Tetrahedron Letters,Vol.30,No.26,pp 3363-3364,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Maxwell Pergamon Macmillan plc

REVISED STRUCTURES OF ANTHELIOLIDES A AND B

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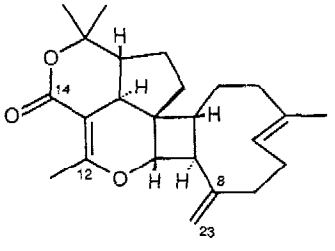
Summary: Revised structures for antheliolides A and B (**3** and **4**), as revealed by single crystal X-ray analysis of **3**, are presented together with corrected NMR assignments and modified biosynthetic proposals.

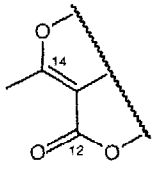
Recently the antheliolides A and B, novel acetoacetylated C_{24} diterpenoids, were isolated from the Red Sea soft coral *Anthelia glauca*. Extensive NMR analysis, in conjunction with other spectroscopic studies, led to the proposal of structure **1** for antheliolide A.[1] Chemical evidence and further spectral data indicated that antheliolide B is an 8,23-epoxy derivative of antheliolide A (i.e., proposed structure **2**).[1] However, it was subsequently recognized that the NMR data did not exclude a closely related permutation of the antheliolide oxacyclic rings. Herein we report a single crystal X-ray analysis of antheliolide A;[2] the crystal structure affirms that the antheliolides must indeed be reformulated as **3** and **4**. The correct structures are formally related to **1** and **2** by an end-to-end transposition of the acetoacetate moiety.

Previous proposals



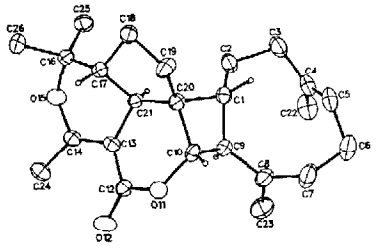
Antheliolide A **1**
Antheliolide B **2**
(8,23-epoxide)

Revised structures



Antheliolide A **3**
Antheliolide B **4**

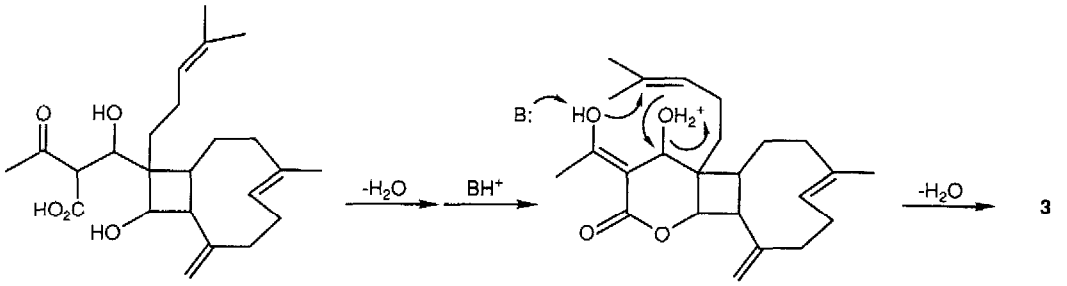
ORTEP drawing of 3



To reconcile the revised structures and the long range proton-carbon correlation 2D-NMR data, the reported ^{13}C chemical shifts of carbons 12 and 14 must be interchanged; for **3**, the correct values are 167.0 and 162.7 ppm, respectively. Interpretations of other spectroscopic data remain unaffected.

The biosynthesis of **3** and **4** can easily be accomodated by a minor modification of the scheme proposed earlier[1] for **1** and **2**. Whereas closure of putative intermediate **5** to furnish the cyclic enol ether moiety of **1** was envisioned previously, an alternative lactonization of **5** would furnish tricyclic intermediate **6** en route to

3. A cationic tandem cyclization involving the sidechain alkene, as invoked earlier, would then afford antheliolide A.



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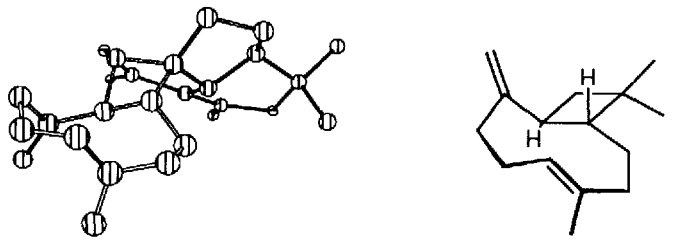
The conformation (7) of the nine-membered ring in crystalline **3** differs markedly from the preferred orientation reported previously for caryophyllene (8).[3] Other notable aspects of antheliolide structure, including solution conformations, absolute configurations, and the relative stereochemistry of the epoxide moiety in antheliolide B, remain to be elucidated.



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Acknowledgement. Support for this investigation was provided by the National Institutes of Health (National Institute of Neurological and Communicative Disorders and Stroke) through grant NS 18254.

References and Footnotes

1. Green, D.; Carmely, S.; Benayahu, Y.; Kashman, Y. *Tetrahedron Lett.* **1988**, *29*, 1605-1608.

2. *Crystal data and details of the structure determination for antheliolide A.* Formula: $C_{24}H_{32}O_3$; formula weight: 368.52 amu; crystal class: orthorhombic; space group: $P2_12_12_1$; Z=4; cell constants: *a*, 8.544(2) Å; *b*, 10.746(1) Å; *c*, 23.146(1) Å; μ: 5.50 cm^{-1}; D_{calc}: 1.152 g/cm^3; radiation: Cu-K_α 1.54184 Å; θ range: 2-65°; *hkl* ranges: $0 \le h \le 10$, $0 \le k \le 12$, $0 \le l \le 27$; no. reflections measured: 2106; no. reflections used in refinement: 1912 [$F_o^2 > 3\sigma(F_o^2)$]; *R*: 0.049; R_w: 0.065; *S*: 1.71. The atomic coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

3. Shirahama, H.; Osawa, E.; Chhabra, B. R.; Shimokawa, T.; Yokono, T.; Kanaiwa, T.; Amiya, T.; Matsumoto, T. *Tetrahedron Lett.* **1981**, *22*, 1527-1528.

(Received in USA 27 March 1989)