Pergamon

Tetrahedron Letters 41 (2000) 3863–3864

TETRAHEDRON
LETTERS

Structure revision of the marine pentacyclic aromatic alkaloid: cystodamine

Evelyne Delfourne,* Nataly Bontemps-Subielos and Jean Bastide

Université de Perpignan, Centre de Phytopharmacie UMR CNRS 5054, 52 avenue de Villeneuve, 66860 Perpignan, France

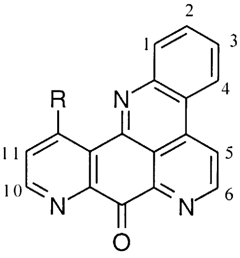
Received 13 March 2000; accepted 23 March 2000

Abstract

The structure of cystodamine, a polycyclic aromatic alkaloid from the mediterranean ascidian *Cystodytes delle chiajei* has been revised to be 11-hydroxyascididemin, by comparison of the spectroscopic data with those of synthetic cystodamine, meridine and 11-hydroxyascididemin. © 2000 Published by Elsevier Science Ltd. All rights reserved.

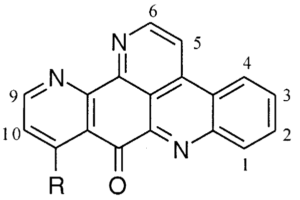
Keywords: natural products; marine metabolites; alkaloids; acridine.

During the past decade, polycyclic aromatic alkaloids have emerged as a class of marine natural products having significant biological activities such as cytotoxicity, antimicrobial activity or in vivo antitumor activity.[1] In 1994, Bontemps et al. reported the isolation of a new pyridoacridine compound named cystodamine from the mediterranean ascidian *Cystodytes delle chiajei* for which, on the basis of spectroscopic data, the meridine-like structure **1a** ($R=NH_2$) was proposed.[2] Three years later, Kitahara et al.[3] proposed a synthesis of this alkaloid. The differences in NMR data between the natural and the synthetic compounds led us to re-examine the structure of the natural product.

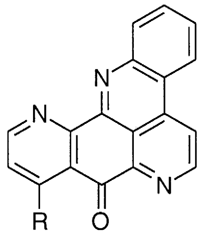


1

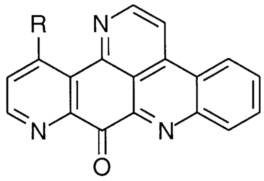
a, $R = NH_2$; **b**, $R = OH$



2



3



4

---

* Corresponding author. Fax: 33 04 68 66 22 23; e-mail: delfourn@univ-perp.fr (E. Delfourne)

PII: S0040-4039(00)00509-8

From the spectroscopic data of the natural product, the four pentacyclic arrangements **1** to **4** are plausible, but the two first ones appear more biosynthetically compatible.[4] The syntheses of the meridine-like structures **1a** and **1b** have been reported, respectively, by Kitahara et al.[3] and Bontemps et al.[5] whereas the synthesis of 11-hydroxyascididemin **2b** (R=OH) was described by Kitahara et al.[6] These different compounds **1a**, **1b** and **2b** were prepared according to these procedures. NMR spectroscopic data were recorded in the same conditions in order to be compared with those of the natural product.

The ^{1}H NMR chemical shift data of these different compounds indicate that the natural product is 11-hydroxyascididemin **2b** (Table 1). This result was also confirmed by ^{13}C chemical shift data and UV-spectroscopy, the spectra of the two compounds being exactly superimposable.

Table 1
^{1}H NMR chemical shift data for cystodamine **1a**, meridine **1b**, 11-hydroxyascididemin **2b** and the natural product in CD_2Cl_2+TFA (ppm)

proton	**1a**	**1b**	**proton**	**2b**	**natural product**
H_{11}	7.38	7.68	H_{10}	7.66	7.67
H_3	7,97	8.19	H_3	8.27	8.26
H_2	8.06	8.26	H_2	8.29	8.28
H_{10}	8.24	8.49	H_1	8.66	8.65
H_1	8.37	8.75	H_9	8.85	8.85
H_4	8.70	8.88	H_4	8.93	8.92
H_5	8.97	9.10	H_5	8.98	8.98
H_6	9.43	9.62	H_6	9.36	9.36

11-Hydroxyascididemin had been first isolated by Schmitz from the other natural marine source *Amphicarpa meridiana*,[4] but in too small amount to allow a direct comparison.

References

1. Molinski, T. F. *Chem. Rev.* **1993**, 1825–1838.
2. Bontemps, N.; Bonnard, I.; Banaigs, B.; Combaut, G.; Francisco, C. *Tetrahedron Lett.* **1994**, *35*, 7023–7026.
3. Kitahara, Y.; Tamura, F.; Kubo, A. *Tetrahedron Lett.* **1998**, *54*, 8421–8432.
4. Schmitz, F. J.; DeGusman, F. S.; Hossain, M. B.; van der Helm, D. *J. Org. Chem.* **1991**, *56*, 804–808.
5. Bontemps, N.; Delfourne, E.; Bastide, J.; Francisco, C.; Bracher, F. *Tetrahedron* **1997**, *53*, 1743–1750.
6. Kitahara, Y.; Nakahara, S.; Yonezawa, T.; Nagatsu, M.; Kubo, A. *Heterocycles* **1993**, *36*, 943–946.