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Two novel 9,11-*seco*-11-norabietanes from the roots of *Taiwania cryptomerioides*

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Abstract—Two novel 9,11-*seco*-11-norabietanes, namely taiwanlactones A (**1**) and B (**2**), together with 3β-hydroxysugiol (**3**) and 6α-hydroxysugiol (**4**), were isolated from the roots of *Taiwania cryptomerioides*. Their structures were elucidated through spectral studies. The absolute configuration of **1** was elucidated by a modified Mosher's method. The biotransformation mechanisms of **1** and **2** were proposed.

The heartwood of *Taiwania cryptomerioides* (Taxodiaceae) was full of large amount of essential oil (over 6%).[1] Therefore, it possessed anti-fungus and decay-resistant characteristic and led to be an important building material. It is an endemic plant and also one genus and one species. Previously, we have investigated the chemical components of its heartwood[2a,b,c] and bark[3a–e] of this plant.

Besides hydrocarbons, α-cadinol is a major component in the essential oil of heartwood of this plant. It shows selectiveness for human colon tumor cell lines.[4] We investigated the biologically active components from this plant and found lignans and cadinane-type compounds, which possessed significant cytotoxicity against three human tumor cell lines.[5] We also discovered α-cadinol with the highest activity against wood-decay fungi.[6] The components of the heartwood of this plant include cadinane, lignan, and abietane diterpene.[7a,b] The bark contains trinorabietane (podocarpane)[3a–e] and abietane diterpenes. No chemical studies on the roots of this plant, we were encouraged to study the diterpene constituents of its roots. We report here two novel 9,11-*seco*-11-norabietanes, namely taiwanlactones A (**1**) and B (**2**), together with two known diterpenes 3β-hydroxysugiol (**3**)[8] and 6α-hydroxysugiol (**4**).[9]

The roots of *Taiwania cryptomerioides* were collected in Nan Tau, Taiwan, in September 1996. These dried roots were crushed to give 15 kg of raw material, which was extracted with acetone at room temperature. The total crude extract was evaporated in vacuo to yield a residue that was then suspended in H_2O, and successively partitioned with ethyl acetate. The combined ethyl acetate layer afforded black syrup that was subsequently chromatographed over silica gel with a hexane/EtOAc gradient solvent system to give taiwanlactones A (**1**) and B (**2**), together with two known diterpenes 3β-hydroxysugiol (**3**) and 6α-hydroxysugiol (**4**).

Taiwanlactone A (**1**) was isolated as a colorless oil; its molecular formula $C_{19}H_{26}O_4$ was established through ^{13}C NMR and HREIMS data, corresponding to seven indices of hydrogen deficiency (IHD). The IR spectrum of compound **1** showed absorptions for hydroxyl (3473 cm^{-1}), γ-lactonedienyl (1739 cm^{-1}), and conjugated carbonyl (1678 cm^{-1}) groups. The ^1H NMR[10] spectrum exhibited signals for three singlet methyl groups [δ_H 0.91 (H_3-19), 1.02 (H_3-18), 1.33 (H_3-20)], one isopropyl groups [δ_H 1.15, 1.17 (each 3H, d, $J = 6.8$ Hz, H_3-17, H_3-16), 2.91 (1H, sep, $J = 6.8$ Hz, H-15)], six methylene protons [δ_H 1.64, 1.65, 1.85 (each 1H, m, H_α-1, H_β-2, and H_α-2, respectively), 2.28 (1H, dt, $J = 13.6$, 3.2 Hz, H_β-1), 2.50 (1H, dd, $J = 17.6$, 13.6 Hz, H_β-6), 2.64 (1H, dd, $J = 17.6$, 3.6 Hz, H_α-6)], one methine proton [δ_H 1.81 (dd, $J = 13.6$, 3.6 Hz, H-5)], one oxymethine proton [δ_H 3.28 (dd, $J = 11.2$, 4.6 Hz, H-3)], and one low-field vinyl proton [δ_H 7.57 (s, H-14)]. The ^{13}C NMR and DEPT data[10] showed five CH_3, three CH_2, four CH, and seven C signals, including those for one oxygen-bearing carbon [δ_C 77.6 (C-3)], four olefinic carbons [δ_C 111.9 (C-8) and 132.5 (C-14), 132.9 (C-13),

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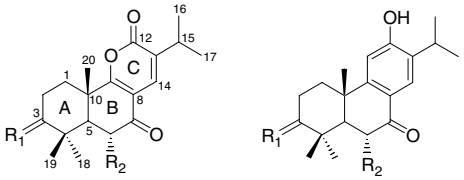
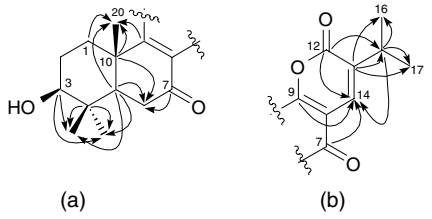
and 178.5 (C-9)], one γ-lactonediene carbonyl carbon [δ_C 160.9 (C-12)], and one conjugated carbonyl carbon [δ_C 194.8 (C-7)]. 3β-Hydroxysugiol (**3**),[8] isolated from the same source, had similar ^{1}H and ^{13}C NMR data as **1** for the A and B rings. From the molecular formula and the above evidence, compound **1** was considered to be an norabietane-type compound. In fact, long range ^{13}C–^{1}H correlations (HMBC) observed as C-1/H_3-20; C-3/H_3-18, H_3-19; C-4/H_3-18, H_3-19; C-5/H_2-6, H_3-18, H_3-19, H_3-20; C-7/H_2-6; C-9/H_3-20; and C-10/H_2-6, H_3-20, respectively, confirmed abietane-type related partial structure of A and B rings (Fig. 1a). α-Isopropyl-γ-lactonediene moiety also can be resolved by long range ^{13}C–^{1}H correlations that were observed as follows: C-7/H-14; C-9/H-14; C-12/H-14, H-15; C-13/H-15, H_3-16, H_3-17; C-15/H-14, H_3-16, H_3-17 (Fig. 1b). NOESY correlations of H-5/H_α-1, H-3, H_3-18; H_3-20/H_β-1, H_β-2, H_β-6, H_3-19 confirmed the assigned structure and relative stereochemistry. The absolute configuration of **1** was determined by the modified Mosher's method.[11] Treatment of **1** with (*R*)- and (*S*)-2-methoxy-2-trifluoromethyl-2-phenylacetyl chloride (MTPACl) afforded the (*S*)- and (*R*)-MTPA esters (**1a** and **1b**, respectively). $\Delta\delta$ values ($\delta_S - \delta_R$) of H_3-18 (+31.6) and H_3-19 (+6.0) showed positive values, while H_3-20 (−8.4) was negative (Fig. 2), thus indicating a 3 *S*-configuration. Therefore, the structure of taiwanlactone A was deduced as shown in formula **1**, with a novel skeleton.



1 R_1= α-H,β-OH; R_2 =H
2 R_1 = O; R_2 = OH

3 R_1= α-H,β-OH; R_2 =H
4 R_1 = H_2; R_2 = OH
5 R_1 = O; R_2 = OH

Taiwanlactone B (**2**) had HREIMS and ^{13}C NMR data consistent with the molecular formula $C_{19}H_{24}O_5$. The IR spectrum of **2** showed the presence of hydroxyl (3480 cm^{-1}), γ-lactonedienyl (1746 cm^{-1}), six-membered ring carbonyl (1719 cm^{-1}), and conjugated carbonyl (1685 cm^{-1}) functionalities that were confirmed by ^{13}C NMR and DEPT experiments. Its NMR[10] spectra suggested that **2** was another norabietane-type diterpenoid, which contained three carbocyclic rings similar to taiwanlactone A (**1**). Comparison of the ^{1}H and ^{13}C NMR data between **1** and **2**[10] revealed that compound **2** contains α-isopropyl-γ-lactonediene moiety. 6α-Hydroxysugiol (**4**),[9] isolated from the same source, has similar ^{1}H NMR data for the B ring suggested the 6α-hydroxy and 7-oxo functionalities. HMQC and HMBC experiments allowed rings A and B to be fully constructed (Fig. 3). Therefore, the structure of Taiwanlactone B was assigned as shown in formula **2**.



(a) (b)

Figure 1. Selected HMBC correlations of **1**.

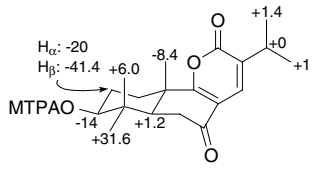


Figure 2. $\Delta\delta$ values [$\Delta\delta$ (in Hz) = $\delta_S - \delta_R$] obtained for the (*S*)- and (*R*)-MTPA esters (**1a** and **1b**, respectively).

The biotransformation of **1** and **2** was proposed from **3** and **5** (an unknown compound, maybe an oxidative product of **4**), respectively, and the pathway was sketched as in Scheme 1. Oxidation of **3** yielded α-ketoaldehyde (**6**) by dioxygenase, which was further oxidized to give α-ketoacid (**7**). Combination with oxygen and dioxygenase,[12] **7** released CO_2 and **8** was produced. Under acidic conditions, **8** was converted into **1**. Compound **2** may be converted from **5** via the same pathway.

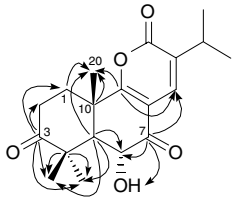
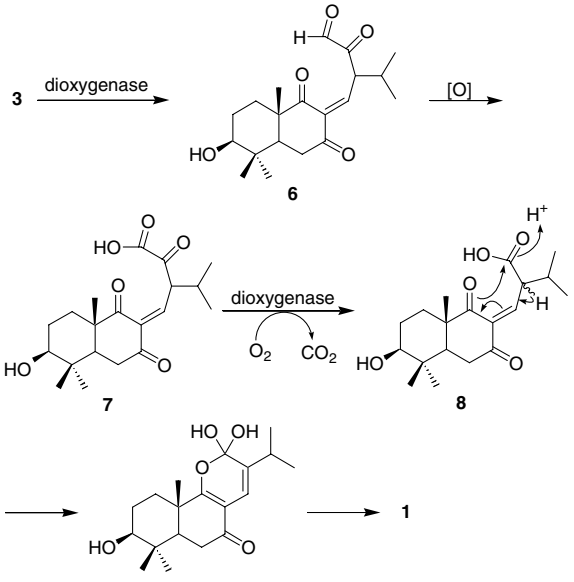


Figure 3. Selected HMBC correlations of **2**.



Scheme 1. Proposed biogenetic pathway for the formation of **1**.

Acknowledgements

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10. Taiwanlactone A (**1**): Colorless gun; $[\alpha]_D^{27}$ +36.6 ($CHCl_3$, *c* 0.7); EIMS *m/z* (rel int): 318(M^+, 38), 303(M^+-CH_3, 9), 300(M^+-H_2O, 6), 285(10), 275(18), 257(13), 179(100); HREIMS *m/z*: 318.1826 (calcd for $C_{19}H_{26}O_4$: 318.1832); IR ν_{max}: 3473, 3090, 1739, 1678, 1633, 1581, 1028, 951, 872, 785, 738 cm^{-1}; UV λ_{max} (log ε) (MeOH) 274.0 (3.93) nm; ^1H NMR (400 MHz, $CDCl_3$): δ 0.91, 1.02, 1.33 (each 3H, s, H_3-19, H_3-18, and H_3-20, respectively), 1.15, 1.17 (each 3H, d, $J = 6.8$ Hz, H_3-17 and H_3-16), 1.64, 1.65, 1.85 (each 1H, m, H_α-1, H_β-2, and H_α-2, respectively), 1.81 (1H, dd, $J = 13.6$, 3.6 Hz, H-5), 2.28 (1H, dt, $J = 13.6$, 3.2 Hz, H_β-1), 2.50 (1H, dd, $J = 17.6$, 13.6 Hz, H_β-6), 2.64 (1H, dd, $J = 17.6$, 3.6 Hz, H_α-6), 2.91 (1H, sep, $J = 6.8$ Hz, H-15), 3.28 (1H, dd, $J = 11.2$, 4.6 Hz, H-3), 7.57 (1H, s, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.2 (C-19, q), 19.0 (C-20, q), 21.0 (C-16, q), 21.2 (C-17, q), 26.7 (C-2, t), 27.4 (C-18, q), 28.5 (C-15, d), 32.0 (C-1, t), 34.5 (C-6, t), 38.7 (C-4, s), 39.6 (C-10, s), 47.9 (C-5, d), 77.6 (C-3, d), 111.9 (C-8, s), 132.5 (C-14, d), 132.9 (C-13, s), 160.9 (C-12, s), 178.5 (C-9, s), 194.8 (C-7, s). Taiwanlactone B (**2**): Colorless gun; $[\alpha]_D^{27}$ +81.3 ($CHCl_3$, *c* 0.1); EIMS *m/z* (rel int): 332(M^+, 100), 317(M^+-CH_3, 10), 314(M^+-H_2O, 9), 303(31), 220(50), 193(55), 149(41); HREIMS *m/z*: 332.1616 (calcd for $C_{19}H_{24}O_5$: 332.1624); IR ν_{max}: 3480, 3085, 1746, 1719, 1685, 1639, 1590, 1130, 1042, 937, 871, 838, 785 cm^{-1}; UV λ_{max} (log ε) (MeOH) 274.0 (3.88) nm; ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (6H, d, $J = 6.8$ Hz, H_3-16 and H_3-17), 1.35 (6H, s, H_3-18, and H_3-20), 1.44 (3H, s, H_3-19), 2.17 (1H, m, H_α-1), 2.39 (1H, ddd, $J = 13.6$, 9.6, 5.2 Hz, H_β-1), 2.45 (1H, d, $J = 12.4$ Hz, H-5), 2.50 (1H, ddd, $J = 16.4$, 9.6, 4.8 Hz, H_α-2), 2.77 (1H, ddd, $J = 16.4$, 11.6, 5.2 Hz, H_β-2), 2.95 (1H, sep, $J = 6.8$ Hz, H-15), 3.69 (1H, s, OH), 4.34 (1H, d, $J = 12.4$ Hz, H-6), 7.54 (1H, s, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.7 (C-19, q), 19.9 (C-20, q), 21.0 (C-16, q), 21.2 (C-17, q), 28.8 (C-15, d), 30.6 (C-18, q), 32.4 (C-1, t), 32.6 (C-2, t), 39.5 (C-10, s), 47.0 (C-4, s), 52.5 (C-5, d), 71.3 (C-6, d), 109.6 (C-8, s), 131.61 (C-14, d), 134.3 (C-13, s), 160.3 (C-12, s), 175.8 (C-9, s), 195.8 (C-7, s), 215.1(C-3, s). (*S*)-MTPA ester of **1** (**1a**): Colorless oil; EIMS *m/z* (rel int): 534(M^+, 4), 301(43), 189(100); ^1H NMR (400 MHz, $CDCl_3$): δ 0.93 (6H, s, H_3-18 and H_3-19), 1.34 (3H, s, H_3-20), 1.17, 1.18 (each 3H, d, $J = 6.8$ Hz, H_3-17 and H_3-16), 1.72, 1.75 (each 1H, m, H_α-1 and H_β-2), 1.94 (1H, dd, $J = 13.6$, 3.6 Hz, H-5), 2.01 (1H, br d, $J = 16.8$ Hz, H_α-2), 2.33 (1H, br d, $J = 13.6$ Hz, H_β-1), 2.51 (1H, dd, $J = 17.6$, 13.6, H_β-6), 2.63 (1H, dd, $J = 17.6$, 3.6 Hz, H_α-6), 2.93 (1H, sep, $J = 6.8$ Hz, H-15), 3.50 (3H, s, OMe), 4.74 (1H, dd, $J = 10.8$, 4.4 Hz, H-3), 7.42 (3H, m), 7.50 (2H, m), 7.57 (1H, s, H-14). (*R*)-MTPA ester of **1** (**1b**): Colorless oil; EIMS *m/z* (rel int): 534(M^+, 8), 301(64), 189(100); ^1H NMR (400 MHz, $CDCl_3$): δ 0.85, 0.92, 1.36 (each 3H, s, H_3-18, H_3-19, and H_3-20, respectively). 1.17, 1.18 (each 3H, d, $J = 6.8$ Hz, H_3-17 and H_3-16), 1.72 (1H, ddd, $J = 14.0$, 13.6, 4.0 Hz, H_α-1), 1.85 (1H, dddd, $J = 16.8$, 13.6, 11.6, 4.0 Hz, H_β-2), 1.93 (1H, dd, $J = 13.6$, 3.6 Hz, H-5), 2.06 (1H, dq, $J = 16.8$, 4.0 Hz, H_α-2), 2.36 (1H, dt, $J = 14.0$, 4.0 Hz, H_β-1), 2.50 (1H, dd, $J = 17.6$, 13.6, H_β-6), 2.62 (1H, dd, $J = 17.6$, 3.6 Hz, H_α-6), 2.93 (1H, sep, $J = 6.8$ Hz, H-15), 3.55 (3H, s, OMe), 4.78 (1H, dd, $J = 11.6$, 4.0 Hz, H-3), 7.41 (3H, m), 7.52 (2H, m), 7.57 (1H, s, H-14).
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