Bazzanane Sesquiterpenoids from the New Zealand Liverwort 
Frullania falciloba

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Two new bazzanane-type sesquiterpenoids have been isolated from the New Zealand liverwort Frullania falciloba. Their structures were confirmed by NMR and CD spectroscopy and chemical reactivity.

Key words liverwort; Frullania falciloba; bazzanane-type; sesquiterpenoid

Liverworts, which contain many different kinds of terpenoids and aromatic compounds, are distributed widely throughout the world.1,2) The southern hemisphere, especially New Zealand, has many more endemic liverworts than the northern hemisphere.3) We have previously reported several peculiar terpenoids and aromatic compounds from some liverworts endemic to New Zealand.4—8) These terpenoids and aromatic compounds are chemosystematically specific to liverworts and are used as genetic markers for the species.

Approximately 30 species of Frullania species have been recorded in New Zealand.9,10) In general, Frullania species contain elaborate sesquiterpene lactones, such as eudesmanolides and eremophilanolides, that cause potent allergenic contact dermatitis and/or contain bibenzyl derivatives.1,2,10) We have now chemically analyzed Frullania falciloba TNL. ex LEHM. The fractionation of the ether extract of F. falciloba resulted in the isolation of two new bazzanane-type sesquiterpenoids 1 and 2. Their structures were determined by spectroscopic and chemical means.

The IR spectrum of 1 established the presence of a conjugated carbonyl group (1685 cm⁻¹) and chemical-ionization mass spectrometry (CI-MS) confirmed a quasimolecular ion at m/z 219 [M+H]+. Its 1H-NMR spectrum (Table 1) contained three methyls (δ 0.99, 1.07, 1.78), an exo-methylene (δ 4.81, 5.04) and an olefinic proton (δ 6.59). The 13C-NMR spectrum (Table 2) exhibited 15 carbons. In combination with the distortionless enhancement by polarization transfer (DEPT) spectrum, we detected the presence of an exo-methylene (δ 158.6 C, 108.0 CH₂), trisubstituted olefinic carbons (δ 143.7 CH, 134.2 C) and a ketone carbonyl carbon (δ 200.7), as well as three methyls, five methylenes and two quaternary carbons. Based on the above spectral evidence, a molecular formula of C₁₅H₂₂O was suggested which indicated the presence of an ether linkage in the molecule.

The stereochemistry of 1 was determined to be the same as bazzanenol (3)11—13) by nuclear Overhauser and exchange spectroscopy (NOESY). To confirm the stereochemistry of 1, bazzanenol (3), already isolated from Bazzania pompeana, was oxidized with tetrapropylammonium perruthenate (TPAP). The stereochemistry at C-2 of 3 was reconfirmed to be S by the circular dichroism (CD) spectrum of its p-bromobenzoate derivative (4). The spectral and optical data of the oxidized product from 3 was completely identical to that of 1. Accordingly, the structure of 1, named 2-oxobazzanene, was established as shown in Fig. 1.

The IR spectrum of 2 showed the presence of a carbonyl group (1703 cm⁻¹) and its molecular formula was determined to be C₁₃H₁₂O₂ (Calcd for 234.1620) by high-resolution electron impact mass spectrometry (HR-EI-MS). The 1H- and 13C-NMR spectra (Tables 1, 2) showed the presence of an exo-methylene (δ 4.95, 5.05; δc 109.0 CH₂, 156.7 C), two methines associated with an oxygen atom (δ 116.0, 119.2; δc 75.3, 79.9), and a ketone carbonyl carbon (δc 211.9), as well as two secondary methyl, two tertiary methyls, a methine, four methylene, and two quaternary carbons. The above spectral data suggested that compound 2 was a tricyclic sesquiterpene ketone. The presence of an ether linkage in the molecule was supported by the results of the IR spectrum that lacked the characteristic absorption of a hydroxy group and the 13C-NMR spectrum that showed two oxygenated methines (δc 75.3, 79.9). The 1H-1H COSY spectrum of 2 exhibited the presence of three partial segments: i)

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CH₂–CH–CH(O–)–CH₂–, ii) –CH₂–, and iii) –CH₂–CH₂–CH(O–). The correlations of each partial segment were confirmed by the HMBC spectrum (Fig. 2). The NOESY spectrum clarified the stereochemistry of 2 as shown in Fig. 3. To obtain further confirmation of the structure, compound 2 was reduced with lithium aluminium hydride (LiAlH₄), followed by acetylation with pyridine and acetic anhydride to give a monoacetate 5 and unreacted monoalcohol 6. The IR, ¹H- and ¹³C-NMR spectra (Tables 1, 2) of 5 (C₁₇H₂₆O₃ Calcd for 278.1882) showed the presence of an acetoxy group (1740, 1240 cm⁻¹; δH 2.09; δC 21.4 CH₃, 170.5 C) and a newly observed oxygenated methine (δH 5.13; δC 69.0). Furthermore, the structure of 5 was determined to be a monoacetate by the ¹H–¹H COSY, HMBC and NOESY spectra. Compound 6 (C₁₅H₂₄O₂ Calcd for 236.1776) was found to be a monoalcohol by spectral analysis (Tables 1, 2). Accordingly, the structure of 2 was determined to be a bazzanane-type sesquiterpene with a ketone at C-2 and an ether linkage between C-4 and C-11. Thus the structure of 2, named bazzanenoxide, was established as shown in Fig. 3. Although the absolute configuration of 2,

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<th>H</th>
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<td>1.47 dd (16.2, 6.0)β</td>
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<tr>
<td>3</td>
<td>2.33 m</td>
<td>2.33 m</td>
<td>1.80 dddd (7.1, 3.3, 3.3, 3.3)</td>
<td>3.79 br s</td>
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<td>4</td>
<td>6.59 d sext. (6.0, 1.4)</td>
<td>4.18 ddd (3.8, 3.8, 1.9)</td>
<td>1.74 ddd (13.2, 4.1, 3.0)α</td>
<td>1.75 ddd (13.2, 4.4, 3.0)α</td>
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<td>5</td>
<td>2.68 br d (18.7)α</td>
<td>1.61 dd (13.5, 1.9)α</td>
<td>1.12 dd (13.2, 1.9)β</td>
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<td>2.07 ddd (18.7, 6.3, 1.6)β</td>
<td>2.08 dt (13.5, 3.8)β</td>
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<td>1.63—1.68 2H, m</td>
<td>1.62 m</td>
<td>1.63—1.68 2H, m</td>
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CH₂–CH(CH₂–CH(O–))–CH₂–, ii) –CH₂– and iii) –CH₂–CH₂–CH(O–). The correlations of each partial segment were confirmed by the HMBC spectrum (Fig. 2). The NOESY spectrum clarified the stereochemistry of 2 as shown in Fig. 3. To obtain further confirmation of the structure, compound 2 was reduced with lithium aluminium hydride (LiAlH₄), followed by acetylation with pyridine and acetic anhydride to give a monoacetate 5 and unreacted monoalcohol 6. The IR, ¹H- and ¹³C-NMR spectra (Tables 1, 2) of 5 (C₁₇H₂₆O₃ Calcd for 278.1882) showed the presence of an acetoxy group (1740, 1240 cm⁻¹; δH 2.09; δC 21.4 CH₃, 170.5 C) and a newly observed oxygenated methine (δH 5.13; δC 69.0). Furthermore, the structure of 5 was determined to be a monoacetate by the ¹H–¹H COSY, HMBC and NOESY spectra. Compound 6 (C₁₅H₂₄O₂ Calcd for 236.1776) was found to be a monoalcohol by spectral analysis (Tables 1, 2). Accordingly, the structure of 2 was determined to be a bazzanane-type sesquiterpene with a ketone at C-2 and an ether linkage between C-4 and C-11. Thus the structure of 2, named bazzanenoxide, was established as shown in Fig. 3. Although the absolute configuration of 2,
shown in Fig. 3, was assumed by the analysis of its CD spectrum ($\Delta \varepsilon_{295} +0.57$), further experiment is needed.

The isolation of sesquiterpenoids and aromatic compounds from $F$. falciloba, e.g., cent-cycloclorolene (7), $\beta$-bazzanene (8), 3-hydroxy-4,3'-dimethoxybenzyl (9), and 3-4' (methoxybenzyl)-5,7-dimethoxyphthalide (10), has previously been reported by our group$^{15,16}$ and Mali et al.$^{17}$ Bazzanene-type sesquiterpenoids are very rare in the plant kingdom.

This type of compound is mainly distributed in the liverwort Bazzania genus, making bazzanenes important chemical markers of the Bazzania species. In the present study, we report the isolation of two new bazzanenes 1 and 2 from $F$. falciloba. The presence of benzyl or phthalide derivatives could not be detected.

Experimental

General Methods Optical rotations were measured on a Jasco DIP-1000 polarimeter. IR spectra were recorded on a Shimadzu FTIR 8400S infrared spectrophotometer. UV spectra were recorded on a Shimadzu UV-1650PC UV-visible spectrophotometer. CD spectra were recorded on a Jasco J-725 spectropolarimeter. 1H- and 13C-NMR spectra were measured on Varian Unity-600 (1H, 600 MHz; 13C, 150 MHz) and Jeol Eclipse-400 (1H, 400 MHz; 13C, 100 MHz) NMR spectrometers. Chemical shift values are expressed in $\delta$ (ppm) downfield from tetramethylsilane as an internal standard ($\delta$-H,NMR), and relative to the solvent CDCl$_3$ ($\delta$-H$_2$NMR).

Plant Material

Frullania falciloba TAYL. EX LEHM. (NZ-267) was collected in Tree Trunk Gorge, New Zealand, in December 2000 and identified by Dr. J. E. Braggins (University of Auckland, New Zealand), and a voucher specimen was deposited in the Faculty of Pharmaceutical Sciences, Tokushima Bunri University.

Extraction and Isolation

The ether extract (205 mg) of $F$. falciloba was divided into seven fractions by column chromatography (CC) on silica gel using n-hexane-EtOAc gradient. Fraction 2 was chromatographed on Sephadex LH-20, silica gel, and preparative HPLC (Hemocors 5Si-U, 17:3 n-hexane-EtOAc) to give 2-oxobazzanene (1, 9.0 mg). Bazzanoxene (2) (12.6 mg) was isolated from Fr. 4 by chromatography on Sephadex LH-20 and preparative HPLC (Amerham Pharmacia Biotech, 1:1 CH$_2$Cl$_2$-MeOH as solvent). TLC spots were visualized under UV (254 nm) light and by spraying with Godin reagent$^{20}$ and 30% H$_2$SO$_4$, followed by heating.

Monacetate (5): Oil, [a]$_{D}^{28}$ $+267.1^\circ$ ($c = 1.74$), FT-IR cm$^{-1}$: 1740, 1240, 1100. 1H- and 13C-NMR: see Tables 1 and 2. HR-EL-MS m/z: 278.1882 (Caled for C$_{11}$H$_{10}$O$_{3}$; 278.1882). EI-MS m/z (int): 278 [M]$^+$ (6), 218 (3), 165 (9), 125 (7), 107 (66), 94 (100), 79 (71), 67 (17), 55 (34), 43 (79).

Monacolhol (6): Oil, [a]$_{D}^{28}$ $+283.8^\circ$ ($c = 0.94$). FT-IR cm$^{-1}$: 3422. 1H- and 13C-NMR: see Tables 1 and 2. HR-EL-MS m/z: 236.1765 (Caled for C$_{16}$H$_{14}$O$_{2}$; 236.1776). EI-MS m/z (int): 236 [M]$^+$ (17), 218 (5), 208 (4), 200 (4), 165 (34), 145 (12), 135 (13), 125 (14), 119 (22), 110 (44), 108 (33), 94 (100), 79 (49), 67 (14), 55 (21), 43 (21).

Exterification of 3 To a suspension of 3 (10 mg) in pyridine (2 ml) and CH$_3$Cl (1 ml) was added p-bromobenzoylchloride (42 mg) and 4-dimethylaminopropylidnorphamide (10 mg) and the mixture was stirred overnight at room temperature. The reaction mixture was filtered and purified on silica gel CC to yield the benzoate derivative 4 (6.2 mg). UV $\lambda_{max}$ (EtOH) mm (log e): 245 (3.73) $\lambda_{max}$ (EtOH): 306.7 $\lambda_{max}$ (EtOH): 219.1738 (Calcd for C$_{15}$H$_{23}$O$_3$: 245.35, 49 [M$^+$]+). HR-EL-MS m/z (int): 307 [M$^+$-CH$_3$] (8), 202 (16), 183 (58), 155 (12), 149 (7), 107 (100), 106 (89), 96 (34), 91 (29), 81 (41), 69 (7), 55 (11), 41 (7).

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References and Notes


