumetosus*, yielded exclusively diterpenoids. Collection of *P. dumetosus* from the Florida Keys yielded the triacetate **3**, while the aldehydes **4–6** were the exclusive diterpenoids isolated from a collection made in the Bahama Islands. The triacetate **3** (20% extract) analyzed for $C_{26}H_{38}O_6$ by interpretation of high-resolution mass and ^{13}C NMR spectral data. The presence of the *E,E*-diacetoxybutadiene functional group, and a primary acetate, were readily illustrated in the ^{1}H and ^{13}C NMR spectra of **3**. The 8° of unsaturation in **3** were accounted for by the three acetate carbonyls and five double bonds in the molecule, thus also indicating this compound to be a linear diterpenoid. The placement of the primary acetate at C17 was indicated by the mass spectral features of this metabolite. An intense fragment which analyzed for $C_{10}H_{15}$ was observed, which indicated cleavage of the bis-allylic C8–C9 bond. Hence, the primary acetate functionality was eliminated as a substituent of carbons 18–20. In addition, ^{13}C NMR bands for **3** were in close accord (for carbons 8–15 and 18–20) with model linear terpenoids.[15] As in earlier compounds, a strong NOE effect between protons at C2 and C16 was observed which confirmed the *E,E* stereochemistry and coplanarity of the bis-enol acetate functionality. The C6–C7 olefin stereochemistry was assigned as *Z* based upon the complete lack of NOE found between the protons on C6 and C17 when either were irradiated.

The aldehyde **4** analyzed for $C_{24}H_{36}O_5$ and again possesed the bis-enol acetate constellation. IR absorptions at 1750 and 1730 cm^{-1} supported the presence of acetate esters and a saturated aldehyde group.

Table 3. ^{13}C-NMR values for major metabolites (values recorded in $CDCl_3$)*

C#	1	2	3	4	8	9
1	[f]136.8d	141.2d	[a]135.5d	[a]135.9d	187.7d	189.0d
2	[b]109.3d	104.9d	113.1d	113.3d	140.5s	139.0s
3	119.1s	128.2s	120.8s	121.3s	158.8s	165.0s
4	69.4d	154.4d	[d]26.8t	[d]29.9t	35.2t	35.0t
5	31.5t	29.7t	[d]26.5t	[d]29.5t	[a]24.7t	[a]24.8t
6	[b]117.9d	118.7d	[c]130.3d	[d]29.1t	45.3d	45.6d
7	[c]138.7s	[a]139.3s	[b]133.5s	51.2d	52.4d	52.8d
8	39.6t	39.5t	35.2t	[d]25.4t	[a]27.2t	[a]27.3t
9	26.6t	26.5t	[d]26.2t	[d]28.5t	[a]26.6t	[a]26.7t
10	123.9d	123.8d	[c]123.9d	[b]123.8d	[b]124.2d	[b]124.2d
11	[c]131.5s	[a]134.9s	[b]135.1s	[c]135.5s	[c]136.3s	[c]136.4s
12	[a]133.9d	193.3d	39.5t	39.7t	39.7t	39.7t
13	16.3q	16.4q	[d]25.2t	[d]26.8t	[a]26.0t	[a]26.2t
14	17.6q	17.7q	[c]123.7d	[b]123.7d	[b]123.2d	[b]123.3d
15	25.6q	25.7q	[b]131.2s	[c]131.5s	[c]131.3s	[c]131.4s
16	--	--	[c]134.3d	[a]134.8d	59.6t	59.5t
17	--	--	61.7t	213.4d	204.6d	205.4d
18	--	--	15.8q	15.7q	16.1q	16.1q
19	--	--	17.5q	17.5q	17.1q	17.7q
20	--	--	25.5q	25.6q	25.7q	25.7q
Acetates	169.9s	167.5s	170.5s	167.1s	170.3s	
	167.7s	20.7q	167.3s	166.7s	20.7q	
	167.0s		166.9s	20.0q		
	20.7q		20.6q	20.0q		
	20.7q		20.6q	*in d_6Br		
	21.0q		20.3q			

The proton NMR spectrum of **4** showed the aldehyde proton as a doublet ($J = 2.7$ Hz) at δ 9.47 confirming the presence of an adjacent proton. As in the triacetate **3**, the mass spectral features of **4** were useful in positioning the aldehyde group. Here again intense cleavage of a $C_{10}H_{15}$ fragment indicated the aldehyde to be at C17. No attempts were made to assess the absolute stereochemistry at C7.

Also present in the Bahamas collections, but as minor metabolites, were the isomeric aldehydes **5** and **6**. Both compounds analyzed for $C_{24}H_{34}O_5$ by the aforementioned methods, and were recognized as isomers of the previously reported diterpenoid udoteal.[4] Comparison of the proton NMR features of **5** and **6** with those of udoteal showed the compounds to be almost identical. It was clear that both possessed α,β-unsaturated aldehyde groups as in udoteal, but positioning the aldehyde presented problems. Fortunately, mass spectral data yielded convincing evidence to position the aldehyde at C18. Intense fragmentation of the C8–C9 bond was again evident yielding two fragments which analyzed for $C_{10}H_{16}O$ and $C_{12}H_{15}O_2$, respectively. The former fragment was assigned as bearing the unsaturated aldehyde group while the latter was assigned as the bis-enol acetate bearing portion of the molecule with additional loss of acetic acid.

The relationship of **5** and **6** as geometrical isomers of the α,β-unsaturated aldehyde double bond was readily illustrated by their ^{1}H NMR features. Aldehyde **5** was assigned the *E* configuration based upon the recorded aldehyde chemical shift of δ 9.35. The aldehyde proton shift for **6** at δ 10.09, conversely supported its assignment in the *Z* configuration.[16] Support for these assignments was also obtained by NOE measurements. Irradiation in **5** of the C18 aldehyde proton produced marked enhancement of the olefin proton at C10. This effect was absent in the isomeric aldehyde **6**.

The algal genus *Udotea* has now been recognized to produce both sesquiterpenoids and diterpenoids (udoteal[4] and udoteatrial[5]). As mentioned earlier, metabolites **1** and **2** were isolated from *U. cyathiformis* as well as *P. capitatus*. We have also subsequently isolated the known sesquiterpenoid flexilin (**7**) from *U. conglutinata* collected in the

Bahama Islands. The spectral features we recorded for compound **7** were identical to those reported for this compound.[8]

More comprehensive studies of the most common Caribbean *Udotea* specie, *U. flabellum*, have also been completed. In addition to udoteal,[4] we have isolated the monocyclic diterpenoids **8** and **9** (5 and 8% of the extract) from a variety of *U. flabellum* with narrowly lacerate blades. The acetate **8** was found by ^{13}C NMR to possess the molecular formula $C_{22}H_{32}O_4$ (Table 3). These latter spectral features, in conjunction with IR absorption at 1735, 1715 and 1670 cm^{-1}, showed the presence of two aldehydes, one saturated and one α,β-unsaturated, and one primary acetate ester. ^{13}C NMR bands were also present for two additional trisubstituted olefins at shifts characteristic of linear terpenoids. As in several previous examples, mass spectral fragmentation of **8** yielded an intense $C_{10}H_{15}$ fragment resulting from cleavage of the allylic C8–C9 bond. Hence, based upon these data, the ring and all oxygenation must involve C1–C8 and C16, C17.

The ^{13}C NMR spectrum of **8** further showed the presence of a polarized tetrasubstituted double bond [δ 158.8 (s) and 140.5 (s)] which was assigned in conjugation with one of the aldehyde groups. Through ^1H decoupling and NOE studies, all protons in acetate **8** were subsequently assigned. The primary acetate was positioned at C16 since these protons were clearly at an allylic chemical shift in the ^1H NMR spectrum (δ 4.63). Strong NOE was also observed between the two aldehyde protons thus placing them within NOE proximity ($\sim$ 3.0Å).

Sodium borohydride reduction of **8**, followed by immediate acetylation (Ac_2O/py) yielded the tris-primary acetate **10**. The ^1H NMR spectrum of **10** clearly showed the newly-formed C1 and C17 methylene protons as characteristic AB and ABM patterns at the expected allylic and non-allylic chemical shifts (experimental). In addition, derivative **10** yielded much more reliable HRMS data to support the molecular formula previously assumed for acetate **8**. Although the structure of **8** was fully defined, no attempts were made to determine the relative nor absolute stereochemistries of the asymmetric centers at C6 and C7.

The polar monocyclic diterpenoid isolated, **9**, was assigned as the corresponding alcohol derivative based upon its facile acetylation to yield acetate **8**. The spectral features for **9** were also in close accord with those of **8** except for the C16 protons which were shifted to higher field, as would be expected. Comparison of the rotations of synthetic **8** produced from **9** ($[\alpha]_D$ – 28°) showed they most likely possessed the identical absolute stereochemistries at the two asymmetric centers. The discrepancy in these values may, however, indicate a degree of racemization at C7 in the synthetic conversion of **9** to **8**.

The new metabolites described here show significant biological activities against several pathogenic marine and terrestrial microorganisms and potential macroscopic predators. Compounds **1**, **3**, **4**, and **7** were active against *Staphylococcus aureus* and **1** and **3** were active against *Bacillus subtilis*. Compounds **1**, **2**, **8**, and **9** were active against the marine bacterium *Serratia marinorubra*. Other marine bacteria, including *Vibrio splendida*, *V. harveyi*, *V. leiognathi* were inhibited by **1–4**, **8** and **9**. Our own isolates of marine bacteria from the surfaces of Caribbean algae were inhibited by compounds **2–4**, **7** and **9**. Marine fungi were also inhibited. Compound **2** was active against *Leptosphaeria* sp., *Lulworthia* sp., *Alternaria* sp., compound **4** was active against *Dreschleria haloides*, *Lulworthia* sp., and compounds **7** and **9** selectively inhibited *Dreschleria haloides* and *Lulworthia* sp., respectively.

Several of these compounds also inhibited cell division in fertilized sea urchin eggs. Compounds **1**, **2**, **4**, **7**, **8**, and **9** all inhibited normal cell division in this recently re-established assay.[18,19] Compounds **1**, **2**, **8**, and **9** were also toxic to herbivorous damselfish causing death within 1 hr.[20]

EXPERIMENTAL

General. IR spectra were recorded on a Perkin–Elmer model 137 spectrophotometer and UV spectra were obtained in MeOH on a Beckman Mk IV instrument. Proton NMR spectra were recorded on a 360 MHz Nicolet–Oxford Magnetics FT spectrometer and ^{13}C NMR spectra were recorded at 50 MHz on a Nicolet NT-200 instrument. High resolution mass spectra were obtained through the Mass Spectrometry Resource Center, School of Pharmacy, UC San Francisco. Algae were collected in various habitats in the Florida Keys (July 1980) and in the Bahama Islands (July–September 1981, July 1982). The freshly collected plants were ground by hand and immediately extracted twice with CH_2Cl_2. The extracts were condensed to dark residues and immediately chromatographed on silica gel with CH_2Cl_2–MeOH solvent mixtures to produce five major fractions representing the complete solvent polarity range. If either frozen algae or crude extracts were allowed to stand or shipped for subsequent analysis, significant decomposition was noted in almost all cases. Final purification of metabolites was effected by preliminary Florisil chromatography (for removal of pigments) followed by preparative silica HPLC with EtOAc/isooctane solvent mixtures.

Triacetate **1**. Collections of *Penicillus capitatus* and *Udotea cyathiformis*, voucher numbers BA-26 and BA-21, Bahama Islands, September 1981, both yielded **1** as a colorless oil (10% of the organic extract) after silica gel HPLC (20% EtOAc/isooctane). Triacetate **1** showed $[\alpha]_D^{25} = 18.0°$ (c = 1.2, $CHCl_3$); IR ($CHCl_3$) 2910, 1700, 1640, 1340, 1200, 1080 cm^{-1}, UV (MeOH) λ_{max} 248, ϵ = 13,000, HRMS M$^+$-C_2H_4O Found: 334.1772, Calc: 334.1781.

Aldehyde **2**. The above collections of *P. capitatus* and *U. cyathiformis* yielded **2** as a minor metabolite, 3% organic extract, after silica gel HPLC (20% EtOAc/isooctane). Compound **2** showed IR ($CHCl_3$) 2925, 2860, 1705, 1685, 1210 cm^{-1}, UV (MeOH) λ_{max} 229 nm, ϵ = 2800, and HRMS Found: 233.1522 for M$^+$ – C_2H_3O, Calc: 233.1541.

Diterpene triacetate **3**. Compound **3** was isolated as the major component of *P. dumetosus* collected in the Florida Keys and the Bahamas Islands, voucher number BS 121, July 1982. Si gel HPLC (15% EtOAc/isooctane) yielded **3** as 20% of the organic extract. Compound **3** showed the following spectral features: $[\alpha]_D^{25} = +1.7°$ (c = 1.3, $CHCl_3$); IR ($CHCl_3$) 3100, 2930, 1750, 1730 broad, 1220, 1080 cm^{-1}, UV (MeOH) λ_{max} 254, ϵ = 11,000; HRMS Found: 386.2435 for M$^+$-$C_2H_4O_2$ (acetic acid) Calc: 386.2457.

Dihydroudoteal **4**. A collection of *P. dumetosus*, voucher number BS3, Bahama Islands, July 1982, yielded **4** as the major metabolite after purification by Si gel HPLC (20% EtOAc/isooctane). Compound **4** showed the following spectral features: $[\alpha]_D^{25} = 0.7°$ (c = 1.3, $CHCl_3$); IR ($CHCl_3$) 2960, 1750, 1730, 1375, 1090 cm^{-1}, UV (MeOH) λ_{max} 250, ϵ = 5,800; HRMS Found 360.2293 for M$^+$-C_2H_4O; HRMS 344.2343 for M$^+$-$C_2H_4O_2$ Calc: 344.2351.

Diterpenoid **5**. *P. dumetosus*, voucher number BS3, yielded **5** as a minor metabolite after Si gel HPLC purification (20% EtOAc/isooctane). Compound **5** showed the following spec-

tral features: IR ($CHCl_3$): 1750, 1680, 1360, 1080 cm^{-1}; UV (MeOH) λ_{max} 243, ϵ = 7300; HRMS Found 342.2199 for $C_{22}H_{30}O_3$ (M^+-HOAc); Calc: 342.2195.

Diterpenoid **6**. *P. dumetosus*, voucher number BS3, yielded **6** as a minor metabolite after Si gel HPLC purification (20% EtOAc/isooctane). UV (MeOH) λ_{max} 246, ϵ = 9700.

Sesquiterpenoid **7**. A Bahama Islands collection (voucher number BS110) of *Udotea conglutinata* (July, 1982) yielded **7** as the major metabolite (20% organic extract) after purification by Si gel HPLC (20% EtOAc/isooctane). Compound **7** was identified as flexilin by comparison with published spectral features.[8]

Diterpenoid **8**. *Udotea flabellum* (voucher number BA86) with narrowly lacerate blades, Bahama Islands, September, 1981, yielded acetate **8** as 5% of the organic extract. Compound **8** was purified by Si gel HPLC (35% EtOAc/isooctane), and showed the following spectral features: $[\alpha]_D^{25} = -28°$ (c = 1.5, $CHCl_3$); UV (MeOH) λ_{max} 248 nm, ϵ = 6500; IR ($CHCl_3$) 2940, 1735, 1715, 1670, 1450, 1370, 1220 cm^{-1}.

$NaBH_4$ *Reduction of* **8**. Compound **8** was reduced with excess $NaBH_4$ in MeOH (0°, 15 min), and immediately acetylated (Ac_2O/py) to yield **10** which showed the following spectral features: $[\alpha]_D^{25} = 1.6°$ (c = 0.5, $CHCl_3$); IR 2920, 1730, 1450, 1370, 1240 cm^{-1}, HRMS Found: 328.2400 for $C_{22}H_{32}O_2$ ($M^+ - 2 \times C_2H_3O_2$), Calc: 328.2402. ^1H NMR (Bz-d_6) 5.25 (2 H, t, J = 6 Hz), 4.82 (1 H, J_{AB} = 13 Hz), 4.75 (1H, J_{AB} = 13 Hz), 4.70 (1 H, d, J_{AB} = 13 Hz), 4.62 (1 H, d, J_{AB} = 13 Hz), 4.10 (1 H, d, d, J = 11, 5 Hz), 3.80 (1 H, dd, J = 11, 7 Hz), 3.00 (1 H, mult), 2.00 (1 H, mult), 1.69 (3 H, s), 1.68 (3 H, s), 1.66 (3H, s), 1.60 (3 H, s), 158 (3 H, s).

Diterpenoid **9**. The extract of *U. flabellum* (voucher number BA86), yielded **9** after Si gel HPLC purification (90% EtOAc/isooctane). Compound **9** showed the following spectral features: $[\alpha]_D^{25} = -26.4°$ (c = 0.9, $CHCl_3$); IR ($CHCl_3$) 3550, 2940, 1715, 1665 cm^{-1}, UV (MeOH) λ_{max} 251 nm (ϵ = 5440); HRMS Found: 300.2090 for M^+-H_2O ($C_{20}H_{28}O_2$) Calc: 300.2089.

Bioassays. Three bioassays were employed to assess the bioactivity of the *Penicillus*- and *Udotea*-derived terpenoids. Antimicrobial assays were performed using the standard agar plate-assay disc method at disc concentrations of 100 μg. Zones of inhibited growth in excess of 4 mm were interpreted as positive inhibitions. The effects of the new terpenoids, both qualitative and quantitative, upon cell division were also assessed using the fertilized eggs of the common Pacific sea urchin *Lytechinus pictus* (16 μg/ml). Details of this assay have been published elsewhere.[18,19] The toxic effects of these compounds were also assessed against the common Caribbean damselfish *Eupomacentrus leucostictus* at 5 and 10 μg/ml concentration for 1 hr in seawater. Details of this assay have also appeared.[20]

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