LITOPHYNINS F, G, AND H, THREE NEW DITERPENOIDS FROM A SOFT CORAL LITOPHYTON SP.

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Abstract-----Three new diterpenoids, litophynins F (**1**), G (**2**), and H (**3**), have been isolated from a soft coral Litophyton sp. and their structures were determined by spectroscopic and chemical methods.

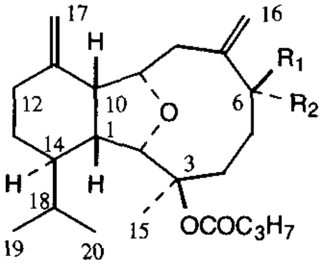
In previous papers,[1] we have described the isolation of five diterpenoids of the eunicellin class from a soft coral Litophyton sp. Further investigation of the same animal has resulted in the isolation of three additional congeners, litophynins F, G, and H, in the yields of 0.0032%, 0.00049%, and 0.00077% (on the basis of wet weight), respectively. The present paper concerns with the structures of these new compounds. Litophynin G exhibits insect growth inhibitory activity against the silkworm, Bombyx mori L.[2]

Litophynin F (**1**)[3] was isolated as an optically active amorphous solid, $[\alpha]_D^{24}$ -9.4° (c 0.43, $CHCl_3$), from the methanol extract of frozen specimens through Sephadex LH-20 (MeOH) and silica gel (hexane/EtOAc) column chromatography, followed by reverse phase HPLC (ODS column, $MeOH/H_2O$). The molecular formula of $C_{24}H_{38}O_4$ was established by high resolution ms (m/z 390.2759, M^+, Δ -1.1 mmu) in combination with the ^{13}C nmr data. It showed ir absorptions indicative of hydroxyl (3610, 3460) and ester (1725 cm^{-1}) groups, and formed a monoacetate **4**,[4] $C_{26}H_{40}O_5$, on acetylation with acetic anhydride-pyridine. The ^1H and ^{13}C nmr spectra of **4** showed the presence of one isopropyl [δ_H 0.75, 0.97 (3H each, d, J=6.8 Hz), and 1.89 (1H, m); δ_C 15.58, 21.96, and 27.45], one tertiary methyl [δ_H 1.62 (3H, s); δ_C 22.08], two exocyclic methylenes [δ_H 4.66, 4.80 (1H each, t, J=1.9 Hz), 5.08, and 5.35 (1H each, d, J=1.0 Hz); δ_C 111.23, 117.88, 146.37, and 147.23], one secondary acetoxyl [δ_H 1.99 (3H, s) and 5.25 (1H, dd, J=11.3 and 4.5 Hz); δ_C 21.39, 75.04, and

170.53], and one butyryl groups [δ_H 0.92 (3H, t, J=7.3 Hz), 1.58 (2H, sext, J=7.3 Hz), and 2.12 and 2.13 (1H each, t, J=7.3 Hz); δ_C 13.63, 18.58, 37.46, and 172.67]. The ^1H-^1H and ^1H-^{13}C COSY spectra displayed the proton connectivities compatible with the carbon frame work of eunicellin (5).[5] In compound 4, however, two exocyclic methylene groups were placed at C_7 and C_{11}. The presence of a long-range coupling between 16-Ha (δ 5.08) and a carbinyl proton (δ 5.25) suggested the location of the acetoxyl group at C_6. Observations of NOEs between 15-Me and 6-H, between 6-H and 8α-H, and between 16-Ha and 17-Ha indicated the β-orientation of the acetoxyl group. This was also supported by the coupling pattern of 6-H (dd, J=11.3 and 4.5 Hz) as illustrated in 4a. Based on these data together with the pertinent ^{13}C nmr data, we assigned the structure (1) for litophynin F.

Litophynin G (2),[6] fine needles, mp 134-136 °C, $C_{24}H_{36}O_4$, $[\alpha]_D^{23}$ -26.1° (c 0.11, $CHCl_3$), showed spectral data similar to those of 1 except that a secondary alcohol was replaced by a ketone (ν_{max} 1690 cm^{-1}; δ_C 205.83) in 2. This was confirmed by oxidation of 1 with pyridinium chlorochromate to 2.

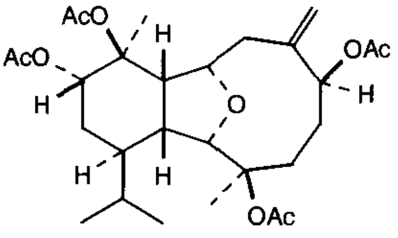
Litophynin H (3)[7] was obtained as an amorphous solid, $C_{24}H_{38}O_5$, $[\alpha]_D^{20}$ +31.4° (c 0.12, $CHCl_3$), and also showed the spectral data very similar to those of 1 except for an additional secondary hydroxyl group [δ_H 4.41 (1H, dd, J=10.4 and 4.0 Hz) and 4.43 (1H, br t, J=2.9 Hz); δ_C 71.75 and 72.37] in 3. The detailed ^1H nmr analysis was consistent with the structure 3. The second hydroxyl group was likely located at $C_{12\alpha}$ judging from the chemical shift and coupling pattern of the carbinyl proton [δ 4.43 (1H, br t, J=2.9 Hz)]. This was also supported by the observation of a long-range coupling between the carbinyl proton and 17-Hb.



1 $R_1 = OH, R_2 = H$

2 $R_1, R_2 = O$

4 $R_1 = OAc, R_2 = H$



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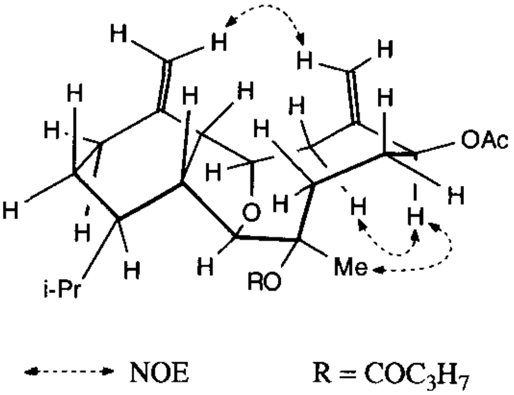
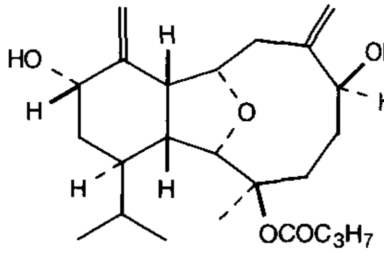


$R = COC_3H_7$

4a



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2) Litophynin G inhibited the growth of the second instar larvae of the silkworm (ED_{50} 42 ppm), while litophynins F and H were inactive at 100 ppm. The ecological role of these compounds in marine habitats will be discussed elsewhere.

3) **1**: Ir (CCl_4) 3610, 3460, 3075, 1640, and 900 cm^{-1}; ms *m/z* 390.2759 (M^+, $C_{24}H_{38}O_4$, Δ -1.1 mmu).

4) **4**: $[\alpha]_D^{22}$ -26.5° (c 0.14, $CHCl_3$); Ir (CCl_4) 3060, 1735, 1640, 1240, and 890 cm^{-1}; ms *m/z* 432.2890 (M^+, $C_{26}H_{40}O_5$, Δ +1.5 mmu); ^1H nmr (400 MHz, $CDCl_3$) δ 0.75 and 0.97 (3H each, d, J=6.8 Hz, 19- and 20-H_3), 0.92 (3H, t, J=7.3 Hz, 4'-H_3), 1.30 (1H, dddd, J=13.0, 12.0, 3.5, and 3.0 Hz, 14-H), 1.58 (2H, sext, J=7.3 Hz, 3'-H_2), 1.62 (3H, s, 15-H_3), 1.89 (1H, m, 18-H), 1.99 (3H, s, Ac), 2.12 and 2.13 (1H each, t, J=7.3 Hz, 2'-H_2), 2.24 (1H, dd, J=12.0 and 7.1 Hz, 1-H), 3.00 (1H, m, 10-H), 3.71 (1H, s, 2-H), 4.12 (1H, dd, J=10.7 and 4.6 Hz, 9-H), 4.66 and 4.80, (1H each, t, J=1.9 Hz, 17-H_2), 5.08 and 5.35 (1H each, d, J=1.0 Hz, 16-H_2), and 5.25 (1H, dd, J=11.3 and 4.5 Hz, 6-H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 13.63

(C-4'), 15.58 (C-19), 18.58 (C-3'), 21.39 (Ac), 21.96 (C-20), 22.08 (C-15), 25.36 (C-13), 27.45 (C-18), 27.92 (C-5), 31.78 (C-12), 32.24 (C-4), 37.46 (C-2'), 38.70 (C-8), 44.24 (C-14), 44.69 (C-1), 47.63 (C-10), 75.04 (C-6), 80.01 (C-9), 84.52 (C-3), 90.94 (C-2), 111.23 (C-17), 117.88 (C-16), 146.37 (C-11), 147.23 (C-7), 170.53 (Ac), and 172.67 (C-1').

5) O. Kennard, D. G. Watson, L. Riva di Sanseverino, B. Tursch, R. Bosmans, and C. Djerassi, *Tetrahedron Lett.*, **1968**, 2879.

6) **2**: Ir (CCl_4) 3070, 1735, 1690, 1640, and 895 cm^{-1}; ms *m/z* 388.2621 (M^+, $C_{24}H_{36}O_4$, Δ + 0.7 mmu); ^{1}H nmr (400 MHz, $CDCl_3$) δ 0.76 and 0.96 (3H each, d, J=6.8 Hz, 19- and 20-H_3), 0.97 (3H, t, J=7.3 Hz, 4'-H_3), 1.29 (1H, br t, J=12.5 Hz, 14-H), 1.50 (3H, s, 15-H_3), 1.64 (2H, sext, J=7.3 Hz, 3'-H_2), 1.77 (1H, m, 18-H), 2.22 (2H, t, J=7.3 Hz, 2'-H_2), 2.77 (1H, dd, J=12.0 and 7.4 Hz, 1-H), 3.05 (1H, dd, J=10.3 and 7.4 Hz, 10-H), 3.68 (1H, s, 2-H), 4.04 (1H, ddd, J=10.3, 5.9, and 2.2 Hz, 9-H), 4.70 (1H, br s, 17-Ha), 4.83 (1H, t, J=1.9 Hz, 17-Hb), and, 5.24 and 5.40 (1H each, s, 16-H_2); ^{13}C nmr (100 MHz, $CDCl_3$) δ 13.66 (C-4'), 15.38 (C-19), 18.52 (C-3'), 21.92 (C-20), 22.76 (C-15), 25.29 (C-13), 27.76 (C-18), 31.57 (C-4), 31.76 (C-12), 37.46 (C-2'), 37.52 (C-5), 38.08 (C-8), 43.64 (C-14), 45.42 (C-1), 48.95 (C-10), 78.55 (C-9), 84.27 (C-3), 91.48 (C-2), 111.17 (C-17), 117.33 (C-16), 146.01 (C-11), 147.89 (C-7), 172.59 (C-1'), and 205.83 (C-6).

7) **3**: Ir ($CHCl_3$) 3600, 3350, 1725, 1640, and 915 cm^{-1}; ms *m/z* 388.2637 (M^+-H_2O, $C_{24}H_{36}O_4$, Δ +2.3 mmu); ^{1}H nmr (400 MHz, $CDCl_3$) δ 0.77 and 0.99 (3H each, d, J=6.8 Hz, 19- and 20-H_3), 0.92 (3H, t, J=7.3 Hz, 4'-H_3), 1.59 (2H, sext, J=7.3 Hz, 3'-H_2), 1.64 (3H, s, 15-H_3), 1.87 (1H, m, 14-H), 1.98 (1H, m, 18-H), 2.12 and 2.13 (1H each, J=7.3 Hz, 2'-H_2), 2.24 (1H, dd, J=12.2 and 8.0 Hz, 1-H), 3.07 (1H, dd, J=10.4 and 8.0 Hz, 10-H), 3.80 (1H, s, 2-H), 4.41 (1H, dd, J=10.4 and 4.0 Hz, 6-H), 4.43 (1H, br t, J=2.9 Hz, 12-H), 4.54 (1H, dd, J=10.4 and 4.7 Hz, 9-H), 4.86 and 5.11 (1H each, d, J=1.8 Hz, 17-H_2), and, 5.10 and 5.45 (1H each, s, 16-H_2); ^{13}C nmr (100 MHz, $CDCl_3$) δ 13.63 (C-4'), 15.51 (C-19), 18.61 (C-3'), 21.74 (C-20), 22.14 (C-15), 27.00 (C-18), 28.71 (C-5), 31.25 (C-13), 35.71 (C-4), 36.02 (C-14), 37.51 (C-2'), 38.63 (C-8), 43.80 (C-1), 45.94 (C-10), 71.75 (C-12), 72.37 (C-6), 81.95 (C-9), 84.81 (C-3), 90.33 (C-2), 115.94 (C-17), 116.48 (C-16), 146.77 (C-11), 151.25 (C-7), and 172.61 (C-1').

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