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Nudenoic acid: A Novel Tricyclic Sesquiterpenoid from the Taiwanese Liverwort *Mylia nuda*

Huei-Ju Liu[1] , Chia-Li Wu[1],* Toshihiro Hashimoto[2] and Yoshinori Asakawa[2]

[1]Department of Chemistry, Tamkang University, Tamsui, Taiwan, R.O.C.
[2] Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770, Japan

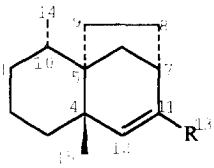
Abstract: *Nudenoic acid, a new sesquiterpene possessing a novel tricyclic skeleton, was isolated from a Taiwanese liverwort Mylia nuda. The structure of nudenoic acid was determined by spectroscopic means and X-ray analysis.*

A reinvestigation[1] of the chemical constituents of the liverwort species, *Mylia nuda,*[2] endemic to Taiwan, has resulted in the identification of a sesquiterpenoid acid possessing a novel tricyclic skeleton, hereby named nudenoic acid, as a minor component.

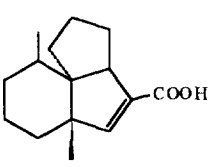
The combined *n*-hexane and EtOAc extract (5.2 g) of the powdered plants (110 g) collected at Taiping Shan (alt. 2000m) was subjected to repeated chromatography on silica gel. The 20% EtOAc-*n*-hexane eluate afforded nudenoic acid (**1**) (6 mg)[3]. Its GC-MS exhibited an [M^+] ion peak at *m/z* 234 (40%) and prominent fragments at *m/z* 88, 91, 146 and 147. The ^{1}H NMR revealed a singlet (δ 1.12) and a doublet (δ 0.82, J=6.6) methyl signals, in addition to a conjugated olefinic proton (δ 6.50 *s*)[3]. The ^{13}C-DEPT NMR indicated the presence of two methyls, 6 methylenes, 3 methines and 4 quaternary carbons including a carboxylic carbon at δ 171.2[3]. Hence nudenoic acid (**1**) has a molecular formula of $C_{15}H_{22}O_2$ and is a tricyclic sesquiterpene. The subsequent HMBC experiment provided clues to limit the choice of two plausible structures, **1** and **2**, that were difficult to be distinguished solely by ^{1}H or ^{13}C NMR spectra. In particular, the prominent mass fragments of m/z 88 and 146 ($C_{11}H_{14}$)[3] could not be easily rationalized on the basis of either structures. Fortunately, colorless crystalline plates of nudenoic acid could be obtained for X-ray crystallographic analysis[4](Fig. 1), which confirmed **1** unambiguously as the correct structure.

In the earlier eluate (5% E-H) of the same chromatographic separation, a mixture of nudenal (**3**)[5] and dihydromylione A[6] was also obtained. The aldehyde **3** was unstable and gradually oxidized to nudenoic acid (**1**) shortly upon contact with air. The GC-MS profile[7] of the crude oil exhibited both nudenal and nudenoic acid at R_t 27 & 60 min., respectively, with pertinent fragmentation patterns. We also examined several other *Mylia* species by GC-MS[8], both sesquiterpenes were observed in *M. nuda* collected at Yuenyang Lake, but only aldehyde **3** was detected in *M. taylorii* collected at Taiping Shan, Taiwan and Giant Mountains, Czechoslovakia[9]. In the specimen of *M. verrucosa* collected at Sanqin Shan, Jianxi, China, however, neither **3** nor **1** could be identified.

We speculate that the novel skeleton of nudenal and nudenoic acid could be derived from the bicyclic spirovetivane (**4**), which has been found in the liverwort species of *Scapania robusta*[10] and *S. maxima*[11] and recently in a *Frullania* species[12].



1 R=COOH
3 R=CHO



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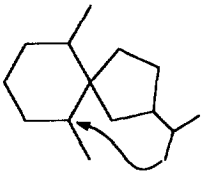

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References and Notes

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2. All species were identified by Dr. K. Yamada (Ise-shi, Japan), to whom we are very grateful. The present research was supported financially by the National Science Council of the Republic of China.
3. **1**: colorless plates; $[\alpha]_D^{25}$ - 21° (c 0.15, $CHCl_3$); UV (EtOH) λ_{max}nm (ε): 229 (3972); IR (film) ν_{max} cm^{-1} : 3200-3500, 1683, 1633; GC-MS *m/z*(rel. int.): 234($[M]^+$, 40), 147(75), 146(95), 91(100), and 88(62); HR-MS: *m/z*234.1612, $C_{15}H_{22}O_2$ requires 234.1620; *m/z*146.1094, $C_{11}H_{14}$ (M^+-88) requires 146.1095, *m/z* 147.1172, $C_{11}H_{15}$ requires 147.1173; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.48 (1H, H-1e), 1.09 (1H, qd, J 13.4, 4.9 Hz, H-1a), 1.66 (1H, H-2), 1.51 (1H, H-2), 1.24 (1H, H-3e), 1.79 (1H, td, J 13.7, 4.9 Hz, H-3a), 1.58 (2H, H-6), 2.99 (1H, br s, H-7), 1.58 (2H, H-8), 1.48 (1H, H-9), 1.58 (1H, H-9), 1.87 (1H, H-10), 6.50 (1H, s, H-12), 0.82 (3H, d, J 6.6 Hz, H-14), 1.12 (3H, s,H-15); ^{13} C NMR (150 MHz, $CDCl_3$) δ 32.2, 20.6, 31.1, 43.3, 48.4, 34.6, 37.1, 24.6, 33.0, 31.3, 131.3, 150.0, 171.2, 15.5, 21.9, from C-1 to C-15, respectively. All undescribed peaks were seriously overlapped.
4. The crystal data for **1** are as follows: orthorhombic crystals from pure hexane with trace EtOAc, crystal size=0.05 x 0.10 x 0.60 mm, cell parameters: a=8.840(3), b=12.693(4), c=23.535(5) Å, space group $P2_12_12_1$ Z=8. The diffraction intensities were collected on a CAD-4 diffractometer using monochromated M_oK_α radiation. The structure was solved by direct methods and the final R and R_w values were 0.063 and 0.067 for 1616 reflections.
5. **3**: GC-MS *m/z*(rel. int.): 218($[M]^+$, 20), 147(60), 146(57), 119(45), 105(83), and 91(100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (1H, H-1), 1.10 (1H, qd, J 12.7, 4.9 Hz, H-1), 1.66 (1H, H-2), 1.55 (1H, H-2), 1.25 (1H, H-3), 1.84(1H, td, J 13.2, 4.4 Hz, H-3), 1.58 (1H, H-6), 1.48 (1H, H-6), 3.05 (1H, br s, H-7), 1.56 (2H, H-8), 1.55 (2H, H-9), 1.87 (1H, H-10), 6.14 (1H, s, H-12), 9.32 (1H, H-13),0.82 (3H, d, J 6.6 Hz, H-14), 1.15 (3H, s,H-15); ^{13} C NMR (75 MHz, $CDCl_3$) δ 32.2, 20.6, 31.1, 44.1, 49.4, 34.3, 34.3, 24.8, 32.7, 31.5, 143.3, 158.9 193.4, 15.5, 21.9, from C-1 to C-15, respectively. All undescribed peaks were seriously overlapped.
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7. GC: DBWAX, 30m x 0.25mm, 50°C to 220°C at 5°C/min; MS: EI, 70 eV.
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9. A specimen given to C.-L. Wu from Prof. S. R. Gradstein (University of Gottingen, Germany).
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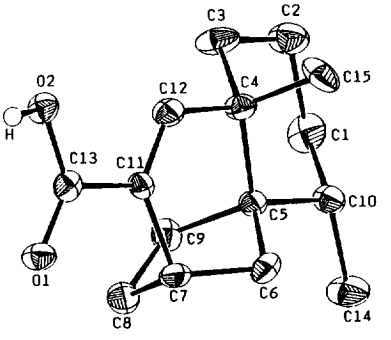

Figure 1. ORTEP diagram of nudenoic acid (**1**)

(relative stereochemistry)

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