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LITOPHYTOLIDES A AND B, TWO NEW LIPID METABOLITES OF A SOFT CORAL LITOPHYTON SP.

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Abstract - The structures of litophytolides A and B, two new branched-chain lipids containing a γ-lactone ring isolated from a soft coral Litophyton sp., have been established as 1 and 2 on the basis of spectral and chemical evidence.

Although the isolation of prostaglandins from marine invertebrates of the Subclass Octocorallia has excited much interest to marine natural products chemists,[1] no different class of lipid metabolites originated from the fatty acid, which is closely related to the precursor of prostanoids, has so far been found in these animals. During a search for the biologically active constituents of a soft coral Litophyton sp.,[2] we encountered methyl (5Z,8Z,11Z,14Z,17Z)-5,8,11,14,17-icosapentaenoate and two new branched-chain lipids with a γ-lactone ring, the latter possessing an unsaturated linear alkyl side chain presumably derived from the former. In this paper, we wish to report the structures of these new lipid metabolites, named litophytolides A and B.

The major lipid, litophytolide A (1), was isolated as an optically active colorless oil (51 mg), $[\alpha]_D^{18}$ -17.2° (c 0.11, EtOH), from the dichloromethane soluble fraction of the methanol extract of frozen specimens (2.0 kg) through Sephadex LH-20 (MeOH) and silica gel (hexane - EtOAc 80:20) column chromatography, followed by reverse phase HPLC (ODS column, MeOH - H_2O 85:15). The structure 1 is assigned for this compound on the basis of the following spectral and chemical evidence. The molecular formula, $C_{27}H_{40}O_4$, was established by high resolution mass spectrometry (m/z 428.2910, M^+, Δ -1.5 mmu). The ir spectrum showed absorptions at 3020, 1655 (C=C), 1780 (γ-lactone), and 1740 (ester) cm^{-1}. The ^1H and ^{13}C nmr spectra[3] in combination with the ^1H - ^1H and ^1H - ^{13}C COSY experiments revealed the presence of the γ-lactone moiety 1a, to which a butyryl group and an unsaturated linear alkyl side chain are attached. The placement of the butyric ester at C-3 was also supported by the conversion of 1 into the butenolide 3, $C_{23}H_{32}O_2$, using DBU in chloroform. The relative configuration of the substituents decorating the γ-lactone ring in 1 was deduced from the inspection of ^1H nmr data. Namely, the 5.1 Hz coupling constant between H_{22} and H_{21} was consistent with cis stereochemistry whereas the rather small coupling constant (3.2 Hz) between H_{21} and H_2 indicated a trans relationship.[4] ^1H nmr signals centered at δ 5.70 (10 H, m) and 2.84 (8 H, m) revealed the presence of five double bonds in a linear alkyl side chain, all of which are doubly allylic. The positioning of these double bonds resulted from the ^1H nmr signals due to a vinylic ethyl group [δ 0.97 (3H, t, J=7.6 Hz) and 2.07 (2H, quint, J=7.6 Hz)] and the ms fragments at m/z 399 ($M^+ - C_2H_5$), 359 ($M^+ - C_5H_9$), 319 ($M^+ - C_8H_{13}$), and 199 ($M^+ - C_{17}H_{25}$). The *Z* geometry of all the double bonds was evident from ^{13}C nmr resonances at δ 25.88 and 25.98 (3C) which are characteristic for methylene carbons shielded by two allylic *Z*-type double bonds.[5,6]

The minor lipid, litophytolide B (2), was obtained as a colorless viscous oil (5.2 mg), $C_{25}H_{36}O_4$, $[\alpha]_D^{22}$ -25.4°(c 0.24, $CHCl_3$), and displayed the spectral data[7] quite similar to those of 1. The only significant difference in their ^1H and ^{13}C nmr data was the replacement of the butyryl group in 1 by the acetyl group [δ 2.12 (3H, s); δ 20.59 and 170.00] in 2. This relationship was verified by the DBU treatment of 2, which gave the butenolide 3.

The co-occurrence of litophytolides and methyl 5,8,11,14,17-icosapentaenoate in the same animal supports the previously proposed biogenesis[8,9] of branched-chain lipids with a γ-lactone ring that involves the condensation of unsaturated fatty acids with pyruvate.

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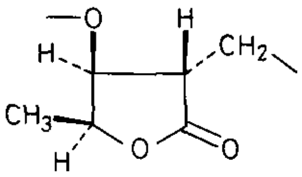
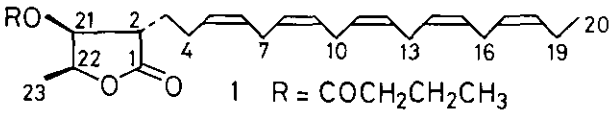
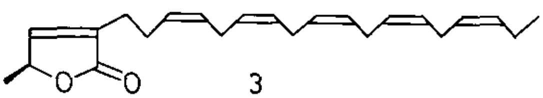


1a



1 R = $COCH_2CH_2CH_3$

2 R = Ac



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3) ^{1}H Nmr (400 MHz, $CDCl_3$) δ 0.96 (3H, t, J=7.3 Hz, 4'-H_3), 0.97 (3H, t, J=7.6 Hz, 20-H_3), 1.32 (3H, d, J=6.6 Hz, 23-H_3), 1.67 (2H, sext, J=7.3 Hz, 3'-H_2), 1.68 and 1.84 (1H each, m, 3-H_2), 2.07 (2H, quint, J=7.6 Hz, 19-H_2), 2.29 (2H, br q, J=7.5 Hz, 4-H_2), 2.34 (2H, t, J=7.3 Hz, 2'-H_2), 2.62 (1H, ddd, J=8.3, 7.1, and 3.2 Hz, 2-H), $\sim$2.85 (8H, m, 7-, 10-, 13-, and 16-H_2), 4.77 (1H, qd, J=6.6 and 5.1 Hz, 22-H), 5.19 (1H, dd, J=5.1 and 3.2 Hz, 21-H), and $\sim$5.70 (10H, olefinic protons); ^{13}C nmr (100 MHz, $CDCl_3$) δ 13.93 (4'), 14.53 (20), 14.59 (23), 18.66 (3'), 20.88 (19), 24.98 (4), 25.88 and 25.98 (3C) (7, 10, 13, and 16), 28.83 (3), 36.20 (2'), 46.52 (2), 75.34 (21), 76.59 (22), 126.89, 127.73 (2C), 127.78, 127.89, 128.18, 128.26, 128.42, 129.63, and 131.81 (5C=C), 172.19 (1'), and 175.53 (1).

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7) Ir (CCl_4) 3020, 1785, 1742, and 1655 cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$) δ 0.97 (3H, t, J=7.6 Hz, 20-H_3), 1.34 (3H, d, J=6.6 Hz, 23-H_3), 1.70 and 1.83 (1H each, m, 3-H_2), 2.08 (2H, quint, J=7.6 Hz, 19-H_2), 2.12 (3H, s, Ac), 2.29 (2H, br q, J=7.4 Hz, 4-H_2), 2.63 (1H, ddd, J=7.7, 7.1, and 2.9 Hz, 2-H), $\sim$2.85 (8H, m, 7-, 10-, 13-, and 16-H_2), 4.77 (1H, qd, J=6.6 and 5.1 Hz, 22-H), 5.19 (1H, dd, J=5.1 and 2.9 Hz, 21-H), and $\sim$5.40 (10H, m, olefinic protons); ^{13}C nmr (100 MHz, $CDCl_3$) δ 14.23 (2C) (20 and 23), 20.59 (2C) (19 and Ac), 24.69 (4), 25.61 and 25.71 (3C) (7, 10, 13, and 16), 28.53 (3), 46.32 (2), 75.54 (21), 76.59 (22), 127.12, 127.95 (3C), 128.11, 128.42, 128.51, 128.67, 129.92, and 132.08 (5C=C), 170.00 (Ac), and 176.06 (1); ms m/z 400 (M^+), 371 ($M^+ - C_2H_5$), 331 ($M^+ - C_5H_9$), 215 ($C_{16}H_{23}^+$), 175 ($C_{13}H_{19}^+$), 135 ($C_{10}H_{15}^+$), and 57 (base peak).

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