HETEROCYCLES, Vol. 68, No. 10, 2006, pp. 2161 - 2164. © The Japan Institute of Heterocyclic Chemistry
Received, 21st June, 2006, Accepted, 27th July, 2006, Published online, 28th July, 2006. COM-06-10823

# A BUTENOLIDE FROM THE MARINE SPONGE *CALLYSPONGIA VAGINALIS*

**Tanya H. Layne and Winston F. Tinto**

Laboratory of Bioorganic Chemistry, Department of Biological and Chemical Sciences, University of the West Indies, Cave Hill Campus, Bridgetown, Barbados, BB10000, West Indies

E-mail: wtinto@uwichill.edu.bb

**Abstract** - A butenolide identified as 5-hydroxy-3-methyl-5-pentyl-2, 5-dihydrofuran-2-one (**1**) was isolated from *Callyspongia vaginalis*. Structural elucidation was achieved via spectroscopic means including 1D and 2D NMR experiments.

*Callyspongia vaginalis* or the Branching Vase Sponge is usually a tubular marine organism. It is commonly found along the Caribbean reefs and ranges in colour from purple to blue to grey, brownish-grey and grey-green.[1] Fan-shaped and vase-shaped varieties also exist, which are located in areas of strong currents along with the tubular variety.[2]

Polyacetylenes, which usually consist of twenty-one or twenty-two carbon atoms, are considered as chemical markers for the genus *Callyspongia*.[3-5] Sulfonated-polyacetylenes are also known[6, 7] and apart from these, terpenes,[8, 9] an alkaloid,[10] a ceramide[11] and polyketide derivatives[12-14] have been obtained. The biological activities exhibited by some of the compounds isolated include cytotoxicity towards human cancer cell lines,[14-17] antifouling,[18, 19] α-glucosidase inhibition,[20] inhibition of starfish fertilization[6] and phosphatidylinositol specific phospholipase C inhibition.[9] As marine sponges are a lucrative source of structurally diverse secondary metabolites we sought to investigate the acetone extract of the marine sponge *Callyspongia vaginalis*. We describe herein the isolation and structural determination of compound (**1**).

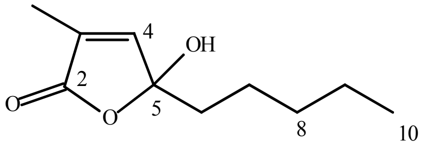
Compound (**1**) was isolated as a white solid and the molecular composition was determined to be $C_{10}H_{16}O_3$ by FABMS. The $^1$H-NMR spectrum indicated the presence of an olefinic proton at δ 6.83 (1 H, br s, H-4) and methyl protons at δ 1.94 (3 H, s, H-11). Upon examination of the HSQC spectrum, it was deduced that the proton at δ 6.83 (H-4) was directly connected to the carbon at δ 146.80 (C-4) and the protons at δ 1.94 (H-11) were directly attached to the carbon at δ10.40 (C-11). Furthermore, the proton at δ 6.83 (H-4) showed an HMBC correlation with the quaternary carbon resonating at δ 121.70 (C-5), while the protons at δ 1.94 (H-11) showed long-range correlations to the $sp^2$-hybridised carbons at δ 146.80 (C-4) and 132.39 (C-3) as well as with the carbonyl carbon at δ 171.55 (C-2). The HSQC spectrum also showed that the protons at δ 1.90 (2 H, t, J= 7.2 Hz H-6), 1.40 (2 H, t, J= 7.2 Hz H-7)) and 1.30 (2 H, m, H-8) were directly bonded to the methylene carbons at δ 37.68 (C-6), 22.99 (C-7) and 31.54 (C-8) respectively, while from the COSY spectrum, cross peaks were observed between H-7 and H-6 and H-8. The HSQC spectrum also indicated that the protons at δ 1.31 (2 H, m, H-9) and 0.89 (3 H, t, J= 5.2 Hz H-10) were directly attached to the carbons at δ 22.42 (C-9) and 13.82 (C-10) in that respective order. The HMBC spectrum showed that long-range coupling occurred between the H-10 methyl protons and C-8 and C-9. From the above information, compound (**1**) was identified as 5-hydroxy-3-methyl-5-pentyl-2, 5-dihydrofuran-2-one.

Table 1. $^{13}$C-NMR, $^{1}$H-NMR and HMBC spectral data for compound (**1**) in $CDCl_3$

| Position | $\delta_C$ | $\delta_H$ (J in Hz) | HMBC |
|---|---|---|---|
| 1 | - | - | - |
| 2 | 171.55 | - | H-11 |
| 3 | 132.39 | - | H-11 |
| 4 | 146.80 | 6.83 br s | - |
| 5 | 121.70 | - | H- 4 |
| 6 | 37.68 | 1.90 t (7.2) | - |
| 7 | 22.99 | 1.40 t (7.2) | - |
| 8 | 31.54 | <1.30> [a, b] m | H-10 |
| 9 | 22.42 | <1.31> [a, b] m | H-10 |
| 10 | 13.82 | 0.89 t (5.2) | - |
| 11 | 10.40 | 1.94 s | - |

[a] Average value for an incompletely resolved $CH_2$ group

[b] overlapped signals



(1)

Compound (**1**) was synthesized prior to its isolation here. The synthetic product has been used in industry for many years as an intermediate for the synthesis of perfume, flavoring agents, antioxidants and sequestering agents for heavy metal ions.[21] However, there has been no report of its isolation from any other organism thus far.

## EXPERIMENTAL

Sponge Material- *Callyspongia vaginalis* was collected off the coast of Brandon's Beach, St. Michael, Barbados at a depth of 30 ft. The sponge was identified by Renata Goodridge, CERMES Division, University of the West Indies, Cave Hill Campus and a voucher specimen has been deposited at the Laboratory of Bioorganic Chemistry located in the Department of Biological and Chemical Sciences on the same Campus.

Extraction and Isolation- *Callyspongia vaginalis* (1.6 kg wet wt.) was stored in a freezer for two days, thawed, macerated in acetone (10 liters) and left to stand for 36 h. The resulting acetone extract was concentrated *in vacuo* and the concentrated aqueous residue extracted with AcOEt (150 ml x 3) to give a dark brown residue (5.18 g). The crude AcOEt extract was fractionated via column chromatography to afford 48 fractions, which were eluted using 10% acetone in 90% hexane, followed by 25% acetone in 75 % hexane and finally by pure methanol. Ten major fractions were obtained and purification of fraction #8 via reverse-phase HPLC gave compound (**1**) as a white solid.

5-Hydroxy-3-methyl-5-pentyl-2,5-dihydrofuran-2-one (**1**). white solid (1.4mg); $[\alpha]^{25}_{D} \pm 0^{\circ}$ (*c* 0.04, $CDCl_3$); IR(film) $\nu_{max}$ 3440, 1752, 1650 $cm^{-1}$ ;$^{1}$H-NMR and $^{13}$C-NMR spectral data refer to Table 1; FABMS :m/z 185 $[M+H]^{+}$, 133; EIMS: 113, 85, 83; HRFABMS: 207.1020 ($C_{10}H_{16}O_3Na$ requires 207.0997).

## Acknowledgments

One of the authors (T. H. L.) wishes to thank the University of the West Indies for the provision of funding and Professor J. Connolly, Glasgow University, for the mass spectrometry data.

## REFERENCES AND NOTES

1. Sea and Sky: Sponges http://www.seasky.org/reeflife/sea2a.htm (May 13th 2005).
2. Charley and the Aquanauts: Endeavours Magazine, UNC- Chapel Hill Winter 2005 http://research.unc.edu/endeavours/win2005/aquanauts.php (May 19th 2005).

3. D. T. A. Youssef, W. Y. Yoshida, M. Kelly, and P. J. Sheuer, *J . Nat. Prod.*, 2000, **63**, 1406.
4. M. Rotem and Y. Kashman, *Tetrahedron Lett.*, 1979, **20**, 3193.
5. A. Umeyama, C. Nagano, and S. Arihara, *J . Nat. Prod.*, 1997, **60**, 131.
6. M. Uno, S. Ohta, E. Ohta, and S. Ikegami, *J . Nat. Prod.*, 1996, **59**, 1146.
7. M. Fujita, Y. Nakao, S. Matsunaga, R. W. M. van Soest, Y. Itoh, M. Seiki, and N. Fusetani, *J . Nat. Prod.*, 2003, **66**, 569.
8. H. S. Garg and S. Agrawal, *Tetrahedron Lett.*, 1995, **36,** 9035.
9. A. Fukami, Y. Ikeda, S. Kondo, H. Naganawa, T. Takeuchi, S. Furuya, Y. Hirabayashi, K. Shimoike, S. Hosaka, Y. Watanabe, and K. Umezawa, *Tetrahedron Lett.*, 1997, **38**, 1201.
10. M. T. Davies-Coleman, D. J. Faulkner, G. M. Dubowchik, G. P. Roth, C. Polson, and C. Fairchild *J.Org.Chem.*, 1993, **58**, 5925.
11. S. Agrawal and H. S. Garg, *Indian J. Chem.*, 1997, **36B**, 343.
12. C. J. Smith, D, Abbanat, V. S. Bernan, W. M. Maiese, M. Greenstein, J. Jompa, A. Tahir, and C. M. Ireland, *J. Nat. Prod.*, 2000, **63**, 142.
13. R. Jadulco, P. Proksch, V. Wray, Sudarsono, A. Berg, and U. Gräfe, *J. Nat. Prod.*, 2001, **64**, 527.
14. M. Kobayashi, K. Higuchi, N. Murakami, H. Tajima, and S. Aoki, *Tetrahedron Lett.*, 1997, **38**, 2859.
15. D. T. A. Youssef, R.W. M. van Soest, and N. Fusetani, *J. Nat. Prod.*, 2003, **66**, 679.

16 D. T. A. Youssef, R.W. M. van Soest, and N. Fusetani, *J. Nat. Prod.*, 2003, **66**, 861.

17. S. I. Toth and F. J. Schmidtz, *J. Nat. Prod.*, 1994, **57**, 123.
18. S. Tsukamoto, H. Kato, H. Hirota, and N. Fusetani, *J. Nat. Prod.*, 1997, **60**, 126.
19. G. Y. S. Wang, M. Kuramato, D. Uemura, A. Yamada, K. Yamaguchi, and K. Yazawa, *Tetrahedron Lett.*, 1996, **37**, 1813.
20. Y. Nakao, T. Uehara, S. Matsunaga, N. Fusetani, and R. W. M van Soest, *J. Nat. Prod.*, 2002, **65**, 922.
21. G. Lardelli, P. Haverkanp-Begemann, P. D. Harkes, and A. S. M. van der Zijden, Unilever Ltd., 1962, Patent No. GB 893322 19620404, 11 pp.