Notes

Cycloshermilamine D, a New Pyridoacridine from the Marine Tunicate *Cystodytes violatinctus*

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A new alkaloid, cycloshermilamine D, was isolated from the marine tunicate *Cystodytes violatinctus*, and its structure (**1**), which is closely related to shermilamine D, was established mainly on the basis of NMR spectroscopic data.

Among marine alkaloids, the pyridoacridines currently seem to be the largest group, with most of the compounds being isolated from sponges and tunicates.[1−3]

A whole variety of pyridoacridines have been isolated from the genera *Cystodytes*.[4] Investigation of *Cystodytes violatinctus* (Monniot 1988) collected in the lagoon of Mayotte, Comoros Islands, northwest of Madagascar, resulted in the isolation of five pyridoacridines, namely, three segolins,[5,6] shermilamines D and E and tintamine, an alkaloid with a new heterocyclic system.[7] The structure of another compound, cycloshermilamine D (**1**), also isolated from the same tunicate in minute amounts (0.4% of the crude extract), is the subject of this report.

Cycloshermilamine D (**1**) was obtained from the $CHCl_3$−MeOH (1:1) extract, after chromatography on Sephadex LH-20 and Si gel columns, as a yellow amorphous powder. The molecular formula of **1** was established by HREIMS (*m*/*z* 372.1045, 100%, M^+, Δmmu = −0.1) and NMR data (Table 1) to be $C_{21}H_{16}N_4OS$, possessing 16 units of unsaturation, indicating an aromatic structure. An IR absorption at 1682 cm^{-1}, together with the δ_C 163.4 ppm signal, in the ^{13}C NMR spectrum, suggested an amide as in the shermilamines.[7] The ^{13}C NMR spectrum (Table 1), showing 21 distinct resonance lines (2 × CH_3, 1 × CH_2, 7 × CH, and 11 quaternary C atoms, determined by a DEPT experiment), accounted for 15 of the 16 protons, leaving one hydrogen to link to a heteroatom. The ^1H NMR spectrum in $CDCl_3$ (Table 1) paralleled the ^{13}C NMR spectrum in showing 15 protons attached to carbon atoms, and an extra proton at δ 9.25 ppm, suggesting an NH group. Characteristic in the ^1H NMR spectrum besides the latter NH signal, was the two proton singlet at δ 3.64 ppm, the same as H_2-12 of the shermilamines,[7] the AB system at δ 8.83 (d, J = 5.2) and 7.96 (d, J = 5.2) (the H-2 and H-3 protons of a pyridine system[8]), the four proton system at δ 7.55−9.13, corresponding to a 1,2-disubstituted aromatic ring, and the $N(CH_3)_2$ singlet at δ 2.96 (6H). The last proton to be accounted for was a singlet at δ 6.78 ppm, which was assigned to H-10 according to its CH-correlations with C-9 and 14d. Furthermore, according to a CH-correlation from the $N(CH_3)_2$ protons to C-9, it was suggested that the C-9(10) double bond creates a new pyrrole ring, condensed to the pyridoacridine system. Searching the literature for such a ring system brought us to stellettamine.[9] Indeed, comparison of the NMR data of the latter compound with the chemical shifts of **1** showed they were nearly identical at C-9 and -10 (δ 150.1 and 94.3 ppm in **1** vs 149.4 and 94.2 ppm for stellettamine) and had high similarity for other common C atoms (Table 1). The relationship between cycloshermilamine D and shermilamine is similar to that between stellettamine and nordercitin.[9] The suggested structure of **1** was confirmed by the measured CH-correlations and NOEs (see Figure 1 and Table 1). Shermilamine is, most likely, the precursor of compound **1**, which is obtained from it by oxidative coupling between the acridine NH group and the side chain.

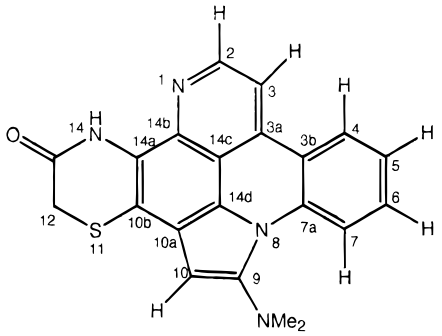

Figure 1.

Experimental Section

General Experimental Procedures. UV spectra were obtained with a Varian Cary 219 spectrophotometer, and IR spectra with a Bruker Vector 22 spectrophotometer. ^1H NMR, ^{13}C NMR, and 2D NMR spectra were recorded on a Bruker ARX-500 spectrophotometer with TMS as internal standard. MS data were recorded on a Fisons Autospec-Q spectrometer.

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Table 1. NMR Data of Cycloshermilamine D (**1**) (125 and 500 MHz, in $CDCl_3$)

C no.	δ_C (m)	δ_C (m)[a]	δ_H (m, *J* in Hz)	COSY	HMBC (H→C)	NOESY
2	143.6 (d)	147.5 (d)	8.83 (d, 5.2)	3	3, 3a, 14b	3
3	109.2 (d)	110.5 (d)	7.96 (d, 5.2)	2	14c, 3b	2, 4
3a	131.5 (s)	133.0 (s)				
3b	120.5 (s)	121.4 (s)				
4	125.7 (d)	125.2 (d)	8.47 (br d, 8.0)	5	3a, 6, 7a	3, 5
5	124.6 (d)	124.3 (d)	7.55 (br t, 7.5)	4, 6	3b, 7, 7a[c]	4, 6
6	132.5 (d)	130.8 (d)	7.80 (br t, 7.5)	5, 7	4, 7a	5, 7
7	118.5 (d)	118.4 (d)	9.13 (br d, 8.0)	6	3b, 5, 7a	6, NMe_2
7a	136.5 (s)	136.4 (s)				
9	150.1 (s)	149.4 (s)				
10	94.3 (d)	94.2 (d)	6.78 (br s)		9, 14d	NMe_2
10a	115.0	110.6 (s)				
10b	113.8 (s)	129.7 (s)				
12	29.6 (t)	149.1 (s)	3.64 (br s)		13, 10b	
13	163.4 (s)					
14NH			9.25 (br s)			
14a	120.3 (s)	145.0 (s)[b]				
14b	137.3 (s)	140.8 (s)				
14c	112.6 (s)	113.3 (s)				
14d	118.8 (s)	122.0 (s)				
NMe_2	45.2 (q)	45.3 (q)	2.96 (br s)		9	7, 10

[a] ^{13}C NMR data of stelletamine in $CDCl_3$. [b] The numbers of C-14a to 14d are according to the numbers of **1**. [c] $^4J_{CH}$ − a long-range correlation that is well-known in polyaromatic systems.

Biological Material. *C. violatinctus* (order Aplousobranchia, family Polycitoridae), a dark purple tunicate, was collected using scuba (−10 m) at the Mayotte Lagoon, Comoros Islands, northwest of Madagascar in April 1996. A voucher specimen (# AM-35) is deposited in the Chemistry Department, University of Réunion.

Extraction and Isolation. After collection, the tunicate was immediately frozen and kept at −25 °C. The frozen tunicate was thawed and then extracted with a mixture of MeOH−$CHCl_3$ (1:2) × 3 to give a dark brown gum (1.26 g). Solvent partition[10] between aqueous MeOH and hexane, CCl_4, and $CHCl_3$ resulted in three fractions (684, 132, and 68 mg, respectively).

The hexane fraction that contained compound **1** was chromatographed on Sephadex LH-20 eluted with MeOH−$CHCl_3$−hexane (1:1:2), and then several times on Si gel columns eluted with hexane and EtOAc mixtures. From the latter chromatographies, **1** was obtained (5 mg, 0.4% of the crude extract); R_f on Si gel plate (eluted with hexanes−EtOAc, 1:1), 0.43.

Compound 1: yellow amorphous powder; IR (neat) ν 1682, 1601, 1560, 1462, 1336, 1221 cm^{-1}; UV (MeOH) λ_{max} (nm) (log ϵ) 208 (4.18), 215 (4.16), 262 (4.04), 299 (3.88), 391 (3.35), 480 (3.19); UV (MeOH, H^+) λ_{max} (nm) (log ϵ) 214 (4.49), 288 (4.06), 427 (3.4); NMR data, see Table 1; EIMS *m*/*z* 372 [M^+] (100), 357 (20), 330 (20), 288 (14); HREIMS *m*/*z* 372.1045 (Δmmu = −0.1).

References and Notes

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