Pergamon

PII: S0031-9422(97)00267-7

Phytochemistry, Vol. 46, No. 1, pp. 169–173, 1997

0031-9422/97 $17.00+0.00

CYCLOADDUCTS OF TERPENE QUINONES FROM *TAIWANIA CRYPTOMERIOIDES*

WANG-HONG LIN, JIM-MIN FANG* and YU-SHIA CHENG

Department of Chemistry, National Taiwan University, Taipei, Taiwan 106, People's Republic of China

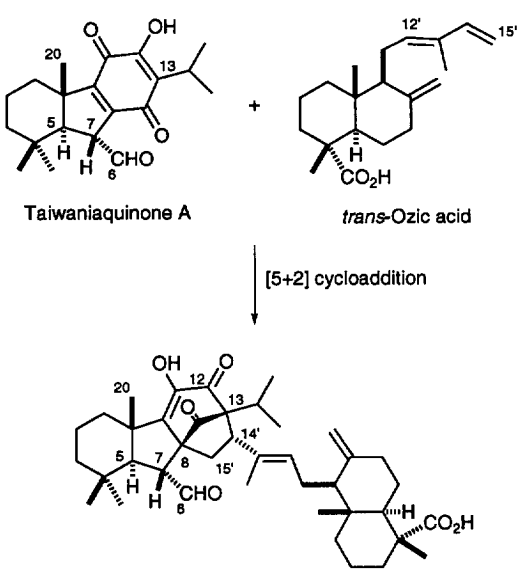
(*Received* 13 *January* 1997)

Key Word Index—*Taiwania cryptomerioides*; Taxodiaceae; leaves; diterpene quinones; ozic acid; cycloadducts.

Abstract—Four [4+2] or [5+2] cycloadducts formed from *trans*-ozic acid and a diterpene or norditerpene quinone were isolated from the leaves of *Taiwania cryptomerioides*. Among them, the [4+2] cycloadduct (taiwaniadduct I) formed from *trans*-ozic acid and a norditerpene quinone underwent an intramolecular [2+2] cycloaddition on standing at room temperature. The structures of these cycloadducts were determined by spectral analyses and of one by X-ray crystallography.

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 [1–3]. Various sesquiterpenes, lignans and bisflavones have been found in the leaves and wood. We recently isolated from this plant five diterpene quinones (taiwaniaquinones A–E), a diterpene quinol (taiwaniaquinol A), a norditerpenequinol (taiwaniaquinol B), and five related [4+2] and [5+2] cycloadducts (taiwaniadducts A–E) derived by the combination of taiwaniaquinone A with β-myrcene or *trans*-ozic acid [4, 5]. We report herein five new cycloadducts **1**–**5** (taiwaniadducts F–J) of such an uncommon type.



Scheme 1.

RESULTS AND DISCUSSION

Compound **1** gave rise to a molecular ion $[M]^+$ at *m/z* 632.4075 consistent with a molecular formula $C_{40}H_{56}O_6$. By detailed analyses of its IR, and ^1H and ^{13}C NMR spectra, the structure was assigned as a [5+2] cycloadduct of two diterpenes, taiwaniaquinone A and *trans*-ozic acid, with the linkages at C-8–C-15′ and C-13–C-14′ (Scheme 1). The ^{13}C and ^1H NMR spectra (Table 1) showed the characteristic resonances of an aldehyde [δ_H 10.23 (*d*) and δ_C 205.9 (*d*)], a ketone [δ_C 201.4 (*s*)], an enone [δ_C 141.7 (*s*), 145.9 (*s*) and 195.1 (*s*)], an acid [δ_C 184.7 (*s*)], a terminal double bond [δ_C 107.9 (*t*) and 147.5 (*s*)], as well as a trisubstituted double bond [δ_C 130.4 (*d*) and 131.5 (*s*)]. The regio- and stereochemistry of **1** was supported by the HMBC and NOESY studies. The HMBC spectrum showed that H-14′ (δ 3.15) was correlated to C-12 (δ 195.1) and C-13 (δ 73.3), whereas the NOESY spectrum showed that H-7 (δ 2.82) was correlated to H-20 (δ 1.21) as well as H-5 (δ 2.00) to H-6 (δ 10.23) and H-15′ (δ 2.44). The large coupling constant (13 Hz) between H-5 and H-7 was consistent with their *trans* relationship. Compound **1** (namely tai-

* Author to whom correspondence should be addressed.

Table 1. ^{13}C and ^{1}H NMR data of compounds **1**, **2m**–**4m** and **5** ($CDCl_3$)

	1		**2m**		**3m**		**4m**		**5**	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	35.9	1.52 (*m*)*	36.6†	*	35.7	1.48 (*m*)*	32.3	*	30.8	1.55 (*m*), 1.88 (*m*)
2	18.3	*	18.5	1.54 (*m*)*	18.4	1.45 (*m*)*	18.1	*	18.1	1.44 (*m*)*
3	41.0	1.14 (*m*), 1.44 (*m*)	43.6	1.06 (*m*), 1.34 (*m*)	41.9	*	41.7	1.38 (*m*)*	41.1	0.96 (*m*), 1.34 (*m*)
4	34.4		34.5		33.4		32.6		32.8	
5	57.3	2.00 (*d*, 13.0)‡	63.5	2.15 (*s*)	55.3	1.42 (*d*, 12.0)	62.3	2.01 (*s*)	60.9	1.57 (*s*)
6	205.9	10.23 (*d*, 4.4)	202.0	10.02 (*d*, 1.4)§						
7	55.1	2.82 (*dd*, 13.0, 4.4)	87.5		77.3	4.35 (*dd*, 12.0, 6.0)	204.8		206.5	
8	66.0		73.8		59.4		66.6		68.1	
9	145.9		142.2		66.1		60.2		55.5	
10	46.8		42.9		47.4		46.6		49.9	
11	141.7		144.1		200.0		198.6		210.5	
12	195.1		194.5		159.8		160.1		92.7	
13	73.3		67.3		140.9		143.2		59.4	
14	201.4		201.8		205.1		192.9		207.1	
15	26.7	2.34 (*m*)	27.5	2.16 (*m*)	25.9	3.16 (*sept*, 6.9)	25.7	3.21 (*sept*, 7.0)	34.3	2.23 (*sept*, 6.8)
16	16.9	1.00 (*d*, 7.0)	17.8	1.06 (*d*, 6.9)	19.6	1.16 (*d*, 6.9)	19.9	1.17 (*d*, 7.0)	20.6	1.23 (*d*, 6.8)
17	18.7	1.01 (*d*, 7.0)	18.1	1.06 (*d*, 6.9)	20.7	1.22 (*d*, 6.9)	20.6	1.15 (*d*, 7.0)	21.6	0.88 (*d*, 6.8)
18	34.1	0.88 (*s*)	33.1	0.97 (*s*)	35.4	0.97 (*s*)	32.6	1.07 (*s*)	32.6	1.07 (*s*)
19	21.3	0.90 (*s*)	23.2	0.88 (*s*)	22.0	0.91 (*s*)	21.5	0.95 (*s*)	21.4	0.89 (*s*)
20	19.1	1.21 (*s*)	24.5	1.48 (*s*)	21.0	0.69 (*s*)	21.3	0.78 (*s*)	23.2	1.01 (*s*)

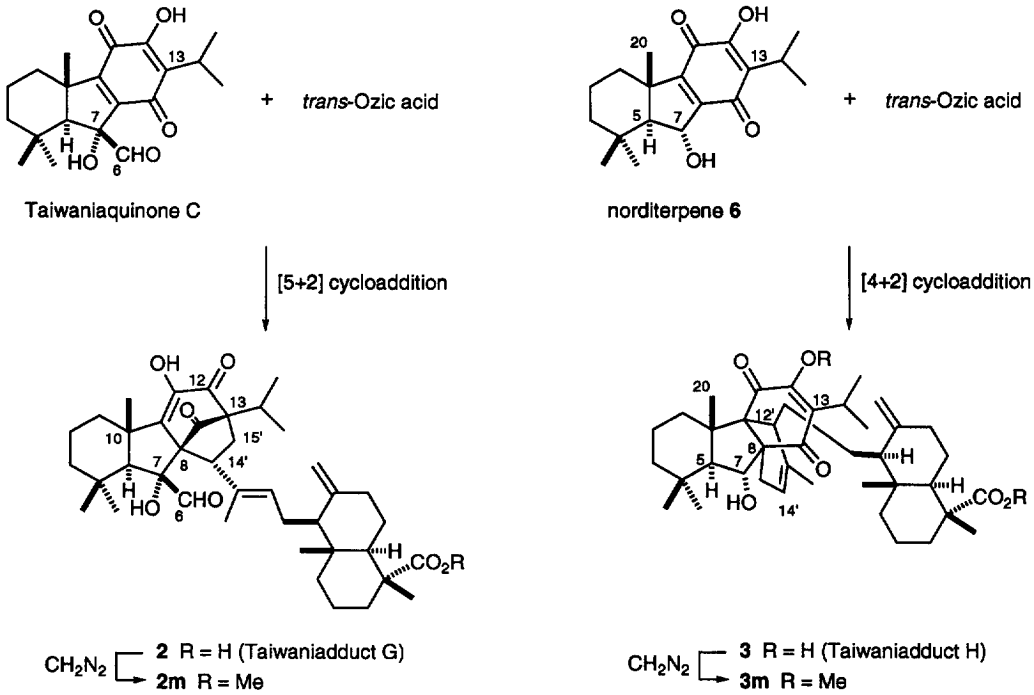
1′	38.0	2.00 (*m*), 1.70 (*m*)	38.1†	*	37.5†	*	37.1†	1.52 (*m*)*	39.2	1.64 (*m*), 0.71 (*m*)
2′	19.1	*	19.5	*	19.2	*	19.0	*	18.6	1.56 (*m*)*
3′	36.9	*	37.0†	*	36.8	1.48 (*m*), 1.93 (*m*)	37.5†	*	36.0	1.44 (*m*), 1.58 (*m*)
4′	47.3		47.7		47.7		47.6		47.7	
5′	49.3	1.90 (*m*)	49.8	1.92 (*dd*, 12.2, 2.7)	50.1	1.83 (*dd*, 12.4, 2.7)	50.2	1.88 (*m*)	48.0	1.35 (*m*)
6′	26.5	1.34 (*m*)*	26.5	1.18 (*m*)*	24.9	1.56 (*m*)*	26.7	*	21.3	1.06 (*m*)*
7′	37.4	2.28 (*m*)*	37.5†	*	37.8†	2.30 (*br d*, 12.0)[a]	37.9†	2.27 (*br d*, 10.9)*	33.8	1.98 (*m*), 1.60 (*m*)
8′	147.5		147.8		147.1		149.0		53.8	
9′	56.9	1.60 (*m*)	56.7	1.76 (*m*)	54.0	1.64 (*m*)	55.9	1.70 (*m*)	48.0	1.16 (*m*)
10′	38.6		38.8		38.8		40.7		39.9	
11′	22.5	2.12 (*m*)*	23.3	*	26.8	*	23.3	*	29.0	2.02 (*m*), 1.80 (*m*)
12′	130.4	5.05 (*br s*)	132.4	5.07 (*br t*, 5.2)	41.3	3.07 (*dd*, 11.8, 3.9)	51.5	*	49.2	2.88 (*m*)
13′	131.5		134.0		143.0		140.8		136.1	
14′	45.5	3.15 (*dd*, 10.6, 6.1)	44.5	3.29 (*t*, 10.0)	122.0	5.64 (*br d*, 7.1)	123.4	5.63 (*br t*, 5.0)	121.6	5.51 (*br d*, 5.6)
15′	38.0	2.44 (*m*)*	33.0	2.32 (*m*)*	30.6	2.17 (*br d*, 15.0), 2.42 (*dd*, 15.0, 7.8)	28.7	2.56 (*m*)*	29.9	2.80 (*m*) 2.45 (*br d*, 20.0)
16′	16.1	1.40 (*s*)	18.8	1.78 (*s*)	24.3	1.72 (*s*)	23.0	1.57 (*s*)	22.2	1.59 (*br s*)
17′	107.9	4.37 (*s*), 4.77 (*s*)	108.2	4.37 (*s*), 4.75 (*s*)	108.7	4.61 (*s*), 4.90 (*s*)	107.0	4.69 (*s*), 4.42 (*s*)	45.4	2.32 (*d*, 12.0), 2.77 (*d*, 12.0)
18′	184.7		179.2		179.2		179.2		178.8	
19′	16.3	1.11 (*s*)	16.7	1.13 (*s*)	16.5	1.08 (*s*)	16.5	1.07 (*s*)	17.1	1.08 (*s*)
20′	14.5	0.67 (*s*)	14.6	0.71 (*s*)	15.2	0.58 (*s*)	14.4	0.64 (*s*)	15.1	0.67 (*s*)
CO_2CH_3			51.9	3.65 (*s*)	51.9	3.63 (*s*)	51.9	3.62 (*s*)	52.0	3.60 (*s*)
OCH_3					60.0	3.99 (*s*)	59.9	3.86 (*s*)	55.1	3.47 (*s*)

* The signal of one or both protons was too weak to be assigned.

† Assignments may be exchanged.

‡ Coupling constants (J in Hz) in parentheses.

§ Coupled with 7-OH (δ 4.24).



Scheme 2.

Scheme 3.

waniadduct F) is a regioisomer of taiwaniadduct E [5], which is a cycloadduct between taiwaniaquinone A and *trans*-ozic acid with the linkages at C-8–C-14′ and C-13–C-15′.

Compound **2** was not readily purified. It was, therefore, subjected to methylation (CH_2N_2, Et_2O) and purified as its methyl ester **2m**. Ester **2m** ($C_{41}H_{58}O_7$), $[M]^+$ at *m/z* 662.4184, showed ^1H and ^{13}C resonances similar to those in taiwaniadduct E methyl ester [5], except for lack of the H-7 signal. The C-7 resonance of **2m** occurred at δ 87.5 (*s*), indicating the presence of a tertiary hydroxyl group at this position. Compound **2** (taiwaniadduct G) was thus a [5+2] cycloadduct between taiwaniaquinone C and *trans*-ozic acid with the linkages at C-8–C-14′ and C-13–C-15′ (Scheme 2). The C-10 methyl group (δ 1.48) and the C-7 aldehyde group (δ 10.02) had to be on the same face as they showed NOE correlation in the NOESY spectrum of **2m**. The HMBC spectrum of **2m** also showed the correlation of C-12 (δ 194.5) with H-15′ (δ 2.32), supporting the regiochemistry of the C-13–C-15′ linkage.

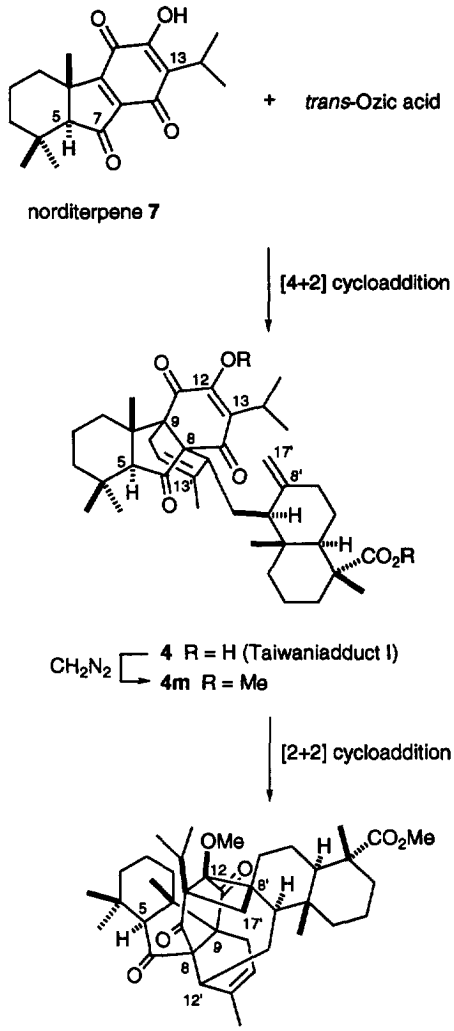
Compound **3** was treated with CH_2N_2 to give a bismethylated product **3m**, in which the two new methyl groups appeared at δ 3.63 and 3.99 attributable to the ester and enol ether moieties. Compound **3m** also had the characteristic resonances for two carbonyl groups [δ_C 200.0 (*s*) and 205.1 (*s*)], a terminal double bond [δ_C 108.7 (*t*) and 147.1 (*s*)], a trisubstituted double bond [δ_C 122.0 (*d*) and 143.0 (*s*)], as well as a secondary hydroxyl group [δ_C 77.3 (*d*)]. Compound **3m** gave rise to a molecular ion $[M]^+$ at *m/z* 648.4394 consistent with the molecular formula $C_{41}H_{60}O_6$. Based on the above spectral data, the parent acid **3** (taiwaniadduct H) was deduced to be a [4+2] cycloadduct of a norditerpene alcohol **6** and *trans*-ozic acid (Scheme 3). The structure was finally deduced from the HMBC spectrum of **3m**, in which the correlation of C-7 (δ 77.3) to C-15′ (δ 30.6) was confirmed. The stereochemistry was established by the NOESY spectrum, in which H-5 (δ 1.42) was correlated with H-12′ (δ 3.07) and H-7 (δ 4.35) with H-20 (δ 0.69). The large coupling constant (12 Hz) for H-5 and H-7 was in agreement with their *trans* relationship. Thus, **3** is formed by combination of two components with the linkages at C-8–C-15′ and C-9–C-12′.

Treatment of compound **4** with CH_2N_2 gave a bismethylated product **4m** ($C_{41}H_{58}O_6$), $[M]^+$ at *m/z* 646.4240. Compound **4m** yielded a crystalline compound **5** on standing at room temperature for three weeks (Scheme 4). The structure of **5** was unambiguously determined by X-ray crystallography (Fig. 1). Thus, **5** (taiwaniadduct J) is derived from **4m** via an intramolecular [2+2] cycloaddition with the linkages at C-12–C-8′ and C-13–C-17′. Compound **4** (taiwaniadduct I) is a [4+2] cycloadduct of the norditerpene **7** and *trans*-ozic acid with the linkages at C-8–C-12′ and C-9–C-15′. The cycloaddition occurs on the less hindered face of **7** to give **4** having the (8*R*, 9*R*, 12′*R*)-configuration.

EXPERIMENTAL

General. HPLC: Hibar Lichrosorb Si 60 column (10 μm, 25 cm × 1 cm i.d.); TLC: Merck silica gel 60F sheets.

Plant material. The dried leaves (1.75 kg) of *T. cryptomerioides* were exhaustively extracted with



Scheme 4.

Me_2CO (7 l × 3). The combined extracts were concd to *ca* 0.8 l, and taken up with $CHCl_3$ (0.8 l × 3). The $CHCl_3$-soluble portion was concd (55 g) and subjected to silica gel CC. The portion obtained from elution with EtOAc–hexane (1:1) was further subjected to flash chromatography and HPLC to give compounds **1** (130 mg), **2** (43 mg), **3** (22 mg) and **4** (27 mg). Acids **2**–**4** were further transformed into their corresponding methyl ester derivatives **2m**–**4m**, which were purified by HPLC.

Taiwaniadduct F (**1**). Solid, mp 128–129°, $[\alpha]_D^{23}$ −120.3° ($CHCl_3$; *c* 6.5). TLC (20% EtOAc in hexane) R_f 0.29; IR ν_{max}^{KBr} cm^{-1}: 3379, 1742, 1700, 1683, 1625; FAB (+): 633.5 $[M+1]^+$; HR-MS for $C_{40}H_{56}O_6$ requires: 632.4079. Found: 632.4075.

Taiwaniadduct G (**2**). Compound **2** (43 mg) was treated with CH_2N_2 in Et_2O to give the monomethylated compound **2m** (38 mg). Solid, mp 112–114°, $[\alpha]_D^{23}$ +27.6° ($CHCl_3$; *c* 1.9). TLC (20% EtOAc in hexane) R_f 0.66; IR ν_{max}^{KBr} cm^{-1}: 3422, 1740, 1716, 1666, 1630; EIMS (70 eV) *m/z* (rel. int.): 662 $[M]^+$ (0.2), 644 (0.4), 601 (1.6), 531 (0.7), 348 (35), 319 (100); HR-MS for $C_{41}H_{58}O_7$ requires: 662.4184. Found: 662.4184.

Taiwaniadduct H (**3**). Compound **3** (22 mg) was treated with CH_2N_2 in Et_2O to give the bismethylated compound **3m** (17.4 mg). Solid, mp 154–156°, $[\alpha]_D^{23}$ +9.3° ($CHCl_3$; *c* 0.87). TLC (20% EtOAc in hexane) R_f 0.66; IR ν_{max}^{KBr} cm^{-1}: 3497, 1715, 1655; FAB (+): 649.6 $[M+1]^+$; HR-MS for $C_{41}H_{60}O_6$ requires: 648.4392. Found: 648.4394.

Taiwaniadduct I (**4**). Compound **4** (27 mg) was treated with CH_2N_2 in Et_2O to give the bismethylated compound **4m** (22 mg). IR ν_{max}^{KBr} cm^{-1}: 1737, 1717, 1666, 1598; EIMS (70 eV) *m/z* (rel. int.): 647 $[M+1]^+$ (15), 646 $[M]^+$ (5), 632 (15), 494 (15), 332 (55), 315 (65), 246 (100), 151 (50); HR-MS for $C_{41}H_{58}O_6$ requires: 646.4235. Found: 646.4240.

Taiwaniadduct J (**5**). The ester **4m** underwent a [2+2] cycloaddition on standing at room temp. to give **5**. Recrystallization from EtOAc–hexane (3:47) gave a colourless sample for X-ray analysis. Mp: 132–134°, $[\alpha]_D^{23}$ +68.7° ($CHCl_3$; *c* 0.68). TLC (20% EtOAc in hexane) R_f 0.66; IR ν_{max}^{KBr} cm^{-1}: 1741, 1720, 1672; FAB (+): 647.3 $[M+1]^+$; HR-MS for $C_{41}H_{58}O_6$ requires: 646.4235. Found: 646.4241.

Acknowledgements—We thank the National Science Council for financial support and Mr Gene-Hsian Lee (Advanced Instrumentation Centre) for the X-ray diffraction.

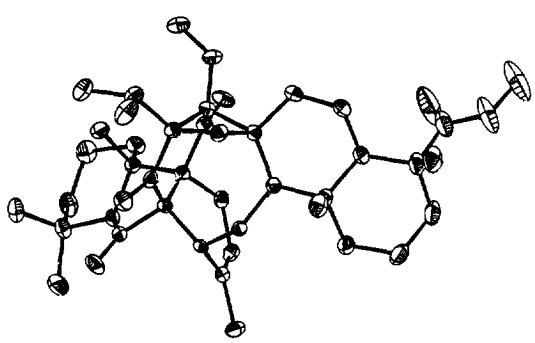


Fig. 1. ORTEP drawing of compound **5**.

REFERENCES

1. Kamil, M., Ilyas, M., Rahman, W., Hasaka, N., Okigawa, M. and Kawano, N., *Journal of the Chemical Society, Perkin Transactions I*, 1981, 553.
2. Kuo, Y.-H., Chen, W.-C. and Lin, Y.-T., *Chemical Express*, 1987, **2**, 105.
3. Fang, J.-M. and Cheng, Y.-S., *Journal of the Chinese Chemical Society (Taipei)*, 1992, **39**, 647.
4. Lin, W.-H., Fang, J.-M. and Cheng, Y.-S., *Phytochemistry*, 1995, **40**, 871.
5. Lin, W.-H., Fang, J.-M. and Cheng, Y.-S., *Phytochemistry*, 1996, **42**, 1657.