Tetrahedron Letters, Vol.31, No.18, pp 2617-2618, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

NOVEL SECO- AND SECONORSESQUITERPENES HAVING A CYCLOPROPANE RING FROM THE OKINAWAN ACTINIA *ANTHOPLEURA PACIFICA* UCHIDA

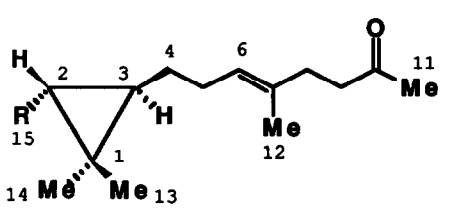
Guo-Chi Zheng, Masako Hatano, Midori O. Ishitsuka, Takenori Kusumi and Hiroshi Kakisawa*

Department of Chemistry, The University of Tsukuba, Tsukuba, Ibaraki 305, Japan

Abstract ——— Two new seco- and seconorsesquiterpenes, which do not obey the isoprene rule, have been isolated from the Okinawan actinia, and their structures and cytotoxicities have been investigated.

Recently, we have isolated bicyclo-*trans*-germacrenes such as 5-hydroperoxylepidoza-1(10),4(14)-diene and 1,10-epoxy-14-hydroperoxy-4-lepidozene, which exhibited potent cytotoxicities against murine melanoma cells, from the Okinawan actinia *Anthopleura pacifica*.[1] This report describes the isolation of two cytotoxic seco-sesquiterpenes that are biogenetically related with the bicyclo-*trans*-germacrenes.

Anthoplalone (**1**),[2] $C_{15}H_{24}O_2$, $[\alpha]_D$ -4.4 ° (c 0.09, $CHCl_3$), exhibited IR absorptions due to two carbonyl groups at 1712 and 1694 cm^{-1}. The ^{13}C-NMR spectrum shows the carbonyl carbon signals at δ 201.8 (d) and 208.8 (s) together with the olefinic carbon signals at δ 123.6 (d) and 135.5 (s), which accounts for three of four degrees of unsaturation of **1**, and, therefore, suggests a monocyclic nature of anthoplalone. The extensive NMR (500 MHz for ^1H) works (H-H and H-C COSY spectra) implied the presence of 4-methyl-3-octen-7-on-1-yl chain, indicating that **1** is composed of a cyclopropane ring. The *trans* relationship of the cyclopropane protons (H-2 and 3) was determined by their coupling constant (J = 6.0 Hz)[3] and the *E* configuration of the olefinic bond was deduced by the ^{13}C chemical shift of the olefinic methyl (δ 16.0; H-12). The rather low wave number (1694 cm^{-1}) of the IR absorption was consistent with the aldehyde group conjugated with the cyclopropane ring, and the coupling constant (J = 6.0 Hz) between the aldehyde proton (δ 9.27, d; H-15) and the cyclopropane methine (δ 1.36, m; H-2), which is rather large for ordinary $C(sp^3)H$-CHO system,[4] was also compatible with the cyclopropanecarbaldehyde moiety. On the basis of these findings the structure **1** was assigned for anthoplalone.[5]



1; R = CHO

2; R = H

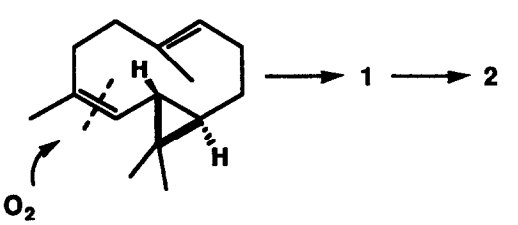


Fig.1 A possible biosynthetic pathway from lepidozene to anthoplalone (1) and noranthoplone (2).

Noranthoplone (2),[6] $C_{14}H_{24}O$, $[\alpha]_D$ -10.5° (c 0.56, $CHCl_3$), showed an intense IR absorption at 1720 cm^{-1} due to an acetyl group [^{1}H-NMR; δ 2.10 (3H, s)]. The lack of an aldehyde function in this compound is obvious from the ^{1}H-NMR spectrum, although it revealed the presence of the *geminal* methyls and the methyl-octenone chain found in **1**, and consideration of the molecular formula suggested the structure **2** for noranthoplone. In fact, the spectrum shows the highly shielded signals characteristic of cyclopropane protons at δ -0.15 (dd, J = 4.5, 5.4 Hz) and 0.33 (d, J = 4.5, 8.6 Hz) assignable as H-2a and H-2b besides the signal at δ 0.40 (m) ascribable to H-3.

Apparently structure **1** is *not* in accord with the isoprene rule. A possible biosynthetic pathway of **1** and **2** from lepidozene is shown in Figure 1. Since the absolute configurations of the lepidozanes in this actinia have been confirmed[1] to be identical with those of lepidozanes found in a terrestrial liverwort,[1,7] we suppose that the present terpenoids should have the absolute stereochemistry as shown in the respective structures. Meanwhile we propose secolepidozane and seconorlepidozane as the designation of the carbon frameworks of **1** and **2**, respectively.

Cytotoxicity of **1** and **2** against B-16 murine melanoma cells is as follows; **1**: 22 μg/ml, **2**: 16 μg/ml.

REFERENCES AND NOTES

(1) G. Zheng, T. Kusumi, M. O. Ishitsuka, A. Ichikawa, H. Yamamoto, H. Kakisawa, *J. Org. Chem.*, in press.

(2) **1**: FTIR ($CHCl_3$) 3030, 2872, 1712 (sh), 1694 cm^{-1}; GCMS m/z 236 (M^+), 221 (M - CH_3)$^+$, 193 (M-CH_3-H_2O)$^+$; ^{1}H NMR (500 MHz)* δ 1.16 (3H, s; H-13/14), 1.28 (3H, s; H-14/13), 1.36 (1H, t, J = 6.0 Hz; H-2), 1.45 (1H, m; H-3), 1.54 (2H, m; H-4), 1.60 (3H, s; H-12), 2.02 (2H, t, J = 8 Hz; H-5), 2.10 (3H, s; H-11), 2.24 (2H, q, J = 7.5 Hz; H-8), 2.44 (2H, t, J = 7.5 Hz; H-9), 5.05 (1H, t, J = 7.5 Hz; H-7), 9.27 (1H, d, J = 6.0 Hz; H-15); ^{13}C NMR (125 MHz, $CDCl_3$)* δ 16.0 (q, C-12), 21.5 (q, C-13/14), 22.3 (q, C-14/13), 22.5 (t, C-8), 26.7 (t, C-4), 30.0 (q, C-11), 31.0 (s, C-1), 35.6 (d, C-3), 39.3 (t, C-5), 43.5 (d, C-2), 43.7 (t, C-9), 123.6 (d, C-7), 135.5 (s, C-6), 201.8 (d, C-15), 208.8 (s, C-10).

(3) W. Brügel, *Handbook of NMR Spectral Parameters*, Vol. 1; Hyden & Sons; London, 1979, p 251.

(4) R. M. Silverstein, G. C. Bassler, T. C. Morrill, *Spectrometric Identification of Organic Compounds*, 4th edition; John Wiley & Sons; New York, 1981, p 235.

(5) Racemic **1** has been incidentally prepared as the intermediate of the total synthesis of (±)-lepidozene. The NMR properties of racemic **1** are identical with those of anthoplalone: See J. E. McMurry, G. K. Bosch, *J. Org. Chem.*, **1987**, 4885.

(6) **2**: FTIR (film) 1720, 1681, 1455, 1411, 1376, 1359, 1269, 1158 cm^{-1}; GCMS *m/z* 208 (M^+), 193 (M-CH_3)$^+$, 190 (M-H_2O)$^+$, 176 , 166 ; ^{1}H NMR (500 MHz)* δ -0.15 (1H, dd, J = 4.5, 5.4 Hz; H-2), 0.33 (1H, dd, J = 4.5, 8.6 Hz; H-2), 0.40 (m; H-3), 1.00 (3H, s; H-13/14), 1.02 (3H, s; H-14/13), 1.30-1.40 (2H, m; H-4), 1.60 (3H, bs; H-12), 2.01 (3H, s; H-11), 2.01 (2H, t, J = 7.5 Hz; H-5), 2.25 (2H, q, J = 7.5 Hz; H-8), 2.44 (2H, t, J = 7.5 Hz; H-9), 5.07 (1H, tq, J = 7.5, 1.2 Hz; H-7); ^{13}C NMR (125 MHz, $CDCl_3$)* δ 15.4 (s; C-1), 16.1 (q; C-12), 19.7 (t; C-2), 20.0 (q; C-14/13), 22.6 (t; C-8), 24.5 (d; C-3), 27.7 (q; C-13/14), 28.6 (t; C-4), 30.0 (q; C-11), 40.2 (t; C-5), 43.9 (t; C-9), 122.4 (d; C-7), 136.8 (s; C-6), 209.0 (s; C-10).

(*Assignments are based on the H-H and H-C COSY spectra.)

(7) A. Matsuo, H. Nozaki, N. Kubota, S. Uto, M. Nakayama, *J. Chem. Soc. Perkin Trans. 1*, **1984**, 203.

(Received in Japan 26 January 1990)