CALICOPHIRINS A AND B, TWO NEW INSECT GROWTH INHIBITORY DITERPENOIDS FROM A GORGONIAN CORAL CALICOGORGIA SP.

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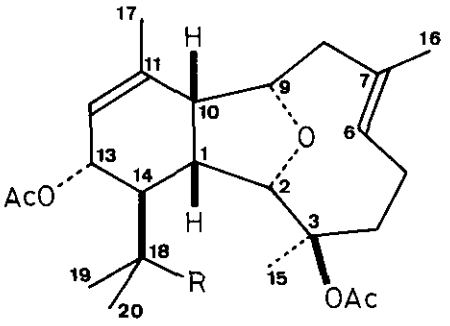
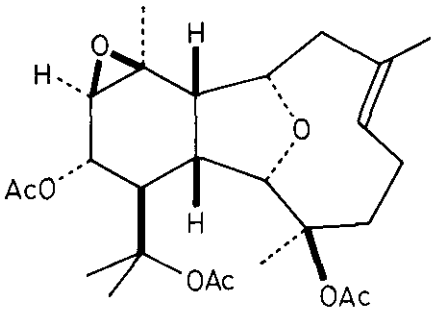
Abstract-----Two new diterpenoids, calicophirins A and B, which exhibit insect growth inhibitory activity against the silkworm, Bombyx mori L., have been isolated from a gorgonian coral Calicogorgia sp. and their structures were fully characterized by extensive 2D-nmr studies.

The gorgonian corals have been shown to possess a wide variety of secondary metabolites, including terpenoids, steroids, and lipids.[1] A number of these terpenoids exhibit interesting biological activities, e.g. ichthyotoxicity, cytotoxicity, and antifouling activity.[1] During a search of the biologically active constituents of marine invertebrates, we have examined the methanol extract of Calicogorgia sp., which found to have an insect growth inhibitory activity against the silkworm, Bombyx mori L. Monitoring fractionations of the methanol extract by artificial diet feeding assay against silkworm larvae[2] led to the isolation of ophirin (**1**)[3] and two new diterpenoids, all responsible to the observed activity.[4] This paper deals with the structures of these new compounds, named calicophirins A and B.

Calicophirin A (**2**)[5] was isolated as an optically active colorless oil, $[\alpha]_D^{19}$ -92.3° (c 0.37, $CHCl_3$), and had a molecular formula of $C_{26}H_{38}O_8$ on the basis of high resolution ms (m/z 478.2593, M^+, Δ +2.7 mmu). The close similarity between **2** and ophirin was predicated by the spectroscopic data.[3,5] The ir spectrum of **2** showed prominent peaks due to acetoxyl groups at 1735 and 1245 cm^{-1}. The ^{13}C nmr spectrum included twenty signals consistent with the ophirin type skeleton. In addition, the ^1H and ^{13}C nmr data, which were completely assigned by the ^1H-^1H and ^1H-^{13}C COSY experiments, revealed the presence of one trisubstituted double bond [δ_H 5.46 (1H, br t, J=8.3 Hz); δ_C 125.60 and 129.78], five deshielded methyl groups





1 R = OAc
3 R = H

2

[δ_H 1.37, 1.43, 1.58, 1.75, and 1.82 (3H each, s); δ_C 18.34, 20.96, 21.36, 25.36, and 25.80], and three acetyl groups [δ_H 1.92, 1.99, and 2.07 (3H, each, s); δ_C 21.74, 22.53, 22.75, 169.52, 169.74, and 170.29]. The only significant difference in their ^1H and ^{13}C nmr data was the replacement of the double bond in **1** by an epoxide [δ_H 3.34 (1H, d, J=5.2 Hz); δ_C 58.30 and 60.41] in **2**. The location of the epoxide at C_{11}-C_{12} was evident from the comparison of the ^1H and ^{13}C nmr data of both compounds. Observations of an NOE between 9-H and 11-Me and a W-coupling between 12-H and 14-H defined the configuration of the epoxide ring as shown in Fig. 1. Thus, the structure (**2**) is assigned to calicophirin A.

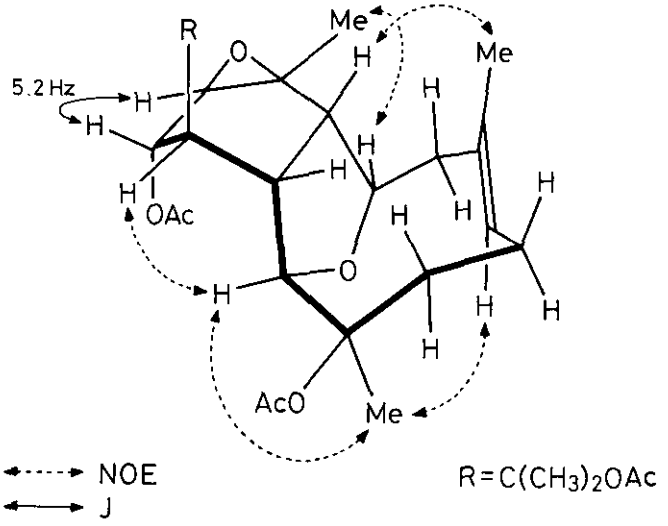


Figure 1

Calicophirin B (3)[6] was obtained as a colorless oil, $C_{24}H_{36}O_5$, $[\alpha]_D^{19}$ -106° (c 0.46, $CHCl_3$), and exhibited spectral data very similar to those of **1** except for the presence of two acetoxyl groups, one fewer than those of **1**. The ^1H and ^{13}C nmr spectra displayed signals due to an isopropyl group [δ_H 0.98 (6H, d, J=6.7 Hz) and 1.67 (1H, m); δ_C 21.00, 21.51, and 31.01], showing the lack of the acetoxyl group at C_{18} present in **1**. Therefore, we deduced the structure (3) for calicophirin B.

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4 The ED_{50}-values, the effective doses for 50% growth inhibition, of calicophirins A and B against Bombyx mori L. were 20 ppm and 52 ppm, respectively.

5 ^1H Nmr (400 MHz, $CDCl_3$) δ 1.37, 1.43, 1.58, 1.75, and 1.82 (3H each, s, 17, 19, 20, 16, and 15-H_3), 1.92, 1.99, and 2.07 (3H each, s, 3Ac), 3.34 (1H, d, J=5.2 Hz, 12-H), 4.28 (1H, d, J=10.4 Hz, 2-H), 4.45 (1H, d, J=6.1 Hz, 9-H), 5.44 (1H, d, J=5.2 Hz, 13-H), and 5.46 (1H, br t, J=8.3 Hz, 6-H): ^{13}C nmr (100 MHz, $CDCl_3$) δ 18.34 (16), 20.96 (17), 21.36 (15), 21.74, 22.53, 22.75 (3Ac), 22.04 (5), 25.36 (19), 25.80 (20), 30.85 (4), 35.80 (1), 43.62 (14), 44.99 (8), 46.75 (10), 58.30 (12), 60.41 (11), 67.27 (13), 79.92 (9), 83.76 (18), 87.58 (2), 90.21 (3), 125.60 (7), 129.78 (6), 169.52, 169.74, and 170.29 (3Ac).

6 ^1H Nmr (400 MHz, $CDCl_3$) δ 0.98 (6H, d, J=6.7 Hz, 19 and 20-H_3), 1.67 (1H, m, 18-H), 1.78 (6H, s, 16 and 17-H_3), 1.80 (3H, s, 15-H_3), 1.89 and 2.01 (3H each, s, 2Ac), 4.28 (1H, dd, J=5.7 and 2.6 Hz, 9-H), 4.49 (1H, d, J=8.2 Hz, 2-H), 5.19 (1H, br d, J=5.5 Hz, 13-H), 5.45 (1H, dd, J=10.7 and 6.7 Hz, 6-H), and 5.59 (1H, d, J=5.5 Hz, 12-H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 18.68 (16), 21.00 (19), 21.35 (15), 21.51 (20), 21.83 (17), 22.06, 22.78 (2Ac), 22.49 (5), 31.01 (18), 31.49 (4), 38.76 (1), 42.19 (14), 44.79 (8), 47.61 (10), 70.19 (13), 81.29 (9), 87.87 (2), 90.28 (3), 120.26 (12), 126.06 (7), 129.75 (6), 139.66 (11), 169.48, and 170.76 (2Ac); ms m/z 404.2587 (M^+, $C_{24}H_{36}O_5$, Δ +2.5 mmu).

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