Chemistry of Natural Compounds, Vol. 44, No. 1, 2008

TRISOXAZOLE MACROLIDES FROM THE SPONGE *Sarcotragus* SPECIES

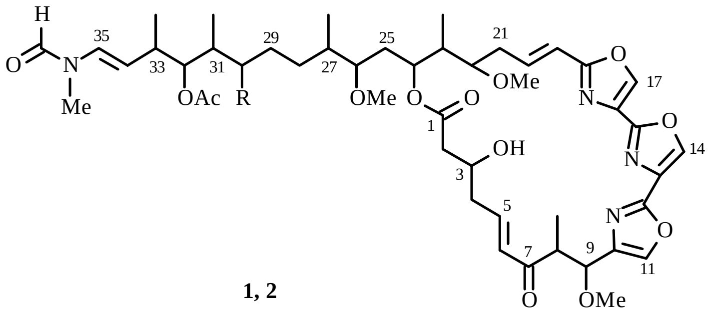
Yonghong Liu,[1*] Hong Ji,[1] Si Zhang,[1]
Jee H. Jung,[2] and Tunhai Xu[3]

UDC 547.945

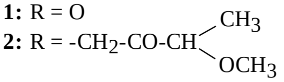
Marine sponges of the order Dictyoceratida have frequently provided a large number of linear furanoterpenoids [1–3]. In the course of our study on the cytotoxic substances of a sponge *Sarcotragus* sp., 35 cytotoxic terpenoids, three cyclitol derivatives, three indole alkaloids, three glycerolipids, and an ω-hydroxyl fatty acid were reported [4–11]. In a continuing study of the same sponge, two known trisoxazole macrolides mycalolide A (**1**) and C (**2**) were isolated [12].

The sponge was collected in July 1998 (15–25 m depth), off Cheju Island, Korea. The specimen has been described elsewhere [4].

Isolation was described in our previous report [4]. Compounds **1** (1.2 mg) and **2** (0.9 mg) were obtained by purification of fraction Fg4-8 by ODS HPLC.



1, 2



$$\mathbf{1}\text{: R = O}$$

$$\mathbf{2}\text{: R = -CH}_2\text{-CO-CH}\begin{matrix}\diagup \mathrm{CH_3} \\ \diagdown \mathrm{OCH_3}\end{matrix}$$

During our search for further cytotoxic constituents of the same sponge, macrolides **1** and **2** were isolated from the same sponge. The macrolides were chemically unique, incorporating three contiguous oxazole rings and a side chain terminating in *N*-methylformamide. Prior to this investigation, several cytotoxic and antifugal macrolides encompassing two or three oxazoles have been isolated from marine organisms such as nudibranchs and their egg masses [13–15], stony corals [16], and sponges of the genera *Halicbondria* [17–19], *Jaspis* [20], *Mycale* [21–23], and *Chondrosia* [24]. Sponge of the genus *Sarcotragus* (order *Dictioceritida*) have not previously been known to contain macrolides. Thus, it appears the distribution of oxazole containing macrolides can be expanded to this genus. The gross structures of the two compounds were elucidated by COSY, HSQC, HMBC, and mass spectroscopy and comparison with reported data [12, 22]. Although compound **1** eluted as a sharp symmetrical peak in RP-HPLC, it showed some doublets in a 1:2 ratio in the ^{1}H NMR spectrum, which suggested the presence of two slowly interconverting conformer. The ^{1}H NMR spectrum immediately revealed three singlets attributable to the trisoxazole moiety (δ 8.62, 8.57, and 8.08) and the 2:1 doublet of the formamide signals ((δ 8.36, 8.10), which are characteristic of the mycalolide,

---

1) Guangdong Key Laboratory of Marine Materia Medica, South China Sea Institute of Oceanology, Chinese Academy of Sciences, Guangzhou 510-301, China, fax: +86 20 84451672, e-mail: yonghongliu@scsio.ac.cn; 2) College of Pharmacy, Pusan National University, Busan 609–735, Korea; 3) School of Chinese Materia Medica, Beijing University of Chinese Medicine, Beijing 100102, China. Published in Khimiya Prirodnykh Soedinenii, No. 1, pp. 107-108, January-February, 2008. Original article submitted November 20, 2006.

kabiramide, ulapualide, halichondramide, and jaspisamide class of compounds. The magnitude of chemical shift differences of the doublets was proportional to the distance from the *N*-methyl formamide unit, suggesting that each pair of doublet signals was due to restricted rotation around the C-N bond of the N-Me formamide group. Comparison of the ^1H and ^{13}C NMR data of compounds **1** and **2** with those reported for the above-mentioned compounds showed that it is identical to mycalolide A and C [12, 22].

ACKNOWLEDGMENT

This study was supported by a grant from the Ministry of Maritime Affairs and Fisheries (Korea Sea Grant Program) and Hundred Talents Project of the Chinese Academy of Sciences.

REFERENCES

1. D. J. Faulkner, *Nat. Prod. Rep.*, **19**, 1 (2002), and earlier reviews cited therein.
2. J. W. Blunt, B. R. Copp, M. H. G. Munro, P. T. Northcote, and M. R. Prinsep, *Nat. Prod. Rep.*, **23**, 26 (2006), and earlier reviews cited therein.
3. Y. Liu, S. Zhang, and P. Abreu, *Nat. Prod. Rep.*, **23**, 630 (2006).
4. Y. Liu, B. K. Bae, N. Alam, J. Hong, C. J. Sim, C-O. Lee, K. S. Im, and J. H. Jung, *J. Nat. Prod.*, **64**, 1301 (2001).
5. Y. Liu, J. Hong, C-O. Lee, K. S. Im, N. D. Kim, J. S. Choi, and J. H. Jung, *J. Nat. Prod.*, **65**, 1307 (2002).
6. Y. Liu, C-O. Lee, J. Hong, and J. H. Jung, *Bull. Korean Chem. Soc.*, **23**, 1467 (2002).
7. Y. Liu, T. A. Mansoor, J. Hong, C-O. Lee, C. J. Sim, K. S. Im, and J. H. Jung, *J. Nat. Prod.*, **11**, 1451 (2003).
8. Y. Liu, J. H. Jung, and S. Zhang, *Biochem. Syst. Ecol.*, **34**, 453 (2006).
9. Y. Liu, J. H. Jung, H. Ji, and S. Zhang, *Molecules*, **11**, 714 (2006).
10. Y. Liu, J. H. Jung, and S. Zhang, *Biochem. Syst. Ecol.*, **34**, 774 (2006).
11. Y. Liu, J. H. Jung, and S. Zhang, *Chem. Nat. Compd.*, **42**, 487 (2006).
12. N. Fusetani, K. Yasumuro, S. Matsunaga, and K. Hashimoto, *Tetrahedron Lett.*, **30**, 2809 (1989).
13. J. A. Roesener and P. J. Scheuer, *J. Am. Chem. Soc.*, **108**, 846 (1986).
14. S. Matsunaga, N. Fusetani, and K. Hashimoto, *J. Am. Chem. Soc.*, **108**, 847 (1986).
15. S. Matsunaga, N. Fusetani, and K. Hashimoto, *J. Org. Chem.*, **54**, 1360 (1989).
16. M. A. Rashid, K. R. Gustafson, J. H. Cardellina, and M. R. Boyd, *J. Nat. Prod.*, **58**, 1120 (1995).
17. M. R. Kernan and D. J. Faulkner, *Tetrahedron Lett.*, **28**, 2809 (1987).
18. M. R. Kernan, T. F. Molinski, and D. J. Faulkner, *J. Org. Chem.*, **53**, 5014 (1988).
19. J. Kobayashi, M. Tsuda, H. Fuse, T. Sasaki, and Y. Mikami, *J. Nat. Prod.*, **60**, 150 (1997).
20. J. Kobayashi, O. Murata, and H. Shigemori, *J. Nat. Prod.*, **56**, 787 (1993).
21. S. Matsunaga, Y. Nogata, and N. Fusetani, *J. Nat. Prod.*, **61**, 663 (1998).
22. S. Matsunaga, T. Sugawara, and N. Fusetani, *J. Nat. Prod.*, **61**, 1164 (1998).
23. P. Phuwapraisirian, S. Matsunaga, R. W. M. V. Soest, and N. Fusetani, *J. Nat. Prod.*, **65**, 942 (2002).
24. J. Shin, H-S. Lee, J-Y. Kim, H. J. Shin, J-W. Ahn, and V. J. Paul, *J. Nat. Prod.*, **67**, 1889 (2004).