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A Novel Skeletal Diterpenoid from the German Liverwort *Barbilophozia hatcheri* (EVANS) LOESKE

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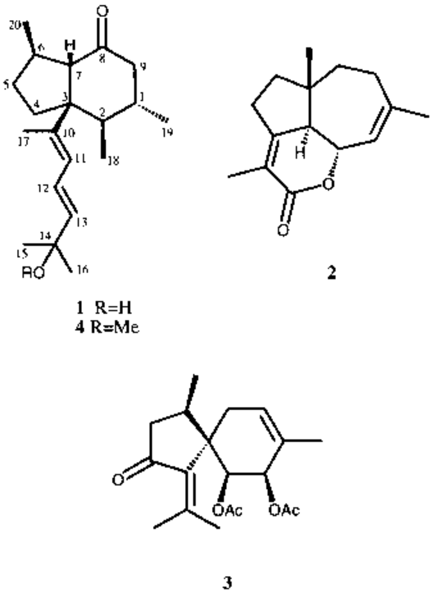
A novel skeletal diterpenoid, named hatcherenone, has been isolated from the German liverwort *Barbilophozia hatcheri*, together with the previously known daucane- and acorane-type sesquiterpenoids, hercynolactone and barbiacoradienone. Their structures were confirmed by NMR techniques.

Key words *Barbilophozia hatcheri*; Lophoziaceae; hatcherenone; hercynolactone; barbiacoradienone

Most *Barbilophozia* species belonging to the Lophoziaceae contain daucane-type sesquiterpenoid and dolabellane- and fusicoccane-type diterpenoids as the main components.[1—3] Therefore these compounds have been regarded as chemical markers of the *Barbilophozia* species.[1,2] The chemical constituents of *B. hatcheri* have already been reported with the isolation of sesqui- and diterpenoids.[4] As part of the search for new chemical constituents from the Hepaticae and investigation of their biological activity, we reinvestigated the German *B. hatcheri* and isolated a novel skeletal diterpenoid, named hatcherenone (**1**), along with two known sesquiterpenoids.

The ether extract of *B. hatcheri* was chromatographed on a silica gel, Sephadex LH-20, medium-pressure liquid chromatography (MPLC) column to give a novel diterpenoid, hatcherenone (**1**), and two known sesquiterpenoids, hercynolactone (**2**),[4] and barbiacoradienone (**3**), the stereostructure of which was established by X-ray crystallographic analysis.[3]



1 R=H
4 R=Me

2

3

Chart 1

Compound **1**[5] was easily converted into **4** through Sephadex LH-20 column chromatography (CH_2Cl_2–MeOH 1 : 1). The electron-impact mass spectrometry (EIMS) of **1** showed *m/z* 304 $[M]^+$ and its molecular formula was confirmed to be $C_{20}H_{32}O_2$ by high-resolution mass spectrometry (HRMS). The IR spectrum of **1** showed the presence of a hydroxyl and a carbonyl group. The ^1H-NMR spectrum contained the signals of three secondary methyls, two tertiary methyls, an olefinic methyl, and three olefinic protons. The ^{13}C-NMR spectrum contained the signals of six methyls, three methylenes, four methines, and two quaternary carbons, along with di- and trisubstituted olefinic carbons, and a carbonyl carbon. The above data suggested that **1** is a bicyclic diterpene ketoalcohol. The ^1H–^1H shift correlation spectroscopy (^1H–^1H COSY) and ^1H-detected heteronuclear multiple quantum coherence (HMQC) spectra indicated the presence of three partial structures [A]—[C] (Fig. 1). The connectivity of each partial structure was clarified by the ^1H-detected heteronuclear multiple-bond correlation (HMBC) spectrum, as shown in Fig. 1. Thus the structure of **1** was established to be a novel bicyclic diterpenoid with a C8 side chain. The nuclear Overhauser and exchange spectroscopy (NOESY) spectrum (Fig. 2) of **1** showed NOEs between (i) H-11 and H-13, (ii) H-17 and H-7, H-12, (iii) H-18 and H-1, H-19, (iv) H-19 and H-2, H-18 and (v) H-20, and H-5, H-7, respectively. Thus the stereostructure of hatcherenone was

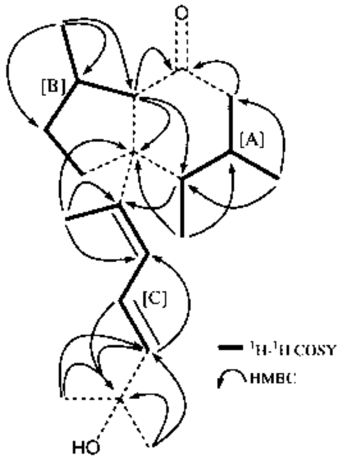


Fig. 1. ^1H–^1H and Long-Range ^{13}C–^1H Correlations of **1**

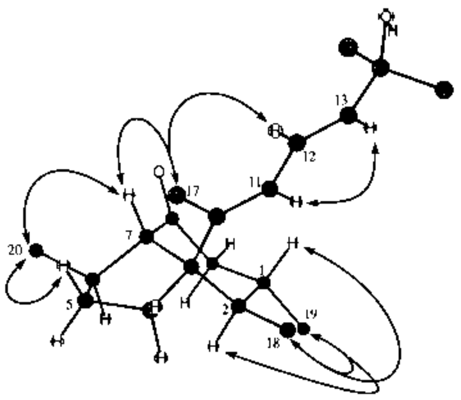


Fig. 2. NOEs of **1**

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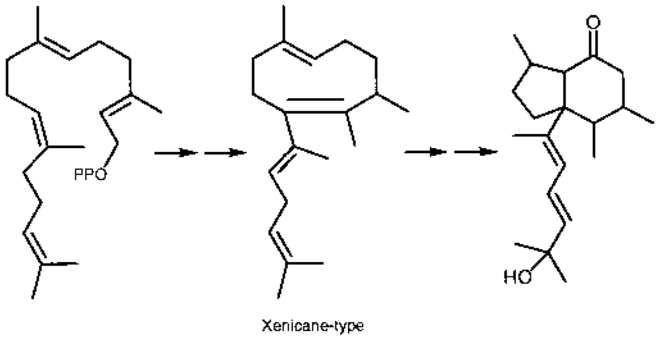

Fig. 3. Possible Biosynthesis of **1**

depicted as **1**. Furthermore, detailed spectroscopic analysis of **4**[6] showed that it possessed a methoxyl group at C-14 in place of the hydroxyl group in **1**. Since compound **1** is an allylic alcohol, it might be easily converted into **4** during chromatography on Sephadex LH-20 using CH_2Cl_2–MeOH as an elute. The absolute configuration of **1** was established by the application of the back-octant rule to the circular dichroic (CD) spectrum of **4** which showed a positive (295 nm) Cotton effect.

Most of the *Barbilophozia* species contain daucane-type sesquiterpenoids.[1,2] The present *B. hatcheri* elaborates a particularly large amount (*ca*. 19% for the crude extract) of hercynolactone (**2**). Thus compound **2** might be a very important chemical marker of *B. hatcheri*. Hatcherenone (**1**) might be biosynthesized from geranyl geranyl pyrophosphate *via* the xenicane-type diterpenoid found in marine organisms,[7] as shown in Fig. 3.

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5) $[\alpha]_D$ +27.4° (*c* 0.73, $CHCl_3$); HREIMS *m/z*: 304.2420 $[M]^+$ $C_{20}H_{32}O_2$ requires 304.2403; IR: 3464, 1691 cm^{-1}; δ_H (C_6D_6) 1.72—1.79 (3H, m, H-1, 4α, 5α), 1.21 (1H, m, H-2), 1.54 (1H, m, H-4β), 1.05 (1H, m, H-5β), 1.98 (1H, m, H-6), 2.33 (1H, dd, J=10.7, 1.4 Hz, H-7), 2.27 (1H, ddd, J=15.7, 4.1, 1.6 Hz, H-9α), 1.95 (1H, dd, J=15.7, 12.9 Hz, H-9β), 5.93 (1H, d-like, J=10.7 Hz, H-11), 6.59 (1H, dd, J=15.1, 10.7 Hz, H-12), 5.73 (1H, d, J=15.1 Hz, H-13), 1.14 (3H, s, H-15 or 16), 1.13 (3H, s, H-16 or 15), 1.68 (3H, d, J=1.1 Hz, H=17), 0.72 (3H, d, J=6.9 Hz, H-18), 0.64 (3H, d, J=6.3 Hz, H-19), 0.99 (3H, d, J=6.6 Hz, H-20); δ_C (C_6D_6) 34.4 (C-1), 41.8 (C-2), 60.9 (C-3), 35.3 (C-4), 31.3 (C-5), 38.3 (C-6), 68.4 (C-7), 211.9 (C-8), 47.0 (C-9), 141.61 (C-10), 122.7 (C-12), 141.6 (C-13), 70.5 (C-14), 30.2, 30.3 (C-15 or 16), 18.3 (C-17), 14.6 (C-18), 20.6 (C-19), 20.4 (C-20), C-11 overlapped in solvent signals.

6) $[\alpha]_D$ +61.9° (*c* 1.34, $CHCl_3$); HREIMS *m/z*: 318.2542 $[M]^+$ $C_{21}H_{34}O_2$ requires 318.2559; IR: 1698 cm^{-1}; δ_H ($CDCl_3$) 1.86 (1H, m, H-1), 1.59 (1H, m, H-2), 2.05—2.18 (2H, m, H-4α, 5α), 1.79 (1H, m, H-4β), 1.35 (1H, m, H-5β), 2.29 (1H, m, H-6), 2.22 (1H, dd, J=10.2, 1.4 Hz, H-7), 2.26 (1H, dd, J=15.9, 12.4 Hz, H-9), 2.31 (1H, ddd, J=15.9, 4.7, 1.4 Hz, H-9), 5.63 (1H, dt, J=10.7, 1.1 Hz, H-11), 6.30 (1H, dd, J=15.4, 10.4 Hz, H-12), 5.59 (1H, d, J=15.4 Hz, H-13), 1.28 (6H, s, H-15, 16), 1.78 (3H, d, J=0.8 Hz, H-17), 0.94 (3H, d, J=6.9 Hz, H-18), 0.95 (3H, d, J=6.3 Hz, H-19), 1.01 (3H, d, J=6.6 Hz, H-20), 3.16 (3H, s, OC$\underline{H}_3$); δ_C ($CDCl_3$) 34.4 (C-1), 41.5 (C-2), 61.1 (C-3), 35.3 (C-4), 31.3 (C-5), 38.5 (C-6), 68.1 (C-7), 214.8 (C-8), 46.9 (C-9), 141.8 (C-10), 127.6 (C-11), 125.2 (C-12), 138.2 (C-13), 75.0 (C-14), 25.9, 26.0 (C-15 or 16), 18.3 (C-17), 14.6 (C-18), 20.7 (C-19), 20.4 (C-20), 50.4 (O$\underline{C}H_3$); CD: $\Delta\varepsilon$ (nm) +1.08 (295), −0.03 (251) (*c* 5.3×10^{-4}, MeOH).

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