

Structures of Four Novel Highly Oxygenated Labdane-Type Diterpenoids, Ptychantins F-I, from the Liverwort *Ptychanthus striatus*

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Four novel highly oxygenated labdane-type diterpenoids, named ptychantins F-I (**1-4**) have been isolated from the liverwort *Ptychanthus striatus*, and their structures including their absolute configurations established by a combination of high resolution NMR and CD spectra, X-ray crystallographic analysis, and chemical degradations.

We have reported the distribution of a number of new terpenoids and aromatic compounds in more than 100 species of liverworts.^{1,2} In the course of our investigation of biologically active substances from liverworts, we recently isolated five novel labdane-type diterpenoids, ptychantins A-E (**5-9**),³ closely related to forskolin (**10**)⁴ isolated from *Coleus forskohlii* showing a number of interesting biological properties such as positive inotropic, and antihypertensive activities, from the ether extract of the liverwort *Ptychanthus striatus* belonging to the Lejeuneaceae. In the continued study, we isolated four novel highly oxygenated labdane-type diterpenoids, ptychantins F-I (**1-4**), biogenetically related to **5-9**, diterpene-ethers found in the same liverwort. Although liverworts belonging to the Lejeuneaceae produce various mono-, sesqui- and diterpenoids¹, these highly acetoxyated diterpenoids have been found only in *P. striatus*. Here we wish to report the isolation and the structure elucidation of **1-4**.

The ether extract (32.7 g) of air-dried *P. striatus* (1.02 kg) collected in Tokushima in 1992 was subjected repeatedly to column chromatography of Sephadex LH-20 (CHCl₃: MeOH = 1 : 1) and of silica gel (*n*-hexane-AcOEt, gradient) to afford ptychantins F (**1**)⁵ (1.09 g), G (**2**)⁶ (143 mg), H (**3**)⁷ (58 mg), and I (**4**)⁸ (128 mg).

The IR spectrum of ptychantin F (**1**, C₃₀H₄₆O₁₁) indicated the presence of a hydroxyl (3400 cm⁻¹) and an acetoxy (1725 and 1230 cm⁻¹) groups. The ¹H NMR spectrum of **1** showed the presence of four tertiary methyl groups [δ 0.92, 1.00, 1.28, 1.67 (each 3H, *s*)], five acetoxy groups [δ 2.02, 2.04, 2.07, 2.08, 2.14 (each 3H, *s*)], one vinyl group [δ 4.95 (*dd*, *J*=10.7, 1.5 Hz), 5.17 (*dd*, *J*=17.1, 1.5 Hz), 5.82 (*dd*, *J*=17.1, 10.7 Hz)], one methylene [δ 4.67, 4.71 (*d*, *J*=12.8 Hz)] and three methine [δ 4.64 (*t*, *J*=2.6 Hz), 5.21 (*dd*, *J*=10.8, 1.3 Hz), 5.50 (*dd*, *J*=4.9, 3.6 Hz)] groups bearing acetoxy groups. Dehydration (POCl₃/pyridine / 0-5 °C) of **1** afforded a mixture of conjugated dienes (**11**) [UV (EtOH)_λmax 213 nm (log ε=3.77)] indicating the presence of a hydroxy group at adjacent to a vinyl group. Reduction (LiAlH₄ / Et₂O) of **1** afforded a hexahydroxy derivative (**12**), which was further converted to an acetonide (**13**) with 2, 2-dimethoxypropane and *p*-TsOH, and to an aldehyde (**14**) by oxidation with NaIO₄ / MeOH, respectively. The structure of **1** was deduced from careful analysis of two-dimension NMR spectra such as HMBC and NOESY spectra of **1**, and NOE difference spectra (Figure 1) of **13** and **14**, and finally established by X-ray crystallography⁹ of **1** as shown in Figure. 2.

Ptychantin G (**2**, C₃₂H₄₈O₁₂) had very similar spectral data to those of **1** except for the signals due to six acetoxy groups [δ 1.93, 1.94, 2.04, 2.11 (each 3H, *s*)] in the ¹H NMR spectrum. As

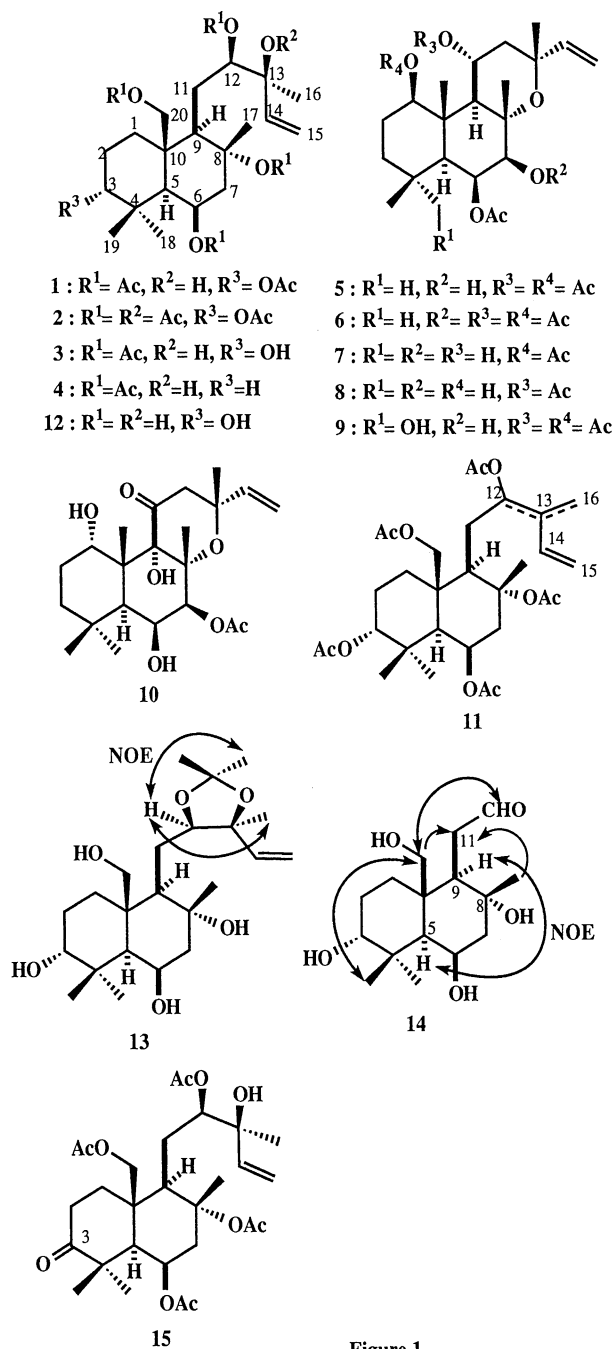


Figure 1.

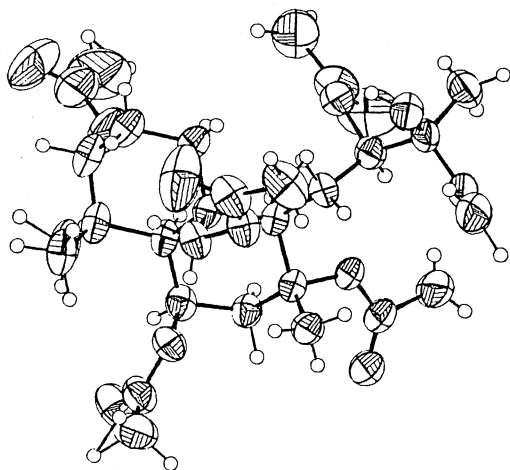


Figure 2. An ORTEP Drawing of 1.

acetylation ($\text{Ac}_2\text{O}/\text{Py}/\text{DMAP}$) of **1** afforded **2**, the structure of **2** was determined as 13-O-acetylptychantin F.

Ptychantin H (**3**, $\text{C}_{28}\text{H}_{42}\text{O}_9$) had very similar spectral data to those of **1** and **2**. The ^1H NMR spectrum of **3** showed the presence of four acetoxyl groups [δ 1.93, 1.94, 2.04, 2.11 (each 3H, s)] and a methine signal [δ 3.45 (dd, $J=2.6, 2.6$)] at C-3, which was 1.3 ppm higher than those of **1** and **2** indicating the presence of a hydroxy group. Oxidation of **3** with PCC- Al_2O_3 afforded a 3-oxo derivative (**15**). As acetylation ($\text{Ac}_2\text{O}/\text{Py}$) of **3** afforded **1**, the structure of **3** was determined as 3-deacetylptychantin F.

The ^1H NMR spectrum of ptychantin I (**4**, $\text{C}_{28}\text{H}_{42}\text{O}_9$) was very similar to those of **1**, **2** and **3** except for the lack of the C-3 methine signal bearing an oxygen function. The structure of **4**

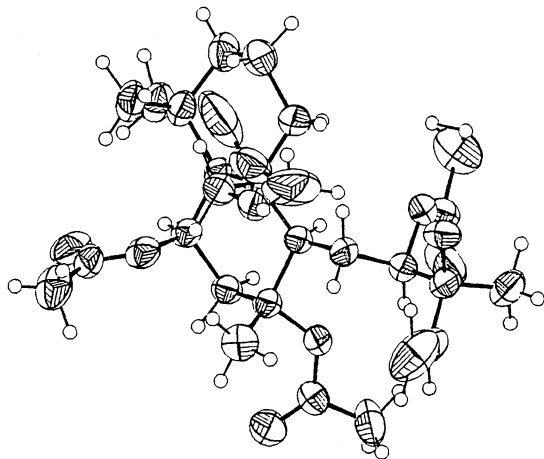


Figure 3. An ORTEP Drawing of 4.

was deduced from careful analysis of the HMBC spectrum of **4** and finally established as 3-deoxyptychantin H by X-ray crystallography¹⁰ of **4** shown in Figure 3.

The absolute configuration of ptychantin F-I was estimated to be as shown in **1-4**, because the CD spectrum¹¹ of compound **15** showed the negative Cotton effect at 317 nm ($\Delta\epsilon -0.11$), and a biogenetic consideration of co-occurring ptychantin A-E, whose absolute configurations have been determined³.

References and Notes

- 1 Y. Asakawa, "Chemical Constituents of Hepaticae," in "Progress in the Chemistry of Organic Natural Products," ed by W. Herz, H. Grisebach, and W. G. Kirby, Springer, Wien (1982). Vol. **42**, p. 1.
- 2 Y. Asakawa, "Biologically Active Terpenoids and Aromatic Compounds from Liverworts and the Inedible Mushroom *Cryptoporus volvatus*," in "Bioactive Natural Products: Detection, Isolation, and Structural Determination," ed by S. M. Colegate and R. J. Molyneux, CRC Press, Florida (1993), p. 319.
- 3 T. Hashimoto, M. Horie, M. Toyota, Z. Taira, R. Takeda, M. Tori, and Y. Asakawa, *Tetrahedron Lett.*, **35**, 5457 (1994).
- 4 S. V. Bhat, B. S. Bajwa, H. Dornauer, N. J. de Souza, and H.-W. Fehlhauer, *Tetrahedron Lett.*, **1977**, 1669.
- 5 **1**: colorless prisms; mp 202-204°; $[\alpha]_D^{21} -11.1^\circ$ (c 0.81, CHCl_3); EI-MS: m/z 462 (M^+-2AcOH), 365, 205; FAB-MS: m/z 605 ($\text{M}+\text{Na}^+$); Anal. Found: C, 61.77%; H, 8.20%; Calcd for $\text{C}_{30}\text{H}_{46}\text{O}_{11}$: C, 61.84%; H, 7.96%; IR (KBr) cm^{-1} : 3561 (OH), 1736 (CO), 1367, 1255, 1103, 1044.
- 6 **2**: amorphous powder; $[\alpha]_D^{25} -6.8^\circ$ (c 0.51, CHCl_3); HR-MS: m/z 582.2626, $\text{C}_{32}\text{H}_{48}\text{O}_{12}$ requires 624.2618; EI-MS: m/z 624 (M^+), 447 (100), 387, 285, 267; FT-IR (KBr) cm^{-1} : 1738 (CO), 1370, 1242, 1150, 1086, 1046.
- 7 **3**: colorless prisms; mp 169-170°; $[\alpha]_D^{21} +4.8^\circ$ (c 0.72, CHCl_3); HR-MS: m/z 540.2626, $\text{C}_{28}\text{H}_{44}\text{O}_{10}$ requires 540.2618; EI-MS: m/z 540 (M^+), 423, 378, 363 (100%), 285; 187, 177; IR (KBr) cm^{-1} : 3497 (OH), 1739, 1715 (CO), 1366, 1242, 1148, 1105, 1040.
- 8 **4**: colorless prisms; mp 137-138°; $[\alpha]_D^{22} +10.9^\circ$ (c 0.76, CHCl_3); EI-MS: m/z 344 (M^+-2AcOH), 313, 291; 253, 231, 213, 187; FAB-MS: m/z 547 ($\text{M}+\text{Na}^+$); Anal. Found: C, 64.08%; H, 8.66%; Calcd for $\text{C}_{28}\text{H}_{44}\text{O}_9$: C, 64.10%; H, 8.45%; FT-IR (KBr) cm^{-1} : 3510 (OH), 2934 (CO), 1736, 1250, 1032.
- 9 The crystal data for **1** are as follows: Orthorhombic; space group $P 2_1 2_1 2_1$ with $a=9.996$ (2), $b=36.998$ (8), $c=8.773$ (3) Å, $V=3245$ (1) Å³, $Z=4$, and Cu K- α ($\lambda=1.54178$) by Mac Science MXC 18 instrument. Final R value was 0.067 for 3035 reflections.
- 10 The crystal data for **4** are as follows: Monoclinic; space group $P 2_1$ with $a=15.996$ (3), $b=10.668$ (2), $c=8.760$ (2), $\beta=8.760$ (2) Å, $V=1484.4$ (5) Å³, $Z=2$, and Cu K- α ($\lambda=1.54178$) by Mac Science MXC 18 instrument. Final R value was 0.054 for 2593 reflections.
- 11 P. M. Scopes, "Applications of the Chiroptical Techniques to the Study of Natural Products," in "Progress in the Chemistry of Organic Natural Products," ed by W. Herz, H. Grisebach, and W. G. Kirby, Springer, Wien (1975). Vol. **32**, p. 167.