# Two Novel Sesquiterpenes from *Neolitsea parvigemma*

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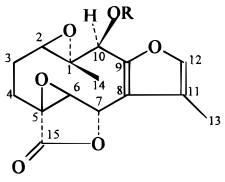
Two novel sesquiterpenes of the furanogermacrane type, parvigemone (**7**) and neolitrane (**8**), along with six known compounds, zeylanidine (**1**), zeylanicine (**2**), linderalactone (**3**), pseudoneolinderane (**4**), linderane (**5**), and deacetylzeylanidine (**6**), have been isolated from the stems of *Neolitsea parvigemma*. The structures of these compounds were elucidated on the basis of spectroscopic techniques, and the structure of compound **8** was confirmed by X-ray crystallographic analysis.

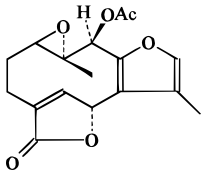
*Neolitsea parvigemma* Kan & Sas (Lauraceae) is a small tree growing in the central and southern mountainous regions in Taiwan.[1] In a previous study, its roots were found to contain five furanosesquiterpene lactones, **1**−**3**, **5**, and **6**.[2] In the course of further investigation on the chemical constituents of this plant, the MeOH extract of its stems was subjected to solvent partitioning and chromatographic separation to afford eight pure substances, comprising the five above-mentioned compounds as well as compounds **4**, **7**, and **8**. The present paper deals with the structural elucidation of the two novel compounds, **7** and **8**.

The identities of known compounds **1**−**6** were verified by comparison of mp, IR, $^1$H-NMR, and/or $^{13}$C-NMR data with those published for zeylanidine,[2−4] zeylanicine,[2−4] linderalactone,[2,4] pseudoneolinderane,[5] linderane,[2,4−6] and deacetylzeylanidine.[2]

Compound **7** was isolated as an oil. The HRMS showed a $[M]^+$ at *m/z* 260.1045 corresponding to the molecular formula $C_{15}H_{16}O_4$ (calcd 260.1048). An IR absorption band at 1760 cm$^{-1}$, a $\lambda$ max at 213 nm in the UV spectrum, and signals at $\delta$ 135.43 (s), 147.63 (d), and 175.79 (s) in $^{13}$C-NMR spectrum provided evidence for an $\alpha,\beta$-unsaturated $\gamma$-lactone.[3] The presence of a trisubstituted furan functionality was indicated by absorptions at 3100, 1710, and 865 cm$^{-1}$ in the IR spectrum, an unresolved quartet at $\delta$ 7.12 in the $^1$H-NMR spectrum, and three singlets ($\delta$ 115.45, 153.97, and 121.82) as well as a doublet ($\delta$ 138.29) in the $^{13}$C-NMR spectrum. On comparison of the $^1$H- and $^{13}$C-NMR data (Tables 1 and 2) of the 10-membered macrocyclic moieties of both compounds **7** and **4**, it was found that a singlet at $\delta$ 0.99 (3H) for $H_3$-14 and a double doublet at $\delta$ 2.79 (1H, $J$ = 11.7, 2.0 Hz) for H-2 in compound **4** disappeared, while two doublets of the AB type at $\delta$ 4.41 ($J$ = 2.0 Hz) and $\delta$ 5.10 ($J$ = 2.0 Hz) for H-14 and a double doublet at $\delta$ 4.29 ($J$ = 9.6; 4.8 Hz) for H-2 were observed for compound **7**. The above information, along with singlets at $\delta$ 76.74 (d), 150.19 (s), and 117.02 (t) in the $^{13}$C-NMR spectrum, clearly indicated that compound **7** contained a hydroxyl group at C-2 and a double bond at C-1 through C-14 instead of an epoxy function between C-1 and C-2 and a methyl group (C-14) as in compound **4**. In order to determine the stereochemistry of the chiral centers at C-2 and C-7, NOESY NMR experiments were performed. Besides the salient common NOE interactions between the




**1** R=Ac
**6** R=H

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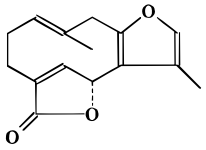


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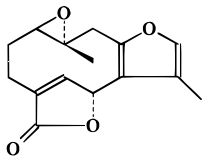


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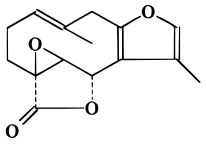


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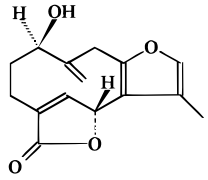
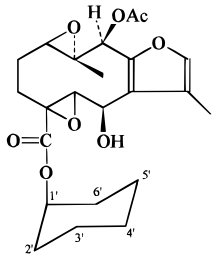



**7**




**8**

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**Table 1.** $^1$H-NMR Chemical Shifts of Compounds **1**, **4**, **7**, and **8**

| | compound | | | |
|---|---|---|---|---|
| proton(s)[a] | **1** | **4** | **7**[b] | **8** |
| H-2 | 3.67 dd (10.0; 1.0) | 2.79 dd (11.7; 2.0) | 4.29 dd (9.6; 4.8) | 4.34 dd (9.9; 1.0) |
| H-3 | 1.50−1.65 m | 1.48−1.54 m | 2.13−2.20 m | 1.46−1.51 m |
| H-3 | 2.20−2.32 m | 2.23−2.27 m | 2.13−2.20 m | 2.61−2.74 m |
| H-4 | 1.83 ddd (14.8; 8.5; 1.0) | 2.55−2.63 m | 2.24−2.36 m | 1.89−1.93 m |
| H-4 | 3.03 ddd (15.6; 9.3; 9.0) | 2.73−2.84 m | 2.47−2.52 m | 1.55−1.62 m |
| H-6 | 3.96 s | 7.12 s | 7.36 d (2.0) | 3.14 d (1.3) |
| H-7 | 5.38 s | 5.88 s | 5.72 d (2.0) | 4.88 dd (10.1; 1.3) |
| H-10 | 6.00 s | 2.35 d (15.4) | 3.24 d (14.4) | 6.26 s |
| | | 3.33 d (15.4) | 3.28 d (14.4) | |
| H-12 | 7.26 s | 7.05 d (1.1) | 7.12 q (unresolved) | 7.18 s |
| H-13 | 2.07 s | 2.08 s | 2.09 d (1.2) | 2.06 s |
| H-14 | 1.15 s | 0.99 s | 4.41 d (2.0) | 1.24 s |
| | | | 5.10 d (2.0) | |
| OAc | 2.05 s | | | 2.04 s |
| H-1′ | | | | 3.75 m |
| H-2′-H-6′ | | | | 1.26−2.03 m |

[a] Measured at 200 MHz, in $CDCl_3$, with TMS as internal standard. Coupling constants (Hz) are in parentheses. Chemical shifts are in $\delta$ values. [b] Measured at 400 MHz.

**Table 2.** $^{13}$C-NMR Chemical Shifts of Compounds **1**, **4**, **7**, and **8**

| | compound | | | |
|---|---|---|---|---|
| carbon[a] | **1** | **4** | **7** | **8** |
| C-1 | 60.83 s | 58.64 s | 150.19 s | 59.21 s |
| C-2 | 56.73 d | 65.71 d | 76.74 d | 57.54 d |
| C-3 | 20.96 t | 23.85 t | 34.94 t | 23.44 t |
| C-4 | 21.27 t | 18.68 t | 19.57 t | 24.71 t |
| C-5 | 61.43 s | 131.48 s | 135.43 s | 63.66 s |
| C-6 | 60.39 d | 147.31 d | 147.63 d | 71.20 d |
| C-7 | 72.57 d | 74.31 d | 75.11 d | 63.28 d |
| C-8 | 116.37 s | 115.29 s | 115.45 s | 126.21 s |
| C-9 | 150.58 s | 150.38 s | 153.97 s | 148.21 s |
| C-10 | 68.33 d | 37.40 t | 28.71 t | 68.92 d |
| C-11 | 121.46 s | 120.80 s | 121.82 s | 120.44 s |
| C-12 | 138.95 d | 137.37 d | 138.29 d | 138.66 d |
| C-13 | 8.37 q | 8.36 q | 8.07 q | 8.29 q |
| C-14 | 16.43 q | 16.36 q | 117.02 t | 14.69 q |
| C-15 | 171.82 s | 174.94 s | 175.79 s | 167.95 s[b] |
| Ac | 169.48 s | | | 168.20 s[b] |
| Ac | 20.60 q | | | 20.80 q |
| C-1′ | | | | 47.97 d |
| C-2′ | | | | 32.94 t |
| C-3′ | | | | 25.53 t |
| C-4′ | | | | 30.32 t |
| C-5′ | | | | 24.86 t |
| C-6′ | | | | 32.14 t |

[a] Measured at 50 MHz, in $CDCl_3$, TMS as internal standard. [b] Assignments may be interchanged.

adjacent protons, an interaction between H-2 and H-14 was also evident although an effect between H-7 and H-14 was not observed. On the basis of the results of NOESY experiments, coupling patterns, and studies of Dreiding models, H-2 was assigned in the α-orientation and H-7 in the $\beta$-orientation. The above observations and the analysis of its COSY and HETCOR NMR spectra led to the establishment of the structure of this compound as **7**.

Compound **8** was isolated as colorless prisms and analyzed for $C_{23}H_{30}O_8$ from the molecular ion at *m/z* 434.1923 in its HRMS (calcd 434.1941). On the basis of $^1$H- and $^{13}$C-NMR spectral analysis (Tables 1 and 2), the structural features in the furanogermacrane moiety of compound **8** were seen to be very close to those of compound **1**. The presence of a furan ring was revealed from the IR (3100, 1650, 1510, and 905 cm$^{-1}$), $^1$H-NMR ($\delta$ 7.18, s), $^{13}$C-NMR ($\delta$ 126.21 s, 148.21 s, 120.44 s, and 138.66 d) and UV data ($\lambda$ max 207 nm). Two epoxy groups were shown by signals at $\delta$ 59.21 (s, C-1), 57.54 (d, C-2), 63.66 (s, C-5), and 71.20 (d, C-6) in the $^{13}$C-NMR spectrum as well as two doublets at $\delta$ 4.34 for H-2 and 3.14 for H-6 in the $^1$H-NMR spectrum. In the $^{13}$C-NMR spectrum, two singlets at $\delta$ 167.95 and 168.20 were ascribed to two ester carbonyls and five triplets at $\delta$ 24.86, 25.53, 30.32, 32.14, and 32.94; a doublet at $\delta$ 47.97 accounted for an oxygenated cyclohexyl group, and a quartet at $\delta$ 20.80 was assigned to an acetate methyl group. On analysis of this available data, it was clear that compound **8** possessed a cyclohexyl ester instead of a $\gamma$-lactone as in compound **1**. The stereochemistry of the chiral centers at C-1, C-2, C-5, C-6, C-7, and C-10 was assumed to be the same as those of compound **1** by comparison of spectral data and coupling patterns of these two compounds. Based on the above information and by correlation with compound **1**, the structure of compound **8** was thus established. The relative (rather than the absolute) configuration of **8** was confirmed by X-ray diffraction analysis (Figure 1).

## Experimental Section

**General Experimental Procedures.** Mps were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. The UV spectra were obtained on a Hitachi 200-20 spectrophotometer, and IR spectra were measured on a Hitachi 260-30 spectrophotometer. $^1$H-NMR spectra were recorded with a Varian Gemini NMR spectrometer at 400 MHz and 200 MHz, and $^{13}$C-NMR spectra were recorded with a Varian Gemini NMR spectrometer at 50 MHz in $CDCl_3$ using TMS as internal standard. EIMS were obtained with a JEOL JMS-HX110 mass spectrometer at 70 eV. Si gel 60 (Merck, 230−400 mesh) was used for column chromatography, precoated Si gel plates (Merck, Kieselgel 60 F-254, 0.20 mm) were used for analytical TLC, and precoated Si gel plates (Merck, Kieselgel 60 F-254, 0.50 mm) were used for preparative TLC.

**Plant Material.** The stems of *N. parvigemma* were collected from Pingtung-Hsien, Taiwan, in June 1992. A voucher specimen is deposited in the Graduate Institute of Natural Products, Kaohsiung Medical College, Kaohsiung, Taiwan, Republic of China.

**Extraction and Isolation.** Air-dried, powdered stems (2.62 kg) of *N. parvigemma* were extracted repeatedly with MeOH at room temperature. The combined MeOH extracts were evaporated and parti-

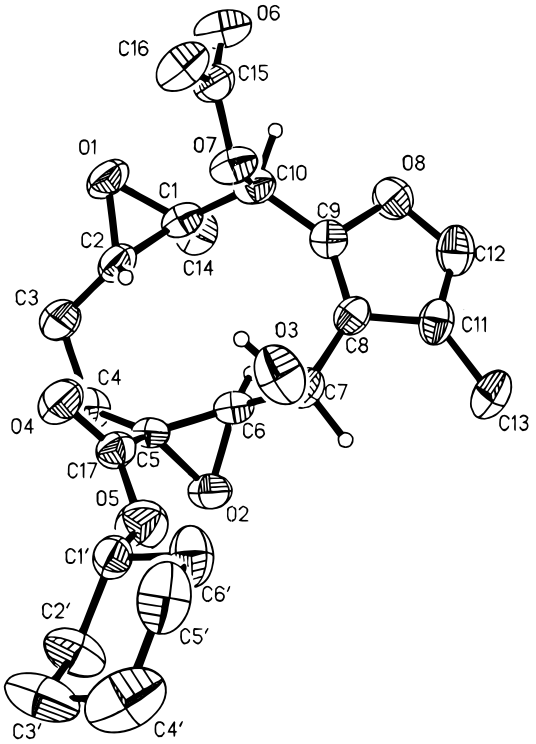


**Figure 1.** Molecular structure (relative configuration) of neolitrane (**8**).

tioned to yield $CHCl_3$- and $H_2O$-soluble extracts. A portion of the $CHCl_3$-soluble extract (41.0 g) was chromatographed over Si gel (1500 g) and eluted with *n*-hexane−$CHCl_3$ mixtures of increasing polarity to yield 45 fractions (120 mL each). The fractions (2.01 g) eluted from *n*-hexane−$CHCl_3$ (10:1) were further purified by Si gel column chromatography using the same solvent system to obtain zeylanidine (**1**) and zeylanicine (**2**). The eluate (1.21 g) with *n*-hexane−$CHCl_3$ (7:1) was repeatedly separated and purified by Si gel column chromatography, and preparative TLC [*n*-hexane−$CHCl_3$ (5:1)] to give linderalactone (**3**), pseudoneolinderane (**4**), and linderane (**5**). The residue (679 mg) eluted with *n*-hexane−$CHCl_3$ (3:1) was rechromatographed on Si gel [*n*-hexane−$CHCl_3$ (1:1)] to yield deacetylzeylanidine (**6**), parvigemone (**7**), and neolitrane (**8**).

**Zeylanidine (1):** white prisms (MeOH) (165 mg); mp 221−223 °C; $[\alpha]^{24}_D$ −175° (*c* 0.21, $CHCl_3$); spectral data consistent with literature values.[2,4]

**Zeylanicine (2):** white prisms (MeOH) (58 mg); mp 233−235 °C; $[\alpha]^{24}_D$ −125° (*c* 0.24, $CHCl_3$); spectral data consistent with literature values.[2−4]

**Linderalactone (3):** white prisms (MeOH) (33 mg); mp 135−136 °C; $[\alpha]^{24}_D$ +98° (*c* 0.48, $CHCl_3$); spectral data consistent with literature values.[2,4]

**Pseudoneolinderane (4):** white prisms (MeOH) (18 mg); mp 204−206 °C; $[\alpha]^{24}_D$ +68° (*c* 0.32, $CHCl_3$); spectral data consistent with literature values.[5]

**Linderane (5):** white prisms (MeOH) (21 mg); mp 185−186 °C; $[\alpha]^{24}_D$ +160° (*c* 0.40, $CHCl_3$); spectral data consistent with literature values.[2,4−6]

**Deacetylzeylanidine (6):** white prisms (MeOH) (19 mg); mp 210−211 °C; $[\alpha]^{24}_D$ +64° (*c* 0.40, $CHCl_3$); spectral data consistent with literature values.[2]

**Parvigemone (7):** pale yellow oil (12 mg); $[\alpha]^{24}_D$ +89° (*c* 0.36, $CHCl_3$); UV (EtOH) $\lambda$ max (log $\epsilon$) 213 (3.46) nm; IR (Nujol) $\nu$ max 3450, 3100, 1760, 1710, 865 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) data, see Table 1; $^{13}$C-NMR ($CDCl_3$) data see Table 2; EIMS *m/z* 260 ($M^+$, 31), 242 (7), 185 (24), 145 (100); HREIMS *m/z* $[M]^+$ 260.1045 (calcd for $C_{15}H_{16}O_4$, 260.1048).

**Neolitrane (8):** white prisms (MeOH) (36 mg); mp 142−143 °C; $[\alpha]^{24}_D$ −120° (*c* 0.21, $CHCl_3$); UV (EtOH) $\lambda$ max (log $\epsilon$) 207 (3.98) nm; IR (KBr) $\nu$ max 3380, 3100, 1650, 1510, 905 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) data, see Table 1; $^{13}$C-NMR ($CDCl_3$) data see Table 2; EIMS *m/z* 433 $[M - 1]^+$ (2), 374 (7), 299 (7), 229 (31), 187 (21), 135 (80), 83 (94), 55 (100); HREIMS *m/z* $[M]^+$ 434.1923 (calcd for $C_{23}H_{30}O_8$, 434.1941).

**Single Crystal X-ray Analysis of Neolitrane (8).**[7] Crystal data: $C_{23}H_{30}O_8$, space group $P2_12_12_1$, $a$ = 10.328(2) Å, $b$ = 15.197 (3) Å, $c$ = 15.362 (3) Å, V = 2411.1 (8) $Å^3$, Z = 4, $D_{calcd}$ = 1.285 mg/$m^3$, $F(000)$ = 1000. Intensity data were collected on a Siemens R3m/V diffractometer using monochromatized Mo Kα radiation ($\lambda$ = 0.71073 Å) via the $\theta - 2\theta$ scan technique; those 2293 data with $I > 2.0\sigma(I)$ were considered observed. The structure was solved by direct methods and refined by full-matrix least-square methods. At convergence, $R_f$ = 5.70%, $R_{wf}$ = 7.28%, and GOOF = 1.21 for 298 variables.

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(7) Atomic coordinates, thermal parameters, bond distances and angles, and observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre and can be obtained upon request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.

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