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Setiformenol, Isolated from the Liverwort *Tetralophozia setiformis*, the First Example of Cembrane-Type Diterpene from Bryophytes

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Abstract: A new diterpene, setiformenol, has been isolated from the liverwort *Tetralophozia setiformis*, which constitutes the first example of cembrane-type diterpene so far from the liverwort.

Liverworts are rich sources of various terpenoids and aromatic compounds, which frequently exhibit interesting biological activities.[1-3] We have been investigating the chemical constituents of the liverwort found in various places in the world.[1] We have recently encountered to obtain the plants from eastern Europe. Now we report on the structure of cembrane-type diterpene, setiformenol, which is the first example from the liverwort, and the chemosystematics of Lophoziaceae liverwort.

The ether extract (0.93g) of *T. setiformis* (Ehrh.) Schljak., collected in Kola-Peninsula, Russia in 1990, was subjected to a combination of the silica gel, Sephadex LH-20, and silver nitrate-impregnated silica gel column chromatography to isolate *ent*-spathulenol (5mg) and setiformenol (**1**) (6mg).

Compound **1**, $C_{20}H_{34}O_2$ (HRMS *m/z* 306.2557), $[\alpha]_D^{17}$ +19.3° (*c* 1.22, $CHCl_3$), exhibits the absorption of a hydroxyl group at 3580 cm^{-1} in its IR spectrum. The ^1H NMR spectrum[4] showed the signals of two tertiary methyl groups, three olefinic methyl groups and an olefinic proton. The ^{13}C NMR spectrum[4] also showed the existence of two olefins and a carbon bearing the hydroxyl group. Since neither IR nor ^1H (^{13}C) NMR shows the absorption of a carbonyl group, the rest of the oxygen must be due to the ether linkages. The ^{13}C NMR exhibits two signals at δ 59.5 (C) and 63.5 (CH) and ^1H NMR at δ 2.76 (dd, *J*=6.2, 3.6 Hz), which are attributable to an epoxide ring. From these observations as well as the TOCSY spectrum (600 MHz), seven

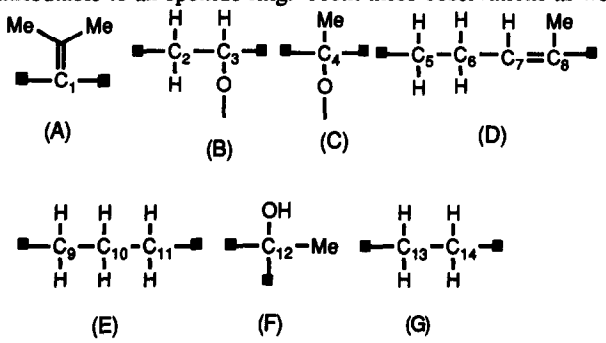
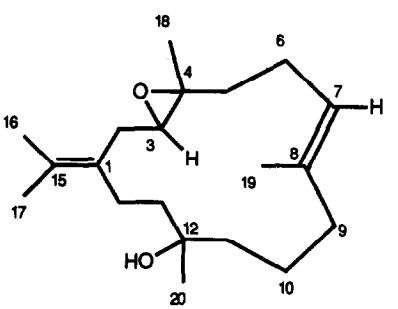


Fig.1. The partial structures of setiformenol (1).



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partial structures (A)-(G) shown in the Fig.1 are suggested. The ^{13}C-^{1}H COSY and HMBC spectra (400 MHz) can connect these partial structures to build up a cembrane skeleton as depicted in the formula **1**.

The geometry of the 7,8-double bond was determined to be *E* by the chemical shift of the C-19 methyl group (δ 16.0) and the NOE between H-7 and H-9. The relative configuration of the epoxide ring was elucidated by the NOE between H-2 and H-18 as shown in the formula. Although some other NOEs were detected in the NOESY spectrum, neither relative configuration of C-12 nor gross conformation of **1** were made clear.

Cembranes are found mostly in soft corals and some higher plants.[5] Quite recently Nakamura *et al.* also found some cembranoids in algae.[6,7] This report is the first example to find a cembrane-type diterpene in the liverwort. Setiformenol (**1**) is a new compound, although a similar compound is recently reported,[8] and these results show that the liverwort may be derived from the algae in the view point of the evolution.[9] *Gymnocolea inflata*,[10] *Lophozia ventricosa*,[11] and *Tritomaria quiquedentata*[12] belonging to Lophoziaceae have been investigated so far and they produce a various types of compounds. A detail of these chemosystematics will be reported elsewhere.

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4. ^{1}H NMR δ 5.07 (t, J=7, H-7), 2.76 (dd, J=6.2, 3.6, H-3), 2.28 (m, H-2), 2.26 (m, H-14a), 2.18-2.12 (m, H-6 and H-9a), 2.09 (m, H-5a), 1.83 (m, H-9b), 1.76 (m, H-14b), 1.69 (s, H-16), 1.68 (s, H-17), 1.68-1.44 (m, H-11, 13), 1.64 (s, H-19), 1.35 (m, H-10), 1.27 (s, H-18), 1.25 (m, H-5b), 1.22 (s, H-20); ^{13}C NMR δ 128.5 (C, C-15), 127.5 (C, C-1), 137.0 (C, C-8), 124.8 (CH, C-7), 72.6 (C, C-12), 63.5 (CH, C-3), 59.5 (C, C-4), 40.0 (CH_2, C-11), 39.5 (CH_2, C-9), 38.7 (CH_2, C-13), 38.5 (CH_2, C-5), 31.0 (CH_2, C-2), 29.0 (CH_3, C-20), 26.8 (CH_2, C-14), 23.8 (CH_2, C-6), 23.2 (CH_2, C-10), 21.0 (CH_3, C-16), 20.5 (CH_3, C-17), 17.0 (CH_3, C-18), 16.0 (CH_3, C-19).
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