Structures and Antimicrobial Activities of Pyridoacridine Alkaloids Isolated from Different Chromotypes of the Ascidian *Cystodytes dellechiajei*

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Three new pentacyclic alkaloids were isolated from different chromotypes of the western Mediterranean ascidian *Cystodytes dellechiajei.* The purple color morph collected in Catalonia contained the known compounds kuanoniamine D (**1**), shermilamine B (**2**), *N*-deacetylkuanoniamine D (**3**), and styelsamine C (**4**) and a new alkaloid named *N*-deacetylshermilamine B (**5**). The green color morph collected in the Balearic Islands contained the known compounds 11-hydroxyascididemin (**6**) and 8,9-dihydro-11-hydroxyascididemin (**7**) and two new alkaloids named cystodimine A (**8**) and cystodimine B (**9**). The blue color morph collected in Catalonia yielded the known compound ascididemin (**10**). The structures of all compounds were elucidated on the basis of spectroscopic data, mainly 1D and 2D NMR data. The antimicrobial potential of the pyridoacridine alkaloids isolated from each color morph was evaluated and compared.

Cystodytes dellechiajei (Della Valle, 1877) (Aplousobranchia, Polycitoridae) is a colonial soft-bodied ascidian widely distributed in both tropical and temperate waters. The general morphology of this species varies greatly in terms of color, spicular composition, and shape without any clear pattern of distribution. However, López-Legentil and Turon,[1] on the basis of genetic studies, concluded that although the differences in color patterns and spicular composition suggested the presence of several species, the morphological traits studied were not consistent enough to differentiate between *Cystodytes* species.

Several pyridoacridine alkaloids have been reported specifically from *Cystodytes dellechiajei*: ascididemin,[2,3] 11-hydroxyascididemin,[4,5] cystodytins A−I,[6,7] and sebastianines A and B.[8] In a previous study, we described two major chemotypes within the most abundant color morphs of *C. dellechiajei* in the northwestern Mediterranean.[9] The first chemotype was characterized by the presence of C9-unsubstituted pyridoacridines such as ascididemin and 11-hydroxyascididemin and was found in blue and green morphs, while the second chemotype found in a purple color morph contained sulfur-containing pyridoacridines such as shermilamine B and kuanoniamine D. These results, obtained using HPLC and MALDI-TOF analysis, were in accordance with the phylogenetic analysis, placing the green/blue and purple morphs in two distinct clades. Regarding the relationship between color and pyridoacridine composition, it should be noted that no alkaloid was detected in a brown color morph collected in the northwestern Mediterranean, while chemical investigations on the same color morph from the Pacific led to the isolation of cystodytins A to I.[6,7] In this study, we have further investigated chemical differences between chromotypes of *C. dellechiajei* from the northwestern Mediterranean and determined the antibacterial properties of their extracts and isolated compounds. Two new C9-unsubstituted and one new sulfur-containing pyridoacridine were characterized using spectroscopic methods. The antimicrobial activity of these three new alkaloids was compared to that of the other pyridoacridines present in the ascidian.

Freeze-dried samples of purple, blue, and green color morphs collected by scuba in 2002 in the northwestern Mediterranean were kept frozen until used. The organic extracts of the blue and purple colonies showed the strongest antibacterial activity, the crude extract of the green morph was less active, and the brown extract was inactive. The HPLC traces of the four extracts obtained from the four different chromotypes (blue, green, purple, and brown) were clearly different and specific. A typical HPLC profile corresponded to each chromotype (see Supporting Information). After successive chromatographic purifications on reversed-phase columns and HPLC, the extract of the purple color morph collected in Catalonia afforded the known kuanoniamine D[10] (**1**), shermilamine B[11] (**2**), *N*-deacetylkuanoniamine D[12] (**3**), and styelsamine C[13] (**4**) and a new compound, *N*-deacetylshermilamine B (**5**). A similar purification pathway for the extract from the green color morph led to the isolation of the known major alkaloid 11-hydroxyascididemin[4,5] (**6**), 8,9-dihydro-11-hydroxyascididemin (**7**),[14] and two new minor compounds: cystodimine A (**8**) and cystodimine B (**9**). A single and known alkaloid, ascididemin[2,3] (**10**), was obtained from the extract of the blue morph.

N-Deacetylshermilamine B (**5**), obtained as a purple TFA salt, was the major alkaloid present in the purple morph. Its structure was elucidated by interpretation of MS and NMR data and comparison with spectroscopic data of shermilamine B. The two compounds exhibited very similar spectroscopic data (UV, NMR, MS). The mass spectrum (EIMS) recorded for **5** exhibited a $[M + H]^+$ pseudomolecular ion at *m/z* 349, which was 42 amu less than for shermilamine B (**2**), corresponding to the loss of the acetyl unit. A fragment ion at *m/z* 332 $[M + H - NH_3]^+$ observed in the ESI spectrum was indicative of the presence of a terminal amino alkyl group in **5**.[12] The molecular formula of the free base was finally established as $C_{19}H_{16}N_4OS$ from positive HRFABMS. The only notable difference with shermilamine B was the lack of the NMR signals corresponding to the *N*-acetyl group and the presence of a broad singlet (3H, δ 7.98) attributable to exchangeable protons, confirming that **5** was the *N*-deacetylated derivative of **2**. Acidic hydrolysis of shermilamine B (**2**) yielded *N*-deacetylshermilamine B (**5**), confirming the suggested structure.

Cystodimine A (**8**) was obtained as a yellow solid, and its molecular formula was determined as $C_{18}H_{12}N_4O$ by HRFABMS (*m/z* 301.1088, $[M + H]^+$). The ^1H NMR spectrum of **8** recorded in CD_3OD showed eight signals ascribable to six aromatic and four aliphatic protons. Interpretation of the $^1H-^1H$ DQF-COSY spectrum suggested that these six aromatic protons could be assigned to two isolated spin systems located on an acridine moiety according to their chemical shifts, the coupling constant values, and the

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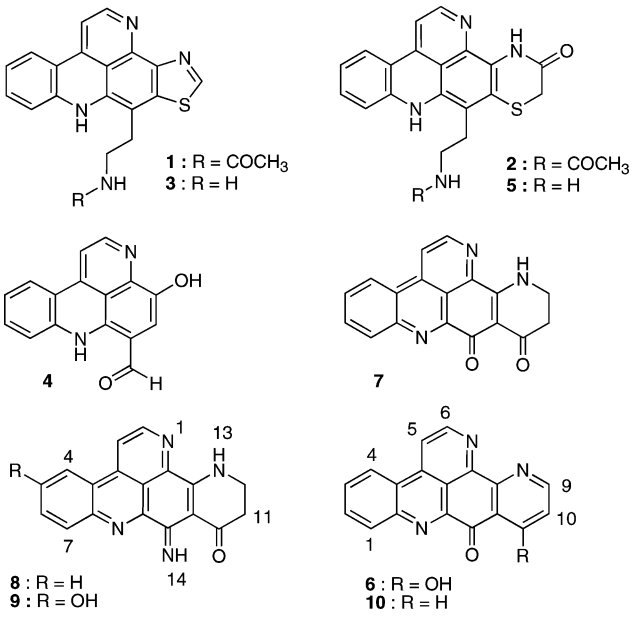

Figure 1. Chemical structures of the pyridoacridine alkaloids isolated from three color morphs of the ascidian *Cystodytes dellechiajei*. The numbering scheme of the ring system for compounds **5**, **8**, and **9** is based on nomenclature rules and is the numbering scheme used for compounds **1** to **3**.[10−12] The numbering scheme for compounds **6**, **7**, and **10** is the one reported in the literature.[2,4,14]

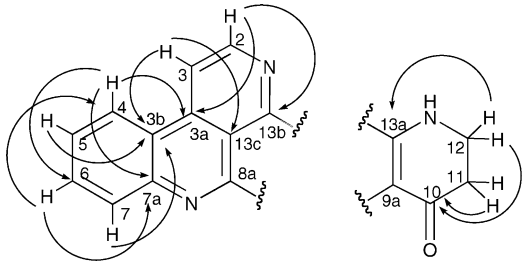

Figure 2. Partial structures of cystodimine A (**8**) with key long-range $^1H-^{13}C$ coupling correlations.

correlations observed in the HMBC experiments (Figure 2). Four proton signals (δ 8.93, 8.03, 8.09, and 8.44) were easily linked to the contiguous carbon atoms of a disubstituted benzene ring (C-4 to C-7), and the other two (δ 8.98, d, $J = 5.5$ Hz and 9.22, d, $J = 5.5$ Hz) were attributed to the α (H-2) and β (H-3) protons of a trisubstituted pyridine system. The signals observed for the third spin system corresponded to two vicinal methylene groups located on a tetrahydropyridone moiety. This deduction was made on the basis of their chemical shifts on the spectrum recorded in CD_3OD (δ 2.98, 2H, t, $J = 7.3$ Hz and δ 4.15, 2H, t, $J = 7.3$ Hz) and of long-range correlations between these protons and the characteristic ^{13}C signal at δ_C 194.6 corresponding to the conjugated ketone (Figure 2). The occurrence of an exchangeable proton located on this ring was confirmed by recording the ^1H NMR spectrum of **7** in DMSO-d_6, where a proton resonance was observed as a broad singlet (δ 11.81, br s, NH-13). The signal corresponding to the methylene protons (δ 4.15, H-12) appeared as a broad triplet that sharpened upon selective irradiation of the NH-13 signal.

The chemical shift of the remaining quaternary carbon atom at δ_C 159.0 (C-9) indicated that it was linked to the remaining nitrogen atom according to the molecular formula given by HRFABMS. The presence of an imino group was confirmed by the observation of two exchangeable protons (δ 10.66 and 11.04, NH_2^+-14) in the ^1H NMR spectrum of **8** in DMSO-d_6, indicative of the formation of a salt at this position. These two signals were coupled in the

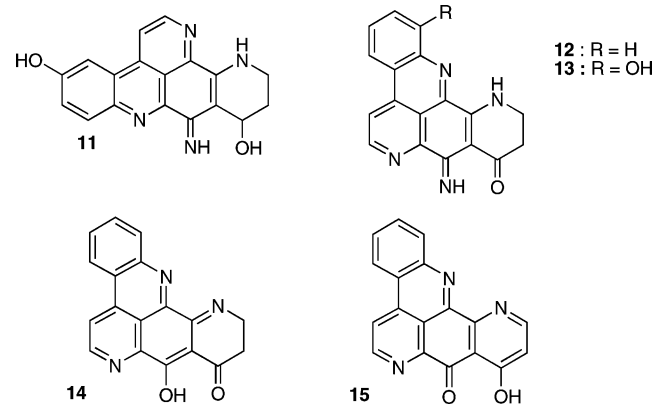

Figure 3. Revised chemical structure of calliactine (**11**) and structures of ecionines A (**12**) and B (**13**), labuanine A (**14**), and 9-hydroxybenzo[*b*]pyrido[4,3,2-*de*][1,10]phenanthrolin-8(^8H)-one (**15**).

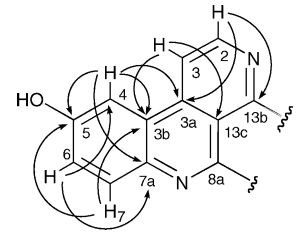

Figure 4. Partial structure of cystodimine B (**9**) with key long-range $^1H-^{13}C$ coupling correlations.

$^1H-^1H$ DQF-COSY spectrum and correlated to the adjacent quaternary carbon resonances (C-8a and C-9a) in the HMBC experiment. The adjacency of the two partial substructures shown in Figure 2 was defined by comparison with the ^{13}C NMR data reported in the literature for calliactine[15] (**11**) (Figure 3), an unstable pigment isolated from the sea anemone *Calliactis parasitica,*[16] taking into account the assignments of the revised structure.[17] The total structure of cystodimine A (**8**) was finally established as shown. The proposed structure for cystodimine A was confirmed by chemical conversion to 11-hydroxyascididemin (**6**) achieved under the conditions described by Lederer et al.[18] The major compound formed during the reaction was concluded to be **6** by comparison with an authentic sample as judged by HPLC, UV spectra, and MS data. Compound **6** was also obtained by oxidative conversion of 8,9-dihydro-11-hydroxyascididemin (**7**), a minor compound that was also isolated from the green color morph. From a biosynthetic point of view, the co-occurrence of **6**, **7**, and **8** appears to be additional proof of the proposed structure for cystodimine A.

Cystodimine B (**9**) was obtained as a yellow solid, and its molecular formula was determined as $C_{18}H_{13}N_4O_2$ by HRFABMS (m/z 317.1039, $[M + H]^+$). The presence of one additional oxygen, as compared with cystodimine A (**8**), suggested that it might be its hydroxylated analogue. This hypothesis was supported by close similarities in ^1H and ^{13}C NMR spectra of **9** recorded in CD_3OD. The major differences were the resonances associated with the spin system of the benzene ring. The $^1H-^1H$ COSY and $^1H-^{13}C$ HSQC experiments indicated that the four-proton spin system (H-4 to H-7) previously observed for **8** was replaced by three protons, H-4, H-6, and H-7, in compound **9**. A hydroxy group could be positioned at C-5 (δ_C 163.2) according to a number of $^1H-^{13}C$ HMBC correlations (Figure 4). As no other substantive changes were observed in the NMR spectra, the total structure of cystodimine B (**9**) was established as shown.

Cystodimines A and B are two pyridoacridine alkaloids based on a "linear" arrangement of the fifth ring on the pyridoacridine skeleton. These two compounds are regioisomers of the recently

Table 1. NMR Spectroscopic Data (400 MHz, DMSO-d_6) for **5**

position	δ_C	δ_H (J in Hz)	HMBC[a]
2	150.5[b]	8.55, d (5.3)	3, 3a, 13b
3	107.3	7.63, d (5.3)	3b, 13c
3a	142.5		3a, 6, 7a
3b	115.4		
4	125.0	8.14, d (8.1)	3a, 6, 7a
5	122.2	7.13, t, (7.9)	3b, 7
6	132.7	7.53, t (7.9)	4, 5, 7a
7	116.9	7.48, d (8.1)	3b, 5
7a	140.0		
8-NH		9.81, bs	
8a	131.5		
9	108.4		
9a	124.4		
11	29.4	3.64, s	9a, 12
12	164.0		
13-NH		9.55, s	9a, 11
13a	121.7		
13b	136.0		
13c	117.1		
14	25.8	3.24, t (8.1)	8a, 9, 9a, 15
15	36.9	2.98, bt	9
16		7.98, bs	

[a] HMBC correlations are from proton(s) stated to the indicated carbon. [b] Not detected in the ^{13}C spectrum; assignment aided by HSQC experiment.

reported ecionines A (**12**) and B (**13**) isolated from the Australian sponge *Ecionemia geodides*[19] based on an "angular" arrangement of the fifth ring. As we demonstrated by chemical conversion (oxidation and hydrolysis), cystodimine A (**8**) is an imine analogue of 11-hydroxyascididemin (**6**). Similarly, we can expect ecionine A to be an imine analogue of the two pyridoacridine alkaloids isolated from the marine sponge *Biemna fortis*,[20] labuanine A (**14**) and compound **15**, the latter being the angular regioisomer of 11-hydroxyascididemin (**6**).

The antimicrobial activities of extracts and isolated compounds from different color morphs of *C. dellechiajei* were determined by a liquid growth inhibition assay based on a NCCLS method.[21] This method has been used to evaluate the antibacterial activity of other pyridoacridine alkaloids, such as isodiplamine, diplamine, cystodytins, and lissoclinidine, against a panel of bacteria and fungi strains (MIC values were from 1 to 29 μM).[22] With this method, ascididemin was found to be active against *Escherichia coli*, *Cladosporium resinae*, and *Bacillus subtilis* but inactive toward *Pseudomonas aeruginosa* and *Trichophyton mentagrophytes*.[23] Extracts and pure compounds from *C. dellechiajei* were tested against the two bacterial strains *Escherichia coli* (Gram negative) and *Micrococcus luteus* (Gram positive). The extracts of blue and purple ascidian color morphs showed the most potent activity against both strains (MIC = 0.3 μg/mL), while the extract of the green color morph was less active (MIC = 1.2 μg/mL) and the brown color morph extract was inactive. These results suggested that the antibacterial activity of the extracts was due to the presence of pyridoacridine alkaloids, as none was detected in the brown color morph. To assess the importance of the isolated pyridoacridine alkaloids for the observed bacterial growth inhibition, each compound was individually tested against both strains (Table 3).

A dose-dependent inhibition of bacteria was observed for all tested pyridoacridines against the two strains. The MIC values (Table 3) ranged from 0.2 to 2.6 μM toward *E. coli* and from 0.3 to 17.4 μM toward *M. luteus*. The latter microorganism exhibited less susceptibility to the pyridoacridine alkaloids. The eight compounds appeared markedly less potent than the clinically active drug gentamicin, with the presence of a free amino group in shermilamine B (*N*-deacetylshermilamine B vs shermilamine B) or kuanoniamine D (*N*-deacetylkuanoniamine D vs kuanoniamine D) having little effect on antibacterial activity, while hydroxylation either on C-11 (ascididemin vs 11-hydroxyascididemin) or on C-5 (cystodimine A vs cystodimine B) resulted in reduced activity. The two strains exhibited similar susceptibility to C-9-unsubstituted pyridoacridines and sulfur-containing pyridoacridines.

In addition, extracts of the blue, purple, and green morphs and ascididemin also deterred fish predation, but not sea urchin predation.[24] Further studies on the antifouling activity of the extracts and pyridoacridine alkaloids are currently being conducted.

The structures of three new alkaloids reported here from the purple and the green color morphs of *C. dellechiajei* are in accordance with previously reported chemotypes.[9] Cystodimine B is a close analogue of the proposed structure of the sea anemone metabolite calliactine (**11**). It is interesting to point out that cystodimines A and B are, with ecionines A and B, the first pyridoacridines described containing a stable imino group that is probably stabilized by a hydrogen bond between the adjacent ketone and the imine hydrogen atom. We believe a biosynthetic relationship between cystodimine A and 11-hydroxyascididemin may also exist. This would imply the presence of the 5,11-dihydroxyascididemin related to cystodimine B in the ascidian, although this compound has not yet been isolated. For the purple color morph, the presence of kuanoniamine D and shermilamine B along with their deacetylated forms has been proven here by isolation and characterization of these compounds. The coexistence of the simple tetracyclic styelsamine C and the pentacyclic pyridoacridines in the purple morph is in accordance with the pyridoacridine family biosynthetic pathway predicted by Skyler and Heathcock.[25] In order to complete the pyridoacridine family tree and achieve a better understanding of the biosynthetic pathway of these compounds, further isolation and characterization of minor pyridoacridines is needed. In particular, other species of the genus *Cystodytes* may provide the missing compounds to resolve the biosynthetic pathway of the pyridoacridines while increasing the pool of marine natural products.

Experimental Section

General Experimental Procedures. UV spectra were recorded on a Hewlett-Packard diode array spectrophotometer. 1D and 2D NMR spectra were recorded on a Jeol EX 400 spectrometer using standard Jeol pulse sequence programs. Mass spectra (MS) were recorded on an automass Unicam spectrometer. HPLC separations were performed on an Interchrom uptisphere 5 μm ODB column using Jasco pumps and a Waters 996 photodiode-array detector. Vacuum column chromatography was performed on Merck Lichroprep RP-8 (0.04−0.063 mm).

Collection and Extraction of *Cystodytes dellechiajei*. Samples of purple, blue, and green morphs of *C. dellechiajei* were collected by scuba diving at 5 to 15 m deep in 2001 and 2002. The purple morph (92 g dry wt) was collected in Catalonia, Northwestern Spain (GPS position 42°06′26″ N, 03°10′30″ E; reference DNA sequence GenBank accession number AY523064). The green color morph (68 g dry wt) was collected in Cabo de Gata, Southern Spain (GPS position 36°53′58″ N, 01°57′58″ W; reference DNA sequence GenBank accession number AY523049). The blue and brown morphs were collected in the Es Vedrà, Balearic Islands (GPS position 38°51′53″ N, 01°11′43″ E; reference DNA sequence GenBank accession numbers AY523046 and AY523042, respectively). Both the morphology and genetics of the four morphs analyzed here have been extensively described by López-Legentil and Turon.[26] All samples were immediately frozen at −30 °C, freeze-dried within a week, and kept frozen until used. Each color morph was extracted exhaustively three times with a MeOH/CH_2Cl_2/TFA (50:50:0.1) mixture. The resulting dry extracts were purple (9 g) and yellow-green (10 g), respectively.

Isolation of Alkaloids from the Purple Morph. The purple extract (9 g) was dissolved in CH_2Cl_2/MeOH (80:20) and mixed with RP-8 silica gel. The solvent was then completely evaporated, and the residue was subjected to a RP-8 reversed-phase column eluted with increasing amounts of MeOH in H_2O. The purple fraction that eluted with 80% H_2O was further purified by semipreparative reversed-phase HPLC (H_2O/MeOH/TFA (60:40:0.1), 2.5 mL/min with UV detection at 340 nm) and yielded the new *N*-deacetylshermilamine B (**5**) (15 mg) along with the known *N*-deacetylkuanoniamine D (**3**) (12 mg) and styelsamine C (**4**) (2 mg). The orange fraction that eluted with 20% H_2O was further

Table 2. NMR Spectroscopic Data (400 MHz, CD_3OD) for **8** and **9**

	compound **8**			compound **9**		
position	δ_C	δ_H (*J* in Hz)	HMBC[a]	δ_C	δ_H (*J* in Hz)	HMBC[a]
2	150.8	9.22, d (5.5)	3, 3a, 13b	150.1	9.17, d (5.6)	3, 3a, 13b
3	122.2	8.98, d (5.5)	2, 3b, 13c	122.2	8.82, d (5.6)	2, 3b, 13c
3a	138.8			137.8		
3b	124.6			127.0		
4	125.3	8.93, dd (8.1, 1.1)	3a, 6, 7a,	108.5	8.10, d (2.5)	3a, 5, 6, 7a
5	133.1	8.03, td (8.1, 1.1)	3b, 7	163.2		
6	133.9	8.09, td (8.1, 1.1)	4, 7a	124.3	7.60, dd (8.7, 2.5)	4, 7a
7	130.0	8.44, dd (8.0, 1.1)	3b, 5	135.3	8.31, d (8.7)	3b, 5
7a	146.2			141.0		
8a	143.9			139.5		
9	159.0			159.4		
9a	100.4			132.5		
10	194.6			194.9		
11	35.7	2.9, t (7.3)	10, 12	35.7	3.00, t (7.3)	10, 12
12	41.9	4.15, t (7.3)	10, 11, 13a	41.8	4.16, t (7.3)	10, 11, 13a
13-NH		11.81, bs[b]				
13a	160.7			160.7		
13b	143.5			143.2		
13c	117.6			117.5		
14a-NH		10.66, bs[b]	8a,[b] 9a[b]			
14b-NH		11.04, bs[b]	9a[b]			

[a] HMBC correlations are from proton(s) stated to the indicated carbon. [b] Observable in DMSO-d_6.

Table 3. Antibacterial Activity of the Pyridoacridine Alkaloids Isolated from *Cystodytes dellechiajei.*

	MIC *E. coli* (μM)	MIC *M. luteus* (μM)
kuanoniamine D (**1**)	2.2	17.4
shermilamine B (**2**)	2.0	8.0
N-deacetylkuanoniamine D (**3**)	2.5	2.5
N-deacetylshermilamine B (**5**)	1.1	4.5
11-hydroxyascididemin (**6**)	2.6	10.5
cystodimine A (**8**)	1.2	2.4
cystodimine B (**9**)	2.6	10.5
ascididemin (**10**)	0.2	0.3
gentamicin	0.08	0.02

purified by semipreparative reversed-phase HPLC (H_2O/MeOH/TFA (40:60:0.1), 2.5 mL/min with UV detection at 340 nm) and yielded the known compounds kuanoniamine D (**1**) (4 mg) and shermilamine B (**2**) (6 mg).

***N*-Deacetylshermilamine B Trifluoroacetate Salt (5):** purple solid; UV ($MeOH_2^+$) λ_{max} (log ε) 231 (4.5); 279 (4.2); 298 (4.8); 314 (4.9); 358 (3.6); 378 (3.6); 540 (3.9); ^{1}H NMR and ^{13}C NMR data (DMSO-d_6) see Table 1; (+)-ESIMS *m/z* 349 $[M + H]^+$; (+)-ESIMS/MS (from the precursor ion *m/z* 349) 332 $[M + H - NH_3]^+$; HRFABMS *m/z* 349.1140 (calcd for $C_{19}H_{17}N_4OS$, 349.1123).

Acidic Hydrolysis of Shermilamine B (2). Shermilamine B (**2**) (2 mg) was dissolved in 1 mL of 6 N HCl and stirred for 5 h under reflux. The reaction mixture was basified with 20% NaOH and extracted with CH_2Cl_2. The organic extract was analyzed by reversed-phase HPLC (H_2O/MeOH/TFA (40:60:0.1)) with photodiode array detection. Comparison of the retention time and the UV spectrum of the synthesized product with those of *N*-deacetylshermilamine B (**5**) indicated that they were identical.

Isolation of Alkaloids from the Green Morph. The yellow-green extract (10 g) was dissolved in CH_2Cl_2/MeOH (80:20) and mixed with RP-8 silica gel. The solvent was completely evaporated, and the residue was subjected to a reversed-phase column eluted with increasing amounts of MeOH in H_2O. The yellow and blue fractions that eluted with 60% MeOH were further purified by semipreparative reversed-phase HPLC (H_2O/MeOH/TFA (50:50:0.1), 2.5 mL/min with UV detection at 300 nm) and yielded two new compounds (**8**, 6 mg, and **9**, 8 mg) along with the known 11-hydroxyascididemin (**6**, 65 mg) and 8,9-dehydro-11-hydroxyascididemin (**7**, 3 mg).

Cystodimine A (8): yellow solid; UV (MeOH) λ_{max} (log ε) 228 (4.2); 282 (3.8); 318 (3.7); 384 (3.8); 440 (3.3); ^{1}H NMR and ^{13}C NMR data (CD_3OD) see Table 2; (+)-ESI-MS *m/z* 301 $[M + H]^+$; HRFABMS *m/z* 301.1088 (calcd for $C_{18}H_{13}N_4O$, 301.1089).

Cystodimine B (9): yellow solid; UV (MeOH) λ_{max} (log ε) 228 (3.8); 278 (3.5); 308 (3.5); 388 (3.1); 450 (3.4); ^{1}H NMR and ^{13}C NMR data (DMSO-d_6) see Table 2; (+)-ESI-MS *m/z* 317 $[M + H]^+$; HRFABMS *m/z* 317.1028 (calcd for $C_{18}H_{13}N_4O_2$, 317.1039).

Oxidation of Cystodimine A (8). Cystodimine A (**8**) (1 mg) was dissolved in 1 mL of 2 N HCl and 0.1 mL of DMSO and stirred for 1 h under reflux. The reaction mixture was directly analyzed by HPLC after filtration (0.2 μm PTFE syringe filter).

Antibacterial Assays. Pyridoacridines and extracts from *C. dellechiajei* were tested for their antibacterial activities toward two strains of bacteria: *Escherichia coli* and *Micrococcus luteus*. Pure compounds or extracts were dissolved in DMSO and liquid media and incubated with the bacteria (2×10^8 cells/mL) in 96-well microplates with PB medium (Bacto-tryptone 1%, NaCl 0.5%, pH 7.5) at 35 °C for 24 h, under constant agitation. Each treatment was realized in triplicate. Growth was measured by reading absorbance at 620 nm. The minimum inhibitory concentration (MIC) is the minimal concentration needed to inhibit growth of bacteria.

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Supporting Information Available: HPLC profiles of the extracts from the green and the purple color morph of *Cystodytes dellechiajei*. ^{1}H, ^{13}C, HSQC, and HMBC NMR spectra of **5**, **8**, and **9**. HRFABMS spectra of **5**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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