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Two novel sesquiterpenes from the roots of *Taiwania cryptomerioides* Hayata

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Abstract—Two novel 3,4-secocadinane and 4,5-seco-8(7→6)-abeoguaiane skeletons, namely taiwaninones A (**1**) and B (**2**), together with khusinodiol (**3**) and 4β,6β-dihydroxy-1α,5β(*H*)-guai-9-ene (**4**) were isolated from the roots of *Taiwania cryptomerioides*. Their structures were elucidated by the spectral methods. The biotransformations of **1** and **2** were proposed from **3** and **4**, respectively.
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Taiwania (*Taiwania cryptomerioides*, Taxodiaceace) is one genus and one species in Taiwan. It is an edemic plant and an important building material due to antifungal and decay-resistant characteristics. Because of yellowish red with distinguished purple–pink streaks on the crossed face of its heartwood and its excellent durability, it is a highly valuable building material. We have previously investigated the chemical components of the heartwood[1a–c] and bark[2a–e] of this plant. Over 6% of essential oil was observed from the heartwood.[3] α-Cadinol is a major component in the essential oil, and it shows selectivity for human colon tumor cell lines.[4] We have found lignan and cadinane-type compounds possessed significant cytotoxicity against three human tumor cell lines.[5] The interesting thing is that the heartwood contained abietane-type diterpenes,[6a,b] but both abietane and podocarpane (trinorabietane) were observed in the bark.[2a–e] The chemical studies of the roots of *T. cryptomerioides* have not been investigated, therefore, we are encouraged to research the chemical principle of this part. We report here two novel 3,4-secocadinane and 4,5-seco-8(7→6)abeoguaiane, namely taiwaninones A (**1**) and B (**2**), together with two known khusinodiol (**3**)[7] and 4β,6β-dihydroxy-1α,5β(*H*)-guai-9-ene (**4**).[8]

Taiwaninones A (**1**) was isolated as a needle crystal (mp 87–88°C). It showed molecular formula $C_{15}H_{26}O_2$ based on ^{13}C NMR and HREIMS data and represents three indices of hydrogen deficiency (IHD). The IR spectrum of **1** exhibited bonds attributable to a hydroxyl group (3416 cm^{-1}), a vinyl group (3069, 1645, 1003 and 914 cm^{-1}), and a ketone group (1705 cm^{-1}). The ^1H NMR[9] spectrum shows signals for an isopropyl group [δ 0.72 and 0.88 (each 3H, d, $J=7.2$ Hz), 1.64 (1H, m)], a methyl singlet (δ 1.11) for attached to a quaternary carbon bearing a hydroxyl group, a propanonyl group [δ 2.06 (3H, s), 2.33 (1H, dd, $J=18.0$, 5.2 Hz, H_a-5), and 2.41 (1H, dd, $J=18.0$, 4.0 Hz, H_b-5)], and a vinyl group [δ 5.12 (1H, dd, $J=16.8$, 2.4 Hz), 5.16 (1H, dd, $J=10.4$, 2.4 Hz) and 5.52 (1H, ddd, $J=16.8$, 10.4, 10.4 Hz)]. The ^{13}C NMR data[9] indicated it is a sesquiterpene ascribing to 15 carbon signals. From DEPT technique revealed four CH_3, four CH_2, five CH, and two C including oxygen-bearing carbon [δ_C 71.5 (C-10)], two vinyl carbons [δ_C 119.6 (C-3) and 138.3 (C-2)], three propanonyl carbons [δ_C 30.6 (C-15), 207.9 (C-4), and 46.5 (C-3)], and three methyl carbons [δ_C 15.3 (C-12), 21.8 (C-13), and 22.2 (C-14)]. Because the IHD of **1** was three including one acetyl and one vinyl functionalities, the number of rings in **1** should be one. Cadinane-type sesquiterpene is a major fraction in the essential oil of Taiwania.[1a–c] Comparison of the ^1H and ^{13}C NMR data of **1** and cadinol derivatives[10] [and khusinodiol (**3**)], **1** was considered contained a 1-hydroxy-*p*-methane moiety with two substituents, a vinyl and an acetonyl on C-2 and C-3 or reverse. A signal at δ 1.82 (1H, dd, $J=11.2$, 10.4 Hz) was assigned as H-1, which exhibited the COSY correlation with H-2 (δ 5.52) and H-6 [δ 1.97 (1H, m)]. The latter proton (H-6) has coupled with H-5 (δ 2.32 and 2.41) and H-7 [δ 1.11 (1H, m)]. One set of consecutive protons, H-7, H-8 and H-9, and the other set of consecutive protons, H-7, H-11, and H-12 (and H-13) are also revealed from

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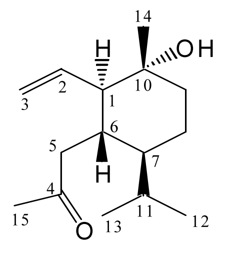
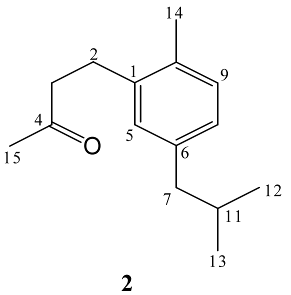
COSY spectrum. The HMBC correlation (see structure **5**) confirmed the structure of **1** as 3-acetonyl-2-vinyl-*p*-menthan-1-ol. As to its relative configuration of all substituents were justified from its NOESY spectrum (see structure **6**). The skeleton of **1** was deduced as 3,4-secocadinane, a novel skeleton.

HREIMS and ^{13}C NMR data revealed taiwaninone B (**2**) to be a sesquiterpene with the formula $C_{15}H_{22}O$ [M$^+$ m/z 218.1069]. The IR spectrum of **2** display peaks for a ketone (1720 cm^{-1}), an isopropyl (1382, 1365 cm^{-1}), and an aromatic groups (1621, 1503 cm^{-1}). Three aromatic ^{1}H NMR signals present at δ 6.86 (1H, br s, H-5), 6.87 (1H, br d, J=8.4 Hz, H-8), and 7.02 (1H, d, J=8.4 Hz, H-9). From these coupling constants and chemical shift, the structure of **2** can be considered as 1,2,4-trialkylbenzene compound. The methyl group appeared at δ 2.25 (3H, s) revealed it was a phenyl methyl group. The secondary alkyl group substituent was judged as 3-oxobutyl group due to the signals at δ 2.83 (2H, t, J=8.8 Hz, H-2), 2.68 (2H, t, J=8.8 Hz, H-3), 2.14 (3H, s, H-15). The third set of signals at δ 2.38 (2H, d, J=6.8 Hz, H-7), 1.80 (1H, m, H-11), 0.87 (6H, d, J=6.8 Hz, H-12, H-13), were assigned as 2-methylpropanyl group. Fifteen ^{13}C NMR signals[9] appeared for six aromatic carbons [with three CH (δ_C 127.0, 129.4, and 130.0) and three C (δ_C 132.9, 138.6, and 139.5)], four CH$_3$, three CH$_2$, one CH, and one carbonyl (δ_C 208.3), and NMBC correlation (see structure **7**) confirmed the assigned structure. As to its relative location of three substituents was revealed from NOESY technique (see structure **8**). Thus, based on the above evidence the structure of **2** was established to be 4-(2-methylpropyl)-2-(3-oxobutyl)toluene. It was a novel skeleton of 4,5-seco-8(7→6)-abeoguaiane or 4,5-secovalerenane.

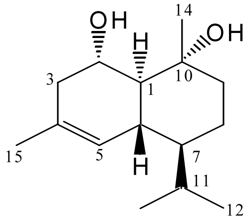
The biotransformations of **1** and **2** were proposed from **3** and **4**, respectively, and the pathway was sketched as in Scheme 1. Hydration of khusinodiol (**3**) yielded triol **9** which was converted to **1** via 1,4-elimination under acid condition. In acidic condition, compound **4** was transferred to cation **10** via ring contraction. After rearrangement, cation **10** become stable valerenane derivative **11**, which was oxidized with monooxygenase to give diol **12**. Through the 1,4-elimination pathway, taiwaninone B (**2**) was yielded from **12**.



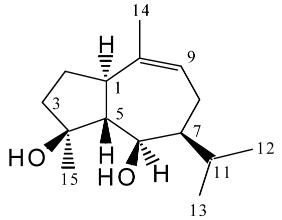
1



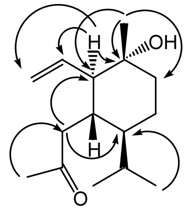
2



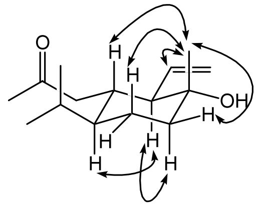
3



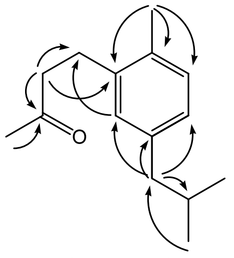
4



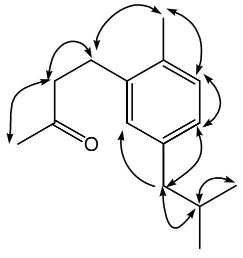
5 (Key HMBC)



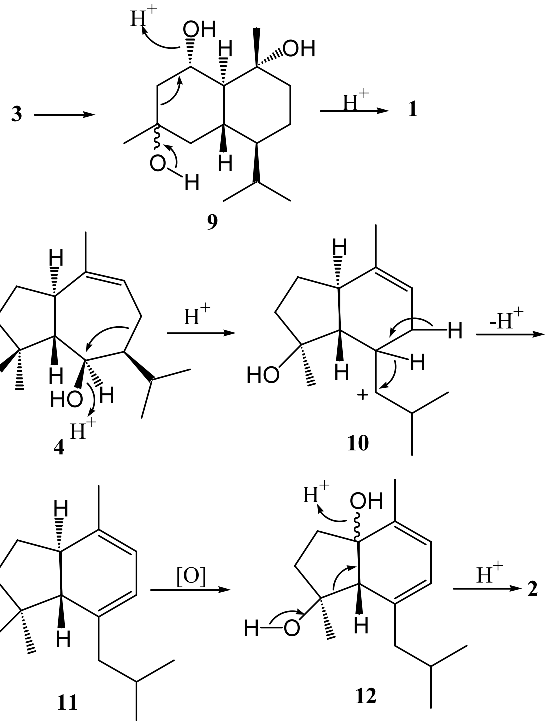
6 (Key NOESY)



7 (Key HMBC)



8 (Key NOESY)



Scheme 1.

Acknowledgements

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9. Taiwaninone A (**1**): mp 87–88°C; $[\alpha]_D^{31}$ −66.7 ($CHCl_3$, *c* 0.5); EIMS m/z (rel. intensity): 238 (M^+, 4), 220 (47), 162 (56), 122 (100), 119 (56); HREIMS m/z 238.1951 (calcd for $C_{15}H_{26}O_2$; 238.1934); IR ν_{max} 3416, 3069, 1705, 1645, 1421, 1364, 1003, 914 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.72, 0.88 (each 3H, d, J=7.2 Hz, H-12, H-13), 1.11, 2.06 (each 3H, s, H-14, H-15), 1.11 (1H, m, H-7), 1.16, 1.59 (each 1H, m, H_2-8), 1.40 (1H, ddd, J=12.8, 12.8, 3.6 Hz, Hα-9), 1.59 (1H, m, H_β-9), 1.64 (1H, m, H-11), 1.82 (1H, dd, J=11.2, 10.4 Hz, H-1), 1.97 (1H, m, H-6), 2.33 (1H, dd, J=18.0, 5.2 Hz, Ha-5), 2.41 (1H, dd, J=18.0, 4.0 Hz, Hb-5), 5.12 (1H, dd, J=16.8, 2.4 Hz, Ha-3), 5.16 (1H, dd, J=10.4, 2.4 Hz, Hb-3), 5.52 (1H, ddd, J=16.8, 10.4, 10.4 Hz, H-2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3 (C-12, q), 21.8 (C-13, q), 21.1 (C-8, t), 22.2 (C-14, q), 27.7 (C-11, d), 30.6 (C-15, q), 35.6 (C-6, d), 39.5 (C-9, t), 46.5 (C-5, t), 46.7 (C-7, d), 60.6 (C-1, d) 71.5 (C-10, s), 119.6 (C-3, t), 138.3 (C-2, d), 207.9 (C-4, s). Taiwaninone B (**2**): viscous gum; EIMS m/z (rel. intensity): 218 (M^+, 13), 200 (50), 175 (100), 157 (70), 117 (50); HREIMS m/z: 218.1669 (calcd for $C_{15}H_{22}O$: 218.1672); IR ν_{max} 3030, 1720, 1621, 1503, 1308, 1365, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); see text; ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.8 (C-14, q), 22.4 (C-12, C-13, q), 27.2 (C-2, t), 30.0 (C-15, q), 30.2 (C-11, d), 44.1 (C-3, t), 45.0 (C-7, t), 127.0 (C-8, d), 129.4 (C-5, d), 130.0 (C-9, d), 132.9 (C-10, s), 138.6 (C-1, s), 139.5 (C-6, s), 208.3 (C-4, s).
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