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# UNCOMMON DITERPENES WITH THE SKELETON OF SIX-FIVE-SIX FUSED-RINGS FROM TAIWANIA CRYPTOMERIOIDES

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Key Word Index-Taiwania cryptomerioides, taxodiaceae; leaves; diterpenes.

Abstract—Four diterpenoid aldehydes and one norditerpenoid ketone having the uncommon skeleton of six-five-six fused-rings were isolated from the leaves of *Taiwania cryptomerioides*.

#### INTRODUCTION

Taiwania cryptomerioides Hayata, is an endemic evergreen species with thick linear-triangular leaves and elongate ovoid cones. The chemical constituents of this plant have been investigated extensively [1-5]. Varied sesquiterpenes, lignans and bisflavones have been found in the essential oil of the leaves and wood. We report herein the isolation of four diterpenes 1-4 and a norditerpene 5, which have the uncommon skeleton of fused 6-5-6 rings, in addition to known diterpenes.

## **RESULTS AND DISCUSSION**

Four known abietane-type diterpenes, ferruginol (6) [6, 7], 6,7-dehydroferruginol (7) [6], 7 $\beta$ -hydroxy-royleanone (8) [8], 7 $\alpha$ -hydroxyroyleanone (9) [8] and a secoabietane dialdehyde (10) [9], were identified by comparison of their physical and spectral data (mp, [ $\alpha$ ], mass, IR, <sup>1</sup>H and <sup>13</sup>C NMR) with those in the literature.

Compound 1, namely taiwaniaquinone A, was isolated as orange crystals, mp 201–203° (decomposed). Its structure was determined by spectral methods. The exact mass  $[M]^+$  at m/z 330.1825 indicated the molecular formula  $C_{20}H_{26}O_4$ . The IR absorptions at 1659 and 1639 cm<sup>-1</sup>, and the UV absorptions at 432 ( $\varepsilon$  579), 284 ( $\varepsilon$  6400) and 207 nm ( $\varepsilon$  12 600) were attributable to the quinone moiety. The <sup>13</sup>C signals of the quinone moiety occurred at  $\delta$  124.6, 149.2, 151.2, 152.8, 181.0 and 185.3 (Table 1). The proton resonance (Table 2) at  $\delta$  9.84 (d, J = 4 Hz) and the carbon signal at  $\delta$  200.2 were attributable to an aldehyde group. The skeleton of 6–5–6 fused-rings were established by means of the C–H COSY and the HMBC experiment. Irradiation of Me-10 (at  $\delta$  1.14) caused 10% nOe of H-7 (at  $\delta$  3.76). The stereochemistry of 1 was thus confirmed.

\* Solution in CDCl<sub>3</sub>. † Solution in acetone- $d_6$ .

TI : 1 C : 1

‡ The signal of methylenedioxy group in 4 appeared at  $\delta$  100.8.

§ The signal of methoxyl group in 5 appeared at  $\delta$  62.1.

H-5 and H-7 were *trans* oriented and had a large coupling constant 11.5 Hz. Compound 1,  $[\alpha]_{D}^{25} - 220.6^{\circ}$ , showed a positive Cotton effect with the maximum at 309 nm ([ $\theta$ ], 22 600). Compound 1 was assigned to have the (5S, 7R, 10S)-configuration by analogy to those abietanes found in the plants of the Taxodiaceae family [4, 5]. The uncommon 6–5–6 rings skeleton was presumably formed (biogenetically) from the pinacol rearrangement of abietane-6, 7-diol as depicted in A (Scheme 1).

Table 1. <sup>13</sup>C NMR spectral data of 1-5 ( $\delta$  value in ppm)

С	1*	2†	3†	<b>4*</b> ·‡	5*·§
1	34.4	35.8	37.6	35.6	30.3
2	19.3	20.2	20.4	19.7	17.5
3	41.1	44.1	44.2	41.7	36.5
4	33.6	35.1	35.2	34.0	34.3
5	61.5	62.1	69.6	61.5	65.1
6	200.2	203.7	201.5	205.0	
7	54.4	88.4	90.2	54.5	211.1
8	149.2	148.8	147.4	113.4	118.3
9	152.8	155.1	154.3	132.3	142.7
10	48.7	50.2	47.3	46.3	42.7
11	181.0	182.8	182.6	135.2	138.4
12	151.2	154.3	153.5	146.8	152.2
13	124.6	125.0	125.6	116.7	126.1
14	185.3	186.1	187.0	146.0	151.1
15	24.2	24.9	24.9	25.1	25.9
16	19.8	20.4	20.5	21.0	20.6
17	19.8	20.4	20.5	21.1	20.6
18	35.0	34.8	33.8	34.4	24.4
19	21.8	23.7	24.6	22.0	33.0
20	20.1	22.8	23.9	22.4	28.8

Table 2. <sup>1</sup>H NMR spectral data of 1–5 ( $\delta$  value in ppm; J value in Hz)

Н	1*	2†	3†	<b>4*</b> ‡	<b>5*</b> §
5	2.13 (d, J = 11.5)	2.04 (s)	2.26 (s)	2.16 (d, J = 11)	2.10 (s)
6	9.84 $(d, J = 4)$	9.82 (s)	10.08 (s)	9.47 $(d, J = 5)$	(-/
7	3.76 (dd, J = 11.5, 4)		.,	3.77 (dd, J = 11, 5)	
15	3.12 (sept, J = 7)	3.12 (sept, J = 7)	3.14 (sept, J = 7)	3.16 (sept, J = 7)	3.25 (sept, J = 7)
16	1.17 (d, J = 7)	1.16 (d, J = 7)	1.18 (d, J = 7)	1.26 (d, J = 7)	1.36 (d, J = 7)
17	1.18 (d, J = 7)	1.16 (d, J = 7)	1.17 (d, J = 7)	1.26 (d, J = 7)	1.36(d, J = 7)
18	0.79 (s)	0.78(s)	1.11 (s)	0.89 (s)	0.86 (s)
19	1.05 (s)	1.20(s)	1.04 (s)	1.06 (s)	1.24 (s)
20	1.14 (s)	1.49 (s)	1.35 (s)	1.10 (s)	1.42 (s)

\* Solution in CDCl<sub>3</sub>.

 $\dagger$  Solution in acetone- $d_6$ .

<sup>‡</sup> The signals of methylenedioxy group in 4 appeared at 5.82 (d, J = 1) and 5.87 (d, J = 1). § The signal of methoxyl group in 5 appeared at  $\delta$  3.78 (s).





The structures of two 7-hydroxylated derivatives 2 (namely taiwaniaquinone B) and 3 (namely taiwaniaquinone C) were determined by similar procedures. Their pertinent <sup>13</sup>C and <sup>1</sup>H signals are listed in Tables 1 and 2. The formyl group in 3 oriented on the  $\beta$ -face as the proton signal at  $\delta$  10.08 showed 10% nOe upon irradiation of Me-10 (at  $\delta$  1.35). Compound 2 showed a positive Cotton effect with maximum  $[\theta]_{304}$  21 100, whereas the epimer 3 showed a negative Cotton effect with minimum  $[\theta]_{316} - 6100$ .

The molecular formula  $C_{21}H_{28}O_4$  for 4, which we have named taiwaniaquinol A, was deduced from its parent peak at m/z 344.1979. Compound 4 was colourless and crystalline, mp 158–160 °C. It showed intense IR absorptions at 3335 and 1686 cm<sup>-1</sup> for the hydroxyl and carbonyl groups. The <sup>1</sup>H NMR spectrum exhibited characteristic signals at  $\delta$  5.87 and 5.82 for the methylenedioxy group. The corresponding carbon signal appeared at  $\delta$  100.8. The structure of taiwaniaquinol A (4) was finally determined by means of the H–H COSY, C–H COSY and HMBC experiments. The nOe effect (13%) of H-7, observed by irradiation of Me-10 (at  $\delta$  1.10), was in agreement with the assigned stereochemistry. The large coupling constant 11 Hz between H-5 and H-7 conformed to their *trans*-relationship.

The NMR analysis revealed that compound 5 ( $C_{20}H_{28}O_4$ ) is a norditerpene containing a methoxyl group ( $\delta_H$  3.78 and  $\delta_C$  62.1). The conjugated ketone showed IR absorption at 1638 cm<sup>-1</sup> and a carbon signal at  $\delta$  211.1. Compound 5, named taiwaniaquinol B, has a *cis*-ring junction as revealed by a nOe experiment, i.e. an 18% enhancement of H-5 (at  $\delta$  2.10) resulting from irradiation of Me-10 (at  $\delta$  1.42).

In summary, compounds 1-4 represent a new class of diterpenes, and 5 is a novel norditerpene. This is the first report of compounds having the uncommon 6-5-6 rings in nature.

## EXPERIMENTAL

General and plant material. The dried leaves (1.75 kg) of T. cryptomerioides were exhaustively extracted with  $Me_2CO(71 \times 3)$ . The combined extracts were concd to ca 0.81, and taken up with CHCl<sub>3</sub> (0.81  $\times$  3). The CHCl<sub>3</sub>soluble portion was concd (55g) and subjected to silica gel CC. The portion obtained from elution with EtOAc in hexane (5-20%) was further purified by HPLC (Hibar Lichrosorb Si 60, 7 or 10  $\mu$ m, 25 × 1 cm) with elution by EtOAc-hexane (1:10) to give compounds 1 (40 mg), 2 (20 mg), 3 (20 mg), 4 (25 mg), 5 (10 mg), 6 (30 mg), 7 (6 mg), 8 (251 mg), 9 (55 mg), 10 (15 mg). Merck Silica sheets were used for analyt. gel 60F TLC (EtOAc-hexane, 1:9).

Taiwaniaquinone A (1). Orange crystals from EtOAchexane (1:9). Mp 201–203 °C (decomposed).  $[\alpha]_{D^5}^{25}$  – 220.6° (CHCl<sub>3</sub>; c 1.3). TLC (EtOAc-hexane, 1:9)  $R_f$  0.5. IR  $\nu_{max}^{KBr}$  cm<sup>-1</sup>. 3331, 1706, 1659, 1639. UV  $\lambda_{max}^{MeOH}$  nm ( $\varepsilon$ ): 432 (579), 284 (6400), 207 (12 600). EIMS (70 eV) m/z (rel. int.): 330 [M]<sup>+</sup> (2), 302 (100), 287 (22), 233 (68), 220 (35), 121 (5), 109 (8). HRMS for C<sub>20</sub>H<sub>26</sub>O<sub>4</sub> requires: 330.1832. Found: 330.1825. CD (MeOH) [ $\theta$ ]<sub>309</sub> + 22600, [ $\theta$ ]<sub>277</sub> – 1900, [ $\theta$ ]<sub>267</sub> – 1100, [ $\theta$ ]<sub>249</sub> – 4400, [ $\theta$ ]<sub>237</sub> – 3600.

Taiwaniaquinone B (2). Orange crystals from EtOAchexane (1:9). Mp 183–185 °C (decomposed).  $[\alpha]_{D}^{31} - 83^{\circ}$ (CHCl<sub>3</sub>; c 0.27). TLC (EtOAc-hexane, 1:9)  $R_{f}$  0.43. IR  $\nu_{max}^{KBr}$  cm<sup>-1</sup>: 3498, 3376, 1720, 1662, 1664. UV  $\lambda_{max}^{MeOH}$  nm ( $\epsilon$ ): 427 (619), 277 (6000), 204 (8900). EIMS (70 eV) m/z(rel. int.): 317 [M - CHO]<sup>+</sup> (56), 299 (4), 209 (100), 187 (5), 115 (10), 109 (68), HRMS for C<sub>20</sub>H<sub>26</sub>O<sub>5</sub>-CHO requires: 317.1754. Found: 317.1749. CD (MeOH) [ $\theta$ ]<sub>353</sub> + 1800, [ $\theta$ ]<sub>304</sub> + 21 100, [ $\theta$ ]<sub>257</sub> - 9800.

Taiwaniaquinone C (3). Orange crystals from EtOAchexane (1:9). Mp 210–212 °C (decomposed).  $[\alpha]_{31}^{31}$  – 266 (CHCl<sub>3</sub>; c 0.27). TLC (EtOAc-hexane, 1:9)  $R_f$  0.45. IR  $\nu_{max}^{KBr}$  cm<sup>-1</sup>: 3497, 3358, 1718, 1648, 1623. UV  $\lambda_{max}^{MeOH}$  nm ( $\varepsilon$ ): 426 (631), 270 (8300), 220sh (22000), 202 (123800). EIMS (70 eV) m/z (rel. int.): 317 [M – CHO]<sup>+</sup> (52), 299 (4), 233 (5), 209 (100), 205 (8), 115 (9), 109 (68). HRMS for C<sub>20</sub>H<sub>26</sub>O<sub>5</sub>-CHO requires: 317.1754. Found: 317.1749. CD (MeOH) [ $\theta$ ]<sub>399</sub> + 2600, [ $\theta$ ]<sub>352</sub> + 6200, [ $\theta$ ]<sub>316</sub> – 6100, [ $\theta$ ]<sub>280</sub> + 17 700, [ $\theta$ ]<sub>248</sub> + 4000, [ $\theta$ ]<sub>228</sub> + 12 000.

Taiwaniaquinol A (4). Crystals from EtOAc-hexane (1:9). Mp 158–160 °C.  $[\alpha]_{21}^{31}$  + 88.2° (CHCl<sub>3</sub>; c 0.64). TLC (EtOAc-hexane, 1:9)  $R_f$  0.48. IR  $\nu_{max}^{\text{KBr}}$  cm<sup>-1</sup>. 3335, 1686. UV  $\lambda_{max}^{\text{MeOH}}$  nm ( $\varepsilon$ ): 293 (4300), 206 (34 200). EIMS (70 eV) m/z (rel. int.): 344 (82), 315 (100), 273 (3), 259 (10), 245 (25), 231 (10), 203 (4). HRMS for C<sub>21</sub>H<sub>28</sub>O<sub>4</sub> requires: 344.1988. Found: 344.1979. CD (MeOH)  $[\theta]_{352}$  + 200,  $[\theta]_{308}$  + 16 800,  $[\theta]_{280}$  - 6400,  $[\theta]_{260}$  - 2500,  $[\theta]_{251}$  - 2800,  $[\theta]_{226}$  + 2000,  $[\theta]_{210}$  - 1000. *Taiwaniaquinol B* (5). Crystals from EtOAc-hexane (1:9). Mp 142-144 °C.  $[\alpha]_{31}^{31} - 37.7^{\circ}$  (CHCl<sub>3</sub>; c 0.27). TLC (EtOAc-hexane, 1:9)  $R_f$  0.63. IR  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 3297, 1638. UV  $\lambda_{\text{max}}^{\text{MeOH}}$  nm ( $\varepsilon$ ): 350 (4900), 276 (10 000), 238 (14 000), 207 (18 700). EIMS (70 eV) m/z (rel. int.): 332 (100), 317 (38), 263 (8), 249 (45), 233 (10), 219 (6), 149 (3). HRMS for C<sub>20</sub>H<sub>28</sub>O<sub>4</sub> requires: 332.1988. Found: 332.1986.

*Ferruginol* (6). Oil solid.  $[\alpha]_D^{20} + 37^\circ$  (CHCl<sub>3</sub>; c 1.2) (lit. [6]  $[\alpha]_D^{16} + 40.6^\circ$ ).

6,7-Dehydroferruginol (7). Oil.  $[\alpha]_D^{24} - 59^\circ$  (CHCl<sub>3</sub>; c 0.5) (lit. [6]  $[\alpha]_D - 60^\circ$ ).

7β-Hydroxyroyleanone (8). Yellow solid. Mp 210–212°C (lit. [10, 11] 212–214°).  $[\alpha]_{D}^{20}$  + 330° (CHCl<sub>3</sub>; c 1.3) {lit. [10, 11]  $[\alpha]_{D}$  + 340° (CHCl<sub>3</sub>)}.

 $7\alpha$ -Hydroxyroyleanone (9). Yellow solid. Mp 175–176°C (lit. [12] 173–175°).  $[\alpha]_{D}^{22} - 135°$  (CHCl<sub>3</sub>; c 1.6) [lit. [12]  $[\alpha]_{D} + 132°$  (CHCl<sub>3</sub>)].

12-Hydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial (10). Solid. Mp 189–191 °C (lit. [9] 191–192 °).  $[\alpha]_D^{30} + 20$  ° (MeOH; c 0.7) {(lit. [9]  $[\alpha]_D^{25} + 22^\circ$  (MeOH; c 1.2)}.

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### REFERENCES

- Fang, J.-M. and Cheng, Y.-S. (1992) J. Chin. Chem. Soc. (Taipei) 39, 647.
- Kamil, M., Ilyas, M., Rahman, W., Hasaka, N., Okigawa, M. and Kawano, N. (1981) J. Chem. Soc., Perkin Trans. 1. 553.
- Kuo, Y.-H., Chen, W.-C. and Lin, Y.-T. (1987) Chem. Express 2, 105.
- 4. Su, W.-C., Fang, J.-M. and Cheng, Y.-S. (1993) Phytochemistry 34, 779.
- 5. Su, W.-C., Fang, J.-M. and Cheng, Y.-S. (1994) *Phytochemistry* **35**, 1279.
- 6. Bredenberg, J. B. (1957) Acta Chem. Scand. 11, 932.
- 7. Lin, Y.-T., Kuo, Y.-H. and Chang, B.-H. (1975) J. Chin. Chem. Soc. 22, 331.
- Hensch, M., Ruedi, P. and Eugster, C. H. (1975) Helv. Chim. Acta 58, 1921.
- Fang, J.-M., Jan, S.-T. and Cheng, Y.-S. (1986) J. Chem. Res. (S) 350.
- Kupchan, S. M., Karim, A. and Marcks, C. (1969) J. Org. Chem. 34, 3912.
- Kupchan, S. M., Karim, A. and Marcks, C. (1968) J. Am. Chem. Soc. 90, 5923.
- Edwards, O. E., Feniak, G. and Los, M. (1962) Can. J. Chem. 40, 1542.