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Alcyonin, a New Cladiellane Diterpene from the Soft Coral Sinularia flexibilis

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The structure of alcyonin, a diterpene isolated from the soft coral Sinularia flexibilis has been determined by spectroscopic and chemical methods.

Marine organisms produce a variety of unique compounds, and much attention has been paid on the marine resources from both biological and chemical aspects.[1] In the course of our study on the biologically active ingredients of marine coelenterates, we found that the methanol extract of the Okinawan soft coral Sinularia flexibilis exhibited considerable cytotoxicity. From the extract, we isolated a new compound designated alcyonin (**1**).

Alcyonin was supposed to be an acetate of a diterpene from its molecular formula ($C_{22}H_{34}O_5$; m/e 378.2403), an acetyl signal (δ 2.10) in the ^{1}H-NMR spectrum, the IR band due to an ester carbonyl at 1730 cm^{-1}, and the coexistence of the known diterpenes, litophynin A[2] and cladiellin.[3] Alcyonin (**1**) exhibits sharp and well-defined ^{1}H and ^{13}C-NMR signals. On the basis of the ^{1}H and ^{13}C-NMR spectra, the presence of the following moieties was deduced; an acetoxyl [^{1}H; δ 2.10 (s): ^{13}C; δ 171.0 (s), 21.4 (q)], an exomethylene [^{1}H; δ 5.28 (s), 5.51 (s): ^{13}C; δ 118.3 (t), 144.9 (s)], a trisubstituted olefin [^{1}H; δ 5.51 (bs): ^{13}C; δ 123.6 (d), 130.6 (s)] bearing a methyl [^{1}H; δ 1.71 (3H, s)], an isopropyl [^{1}H; δ 0.75 (3H, d), 0.94 (3H, d), 1.88 (m)], and a tertiary methyl [^{1}H; δ 1.34 (3H, s)]. Besides these, there are four methines [^{1}H; δ 3.92 (d), 4.03 (ddd), 4.76 (dd), 5.06 (dd): ^{13}C; δ 73.1 (d), 82.9 (d), 83.7 (d), 88.5 (d)] and one quaternary carbon [^{13}C; δ 74.5 (s)] possessing oxygen atoms. Consideration of the molecular formula and the number of double bonds (two from ^{13}C-NMR) led to the tricyclic nature of alcyonin, and the existence of two hydroxy groups was deduced by the difference between the proton number anticipated from the molecular formula and that calculated from the ^{13}C-NMR (DEPT) spectrum, together with an intense IR band at 3300 cm^{-1}. By extensive decoupling difference experiments and ^{1}H-^{1}H COSY spectrum, the connectivity of the protons was firmly established,[4] and the structure **1** (without stereochemistry) was proposed for alcyonin. The structure was verified by the COLOC spectrum (J = 10 Hz) which enabled to connect the

proton networks separated by the quaternary carbons as shown by the arrows (^{1}H-^{13}C long-range coupling) in structure **1**. The phase-sensitive NOESY spectrum exhibits a number of NOE cross peaks, and by considering the NOEs, the stereochemical feature of alcyonin was deduced to be **1a**. The coupling pattern of the protons[4] is quite agreeable with the conformation.

In the attempted benzoylation (PhCOCl/DMAP/CH_2Cl_2/NEt_3, room temperature, 12 h), an unexpected product was obtained instead of the benzoate. The structure **2** of the product was determined by the high resolution MS ($C_{22}H_{32}O_5$; m/e 376.2261), the ^{1}H-^{1}H COSY, and phase-sensitive NOESY spectra. It is likely that this compound was produced by the acetalization of 3-OH to 6-carbonyl group that was formed by air-oxidation of 6-OH. Formation of the acetal **2** settled the position of the acetyl group on 4-oxygen.

Alcyonin (**1**) shows cytotoxic activity against Vero cells at IC_{50} 55 μg/ml.

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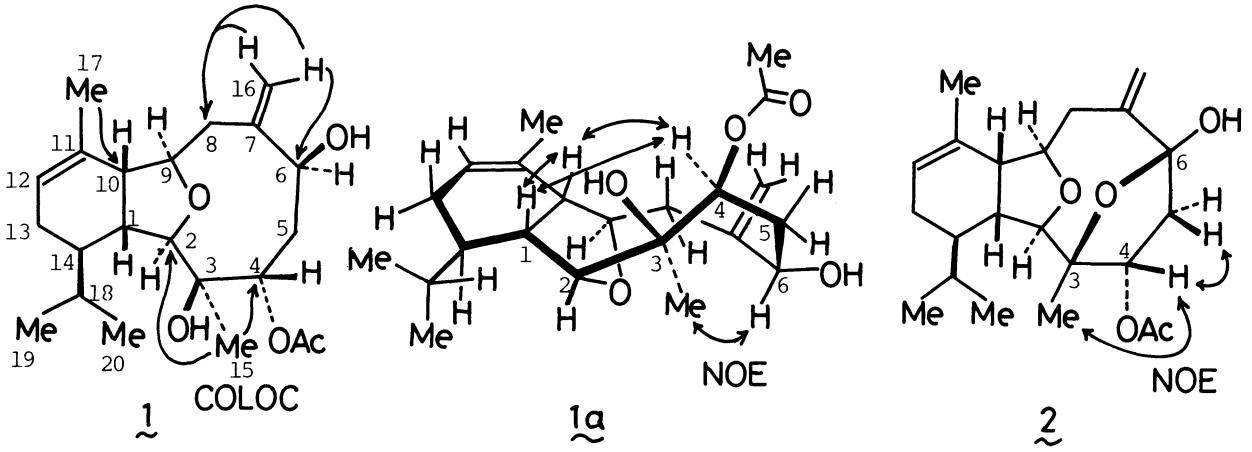

1 **1a** **2**

References

1) D. J. Faulkner, Nat. Prod. Rep., 4, 539 (1987).

2) M. Ochi, K. Futatsugi, H. Kotsuki, M. Ishii, and K. Shibata., Chem. Lett., 1987, 2207.

3) R. Kazlauskas, P. T. Murphy, R. J. Wells, and P. Schonholzer, Tetrahedron Lett., 1977, 4643.

4) **1**: ^{1}H-NMR (500 MHz; $CDCl_3$) δ 0.75, 0.94 (each 3H,d,J=7;19,20-H), 1.34 (s, 3H;15-H), 1.38 (m;14-H), 1.71 (3H,s;17-H), 1.80 (m;13-H), 1.88 (m;18-H), 1.95 (ddd,J=4.0,10.5,14.1;5-H), 1.97 (m;13-H), 2.10 (s,3H;Ac), 2.34 (ddd,J=4.5,9.5,14.1;5-H), 2.46 (ddd,J=3.5,8.2,10.5;1-H), 2.52 (dd,J=2.0,14.0;8-H), 2.58 (dd,J=8.2,8.5;10-H), 2.77 (dd,J=5.0,14.0;8-H), 3.92(d,J=3.5;2-H), 4.03 (ddd,J=2.0,5.0,8.5;9-H), 4.76 (dd,J=4.5,10.5;6-H), 5.06 (dd,J=4.0,9.5; 4-H), 5.28 (s;16-H), 5.51 (s;16-H), 5.51 (bs;12-H). ^{13}C-NMR ($CDCl_3$) δ 16.5 (20), 21.4 (Ac), 21.9 (19), 23.2 (13), 23.2 (15), 23.3 (17), 27.5 (18), 35.6 (5), 40.0 (14), 41.1(1), 41.7 (8), 44.6 (10), 73.1 (4), 74.5 (3), 82.9 (9), 83.7 (6), 88.5 (2), 118.3 (16), 123.6 (12), 130.6 (11), 144.9 (7), 171.0 (Ac).

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