# New Acetyl Derivatives from Antarctic *Delisea fimbriata*

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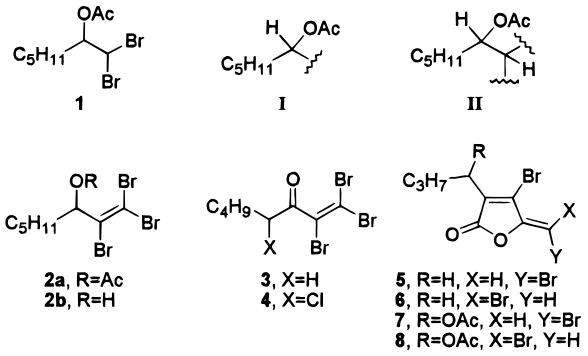
Compounds with three characteristic skeletons of members of the family Bonnemaisoneaceae were found to coexist in the alga *Delisea fimbriata*. The two new acetates **1** and **2a** were also isolated; this is the first isolation of acetates from this genus. The structures, chemical transformation, and biogenetic significance of **1** and **2a** are described.

The significant *in vitro* antimicrobial and antifungal activity of the extracts of several species of red algae within the family Bonnemaisoniaceae has led to the search for new metabolites from collections covering a wide geographic range. Seaweed from the genera *Asparagopsis*, *Delisea*, *Ptilonia*, and *Bonnemaisonia* have been studied and have proven to be a rich source of secondary metabolites based almost exclusively on acetate biosynthesis, which appears to be characteristic of the family.[1] The genus *Asparagopsis* has the particular property of producing halogenated substances[2] whose framework contains up to four carbon atoms, including methane, acetones, propanols, butenones, and acrylic and acetic acid derivatives, while genera such as *Delisea*, *Ptilonia*, and *Bonnemaisonia* display a variety of polyhalogenated compounds with between seven[2−6] and nine[7−17] carbon atoms, with the exception of a 12-carbon-atom metabolite recently isolated.[8]

Here, we report on the new metabolites **1** and **2a** from *Delisea fimbriata* (Lamour) as well as the reisolation of the polyhalogenated unsaturated ketones **3** and **4**[7] and the fimbrolides **5**−**8**[11−12] showing for the first time the coexistence of compounds derived from seven (compound **1**), eight (**2a**, **3**, and **4**), and nine (**5**−**8**) carbon atom skeletons found in the same species. *D. fimbriata* was collected by scuba off King George Island (South Shetland, Antarctic) at a depth of 30 m. Fractions of A−C were obtained by flash chromatography of the crude algal extract. The hexane:EtOAc (9:1) fraction from the chromatography column of portion B yielded a mixture of four components from which compounds **1** and **2a** were separated by recycling-HPLC.

Compound **1** was a colorless oil. The EIMS showed the molecular ion at *m*/*z* 313/315/317 with relative intensity for two bromine atoms in accordance with the empirical formula $C_9H_{16}Br_2O_2$. The ions at *m*/*z* 143 and *m*/*z* 83 were assigned to the fragments **I** and **I**−AcOH, respectively. The $^1$H NMR spectrum (200 MHz, $CDCl_3$) showed signals for the methyl group of an acetate [$\delta$ 2.15 (3H, s)] and an *n*-pentyl chain at $\delta$ 1.82 (2H, m), 1.32 (6H, m), and 0.96 (3H, broad s), which suggested the presence of fragment **I**. Other $^1$H NMR signals appeared at $\delta$ 5.08 (1H, dt) and at $\delta$ 5.75 (1H, d, $J$ = 3.35 Hz). Homonuclear proton-decoupling experiments




allowed the establishment of fragment **II**. The proton signal at $\delta$ 1.82 showed coupling to the doublet of triplets proton at $\delta$ 5.08, and irradiation of the methylene at $\delta$ 1.82 collapsed the signal at $\delta$ 5.08 to a doublet that possesses a coupling constant similar to that of the proton situated at $\delta$ 5.75. This shows that the two methines at $\delta$ 5.08 and $\delta$ 5.75 are adjacent, thus allowing the partial establishment of structure **II**. Consequently, the complete structure for the compound can be established as **1**, where the bromine atoms are the substituents at C-1.

Compound **2a** was also a colorless oil. The IR spectrum gave an absorption for an acetate group at 1743 cm$^{-1}$. The CIMS showed the molecular ion ($M^+ + 1$) at *m*/*z* 405/407/409/411 with relative intensity for three bromine atoms in accordance with the empirical formula $C_{10}H_{15}Br_3O_2$. The EIMS gave fragments at *m*/*z* 325/327/329 ($M^+ - Br$) and *m*/*z* 83 ($C_6H_{11}$). The $^1$H NMR spectrum showed signals at $\delta$ 2.10 (3H, s) and $\delta$ 5.70 (1H, t, $J$ = 7.16 Hz) for the methyl and geminal protons, respectively, corresponding to a secondary acetate group. At $\delta$ 0.89 (3H, broad s), 1.73 (2H, m), and 1.25 (6H, m), typical signals for an *n*-pentyl chain appeared. The $^{13}$C NMR showed the following 10 signals: two methyl groups at $\delta$ 20.79 (q) and 13.93 (q), four methylenes at $\delta$ 22.40 (t), 24.28 (t), 31.34 (t), and 32.82 (t), two olefinic carbons at $\delta$ 128.98 (s) and 91.16 (s), and the signals at $\delta$ 74.80 (d) and 169.72 (s) belonging to a methine and carbonyl group, respectively.

According to the degree of unsaturation expressed in the empirical formula, the compound should be linear. Because the molecule contains a tetrasubstituted double bond and an acetyl group, because five of the 10 carbon

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atoms of the molecule form an *n*-pentyl chain, and because the multiplicity of the proton on the carbon-bearing acetate group is a triplet, it can be stated that the substituents on the olefinic double bond are bromine and that the structure for the compound must be **2a**. The structure **2a** was confirmed by partial synthesis starting from **3**. Reduction of **3** with $NaBH_4$ in methanol at room temperature for 1 h gave the alcoholic derivative **2b** ($\delta$ 4.72, 1H, t, $J$ = 6.0 Hz), which was acetylated to give a material whose $^1$H-NMR spectrum was identical to the natural compound.

Fraction A, eluted with hexane−EtOAc (9:1), was chromatographed on R-HPLC using chloroform as eluent, affording the known compounds **3** and **4**, which have $^1$H-NMR data identical to those previously reported.[7,10] Likewise, the other two products **5** and **6** of the fraction B were purified and their structures identified.[11]

Fraction C, which eluted with hexane−EtOAc (8:2), was chromatographed on R-HPLC ($CHCl_3$), yielding **7** and **8**, which were identical ($^1$H-NMR) to the acetoxyfimbrolides previously isolated[11] from *D. fimbriata*.

From a study of the marine chemical literature of the Bonnemaisoniaceae it was interesting to note[1,3−17] that, within the family, the naturally occurring halogenated metabolites containing an acetate function appeared to be exclusive to the genera *Bonnemaisonia* and *Ptilonia*. The ocurrence of the acetylate compounds **1** and **2a** in *Delisea* is a novelty because until now the genus has been characterized by producing only polyhalogenated ketones. The compound **1** is also interesting from a biogenetic point of view. It appeared as the simplest, and probable biogenetic precursor, of most of the metabolites with a seven-carbon-atom skeleton coming from members of the family of the red algae Bonnemaisoniaceae.

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter using a Na lamp at 25 °C. IR spectra were obtained with a Perkin-Elmer 1650/FTIR spectrometer in $CHCl_3$ solutions. EI mass spectra (EIMS) spectra were taken on a Hewlett-Packard 5995; CIMS were determined with a Hewlett-Packard 5998 using methane as the reactive gas and HRMS on a VG Micromass ZAB-2F spectrometer. $^1$H NMR and $^{13}$C NMR spectra were measured employing a Bruker AMX 200 instrument operating at 200 MHz for $^1$H NMR and 50 MHz for $^{13}$C NMR, using TMS as internal standard. Recycling-HPLC separations were performed with a Japan Analytical LC-908, and the solvent utilized was chloroform. Merck silica gel 7734 and 7729 were used for column chromatography. The spray reagent for TLC was $H_2SO_4$:$H_2O$:AcOH (1:4:20).

**Plant Material.** *D. fimbriata* was collected by scuba off King George Island (South Shetland, Antarctic) at a depth of 30 m. A voucher specimen has been deposited at the Museo de Historia Natural, Santiago de Chile (no. R23B78Df).

**Extraction and Isolation.** The dried alga (61 g) was extracted with acetone at room temperature, and the acetone extract was concentrated to give a dark green residue (404 mg). This extract was chromatographed by flash chromatography on silica gel. Fraction A, which eluted with hexane−EtOAc (9:1) (53 mg), was chromatographed on R-HPLC ($CHCl_3$), affording **3** (27.4 mg) and **4** (2.0 mg). Fraction B, which also eluted with hexane−EtOAc (9:1) (83.3 mg), was chromatographed on R-HPLC ($CHCl_3$), affording **1** (27.4 mg), **2a** (2.0 mg), **5** (14.4 mg), and **6** (5.6 mg). Fraction C, which eluted with hexane−EtOAc (8:2) (98.8 mg), was chromatographed on R-HPLC ($CHCl_3$), affording **7** (4.7 mg) and **8** (22.8 mg).

**Compound 1:** colorless oil; $[\alpha]_D$ 0° (*c* 0.2, $CHCl_3$); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.90 (3H, broad s), 1.33 (6H, m), 1.82 (2H, m), 2.15 (3H, s), 5.08 (1H, dt), 5.75 (1H, d, $J$ = 3.55 Hz); EIMS *m*/*z* 314/316/318 [$M^+$], 197/199/201 [$C_3H_3Br_2$], 143 [$M^+ - CHBr_2$], 117/119 [$C_3H_2Br$], 83 [$C_6H_{11}$].

**Compound 2a:** colorless oil; $[\alpha]_D$ 0° (*c* 0.28, $CHCl_3$); IR ($CHCl_3$) $\nu$ max 1743 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.89 (3H, broad s), 1.25 (6H, m), 1.73 (2H, m), 2.10 (3H, s), 5.70 (1H, t, $J$ = 7.16 Hz); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$ 13.93 (q), 20.79 (q), 22.40 (t), 24.28 (t), 31.34 (t), 32.83 (t), 74.80 (d), 91.16 (s), 128.89 (s), 169.72 (s); EIMS *m*/*z* 325/327/329 [$M^+ - Br$], 283/285/287 [$M^+ - Br - (CH_2)_3 - AcOH$], 83 [$C_6H_{11}$], CIMS 403/405/407/409 [$M^+ - 1$], 405/407/409/411 [$M^+ + 1$], 433/435/437/439 [$M^+ + 29$], 445/447/449/451 [$M^+ + 41$], HRMS *m*/*z* [$M^+ - Br$] 328.9415, calcd for $C_{10}H_{15}O_2{}^{81}Br_2$ found 328.9561.

**Reduction of 3.** A solution of **3** (10 mg) in dry EtOH (2 mL) was treated with $NaBH_4$ and stirred at room temperature for 1 h. The solution was poured into water and extracted with $CHCl_3$. The organic layer was washed with $H_2O$, dried ($Na_2SO_4$), and concentrated to obtain 10 mg of **2b**.

**Compound 2b:** colorless oil; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.88 (3H, broad s), 1.32 (6H, m), 1.62 (2H, m), 4.72 (1H, t, $J$ = 6.0 Hz); EIMS *m*/*z* 283/285/287 [$M^+ - Br$], 265/267/269 [$M^+ - Br - H_2O$], 223/225/227 [$M^+ - Br - H_2O - (CH_2)_3$], 83 [$C_6H_{11}$].

**Acetylation of Compound 2b.** A solution of **2b** (10 mg) in dry $C_5H_5N$ (2 mL) was treated with $Ac_2O$ (0.25 mL) and stirred at 0 °C for 1.5 h, and then it was poured into 10% aqueous HCl and extracted with $CHCl_3$. The organic layer was washed with $H_2O$ and brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by R-HPLC to give 4 mg of **2a**, identical ($^1$H-NMR) to the naturally occurring compound.

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