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REVISED STRUCTURES FOR FOUR ACETOPHENONES FROM *CYNANCHUM TAIWANIANUM*

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Key Word Index—*Cynanchum taiwanianum*; Asclepiadaceae; roots; acetophenones; cynandiones B-D; cynanchone A; revised structures.

Abstract—The structures of the acetophenones, cynanchone A and cynandiones B–C, from *Cynanchum taiwanianum*, elucidated on the basis of spectral and chemical evidence have been revised. Cynandione D was proved to be cynandione C, whereas cynanchone A and cynandiones B–C are probably artificial products from cynandione A.

INTRODUCTION

The roots of *Cynanchum taiwanianum* have been used as a folk medicine for treating tumours in Taiwan. Previously, chemical studies afforded pregnane glycosides [1, 2] and Huang *et al.* [3, 4] have isolated five acetophenone derivatives. Recently, we have revised the structure of cynandione A to **1** [5]. In the present paper, we have now revised the structures of cynanchone A, cynandiones B and C to **2**, **3** and **4**, respectively, and proved that cynandiones C and D are the same compound. In addition, we also proved that cynanchone A, cynandiones B and C are artificial products.

RESULTS AND DISCUSSION

By assignment of spectra data to cynanchone A, structure **2** is the most appropriate rather than the structure assigned previously [4]. In addition, NOESY (correlations between H-8 and OMe, H-4′ and H-8′) and HMBC (between H-8 and C-2, H-5′ and C-1′, H-4′ and C-2′, H-5′ and C-1, H-4 and C-2), further confirmed the structure of cynandione A as **2**. Under acidic conditions, cynanchone A (**2**) was converted to mainly cynandione A (**1**). Methylation of **2** with MeI and K_2CO_3 in acetone afforded three products, **5**–**7**. Compound **5** was partially hydrolyzed to afford **8** when dissolved in $CDCl_3$ solution for 7 days. Structural elucidation of every product (**5**–**8**) was performed by spectral methods, including NOESY and NOE techniques. These provided additional proof for the structure of cynanchone A.

By comparison with the UV absorption of cynandiones B–D reported in the literature [3, 4], cynandione B exhibited absorption signals at λ^{MeOH} nm (log ε) 208 (4.55), 222 (4.45) (sh), 268 (4.40), 300 (4.20) and 400 (3.61) (sh) and cynandione C at 208 (4.64), 220 (4.66) (sh), 261 (4.57), 308 (4.37) and 405 (3.21) (sh). The designated structures B and C as diastereomers is compatible based on their similar UV absorption. However, the UV absorption bands of cynandione D were expressed at λ_{max}^{MeOH} nm (log ε) 221 (4.62), 263 (4.46) (sh), 305 (4.26) and 357 (4.04) (sh). These data were not in agreement with cynandione D being a diastereomer of cynandiones B and C. The ^1H and ^{13}C NMR data of cynandiones B and C were recorded in pyridine-d_5 and those of cynandione D in CD_3OD [4]. The chemical shifts of cynandione D are considerably different from those of cynandiones B and C. Therefore, cynandione D is probably not a stereoisomer of cynandiones B–C. In our experiments, cynandiones B and C were slightly soluble in CD_3OD, so that ^1H NMR spectra of cynandiones B–C were measured in $CDCl_3$ (Table 1). ^1H and ^{13}C NMR data of cynandione C were similar to cynandione D (C.N. Lin, personal communication). Therefore, we suggest that cynandione D is cynandione C. In addition, some incorrect data were reported previously [3, 4], such as the methyl groups (C-17) of cynandiones C-D and the methyl group (C-8) of cynanchone A being singlets instead of doublets.

Cynandiones B and C were identified by comparison of their ^1H and ^{13}C NMR data in pyridine-d_5 with published information [4]; data measured in

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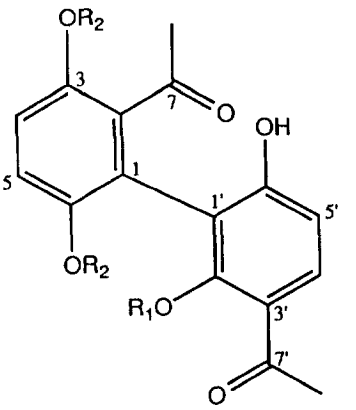
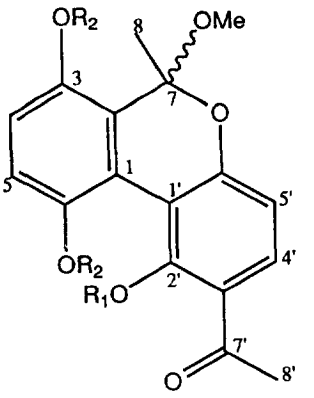
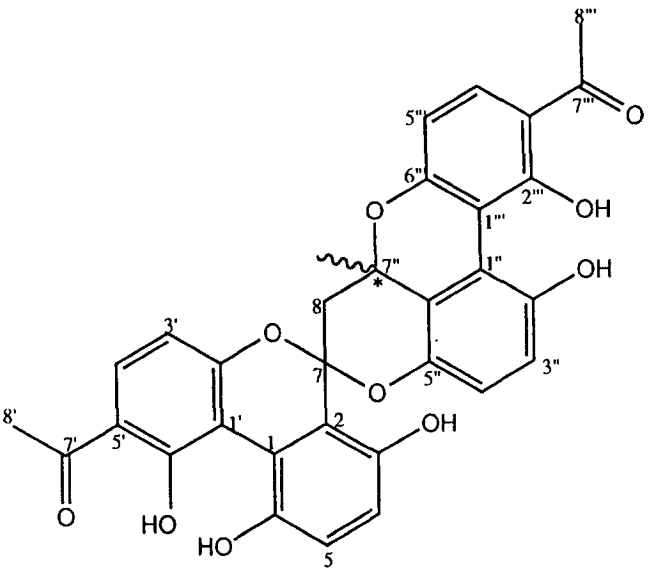


	1	7	8
R_1	H	H	Me
R_2	H	Me	Me

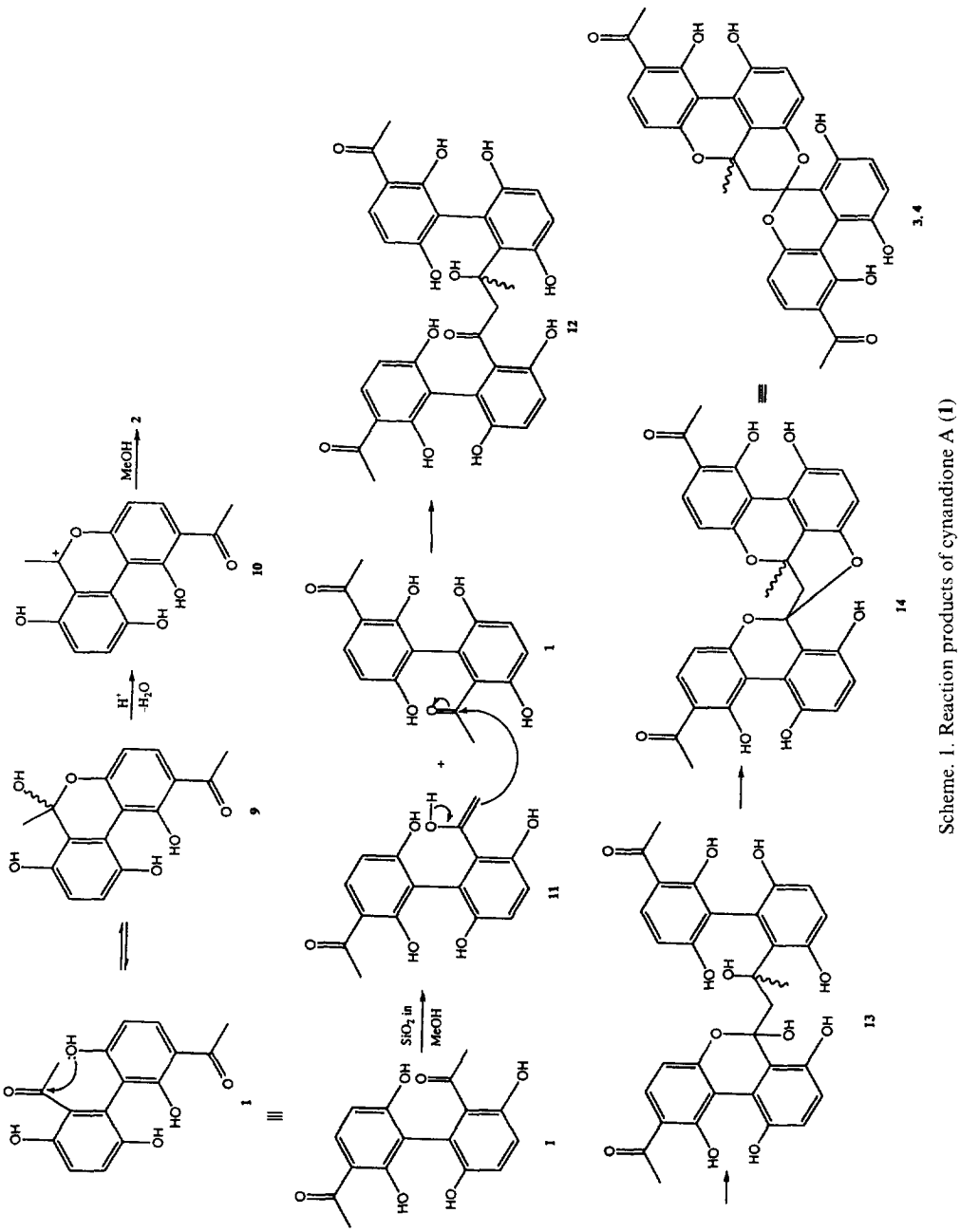


	2	5	6
R_1	H	Me	H
R_2	H	Me	Me



3, 4

$CDCl_3$ are recorded in Table 1. Both compounds contain two acetyl groups, one methyl group, one methylene group, four pairs of *ortho*-phenyl protons and five phenolic protons (δ 6.80, 8.21, 8.73, 15.53 and 15.59 in cynandione B and δ 7.37, 8.25, 8.93, 15.53 and 15.59 in cynandione C). Their structures were revised to **3** and **4**, with reference to their ^{1}H NMR, ^{13}C NMR, HMQC and HMBC data. Cynandiones B and C were treated in acidic acetone solution and both yielded mainly cynandione A (**1**). Cynanchone A (**2**) and cynandiones B and C (**3** and **4**) were proved to be artificial products on the basis of the following evidence. Cynandione A (**1**) was stirred in methanol solution in the presence of SiO_2 as catalyst; four products were detected after 7 days. The ratio between the four products, **1**, **2**, **3** and **4** is 19.0:6.0:0.5:1.0. The formation of each product is summarized in Scheme 1; this also confirms the structures of cynandiones B and C (**3** and **4**). Two low-field signals (δ 15.59 and 15.53) are present in compounds **3** and **4**. Therefore, the two acetyl groups in both compounds should be located at C-5′ and C-3‴. The specific rotations of cynanchone A (**2**), cynandione B (**3**) and cynandione C (**4**) obtained from natural sources are all near to 0° ($CHCl_3$). One confusing piece of evidence is that the reported specific rotations of cynanchone A, cynandiones B, C and D are +20.0°, +30.0°, −18.2°, and +70.4° (in MeOH), respectively [3, 4]. However, cynandiones B and C were found to be only slightly soluble in methanol in the present work.



Scheme. 1. Reaction products of cynandione A (**1**)

Table 1. ^1H and ^{13}C NMR spectral data of compounds **3** and **4** (300 and 75 MHz in $CDCl_3$)

	3		**4**	
C	δ_H	δ_c	δ_H	δ_c
1		113.8		114.8
2		120.5		120.5
3		146.3		146.1
4	7.08(*d*, 8.7)	120.5	7.08(*d*, 9.0)	120.4
5	7.12(*d*, 8.7)	121.3	7.12(*d*, 9.0)	120.5
6		150.9		150.7
7		103.0		102.6
8	2.74(*d*, 14.6)	39.5	2.74(*d*, 15.6)	44.4
	2.76(*d*, 14.6)		2.91(*d*, 15.6)	
1′		113.8		113.7
2′		158.2		161.0
3′		111.5		111.3
4′	6.56(*d*, 8.7)	132.2	7.72(*d*, 8.7)	132.0
5′	7.77(*d*, 8.7)	115.1	6.56(*d*, 8.7)	115.0
6′		158.3		158.3
7′		204.9		204.5
8′2.66*s*		26.7	2.66*s*	26.3
1″		112.8		112.5
2″		147.3		147.6
3″	6.98(*d*, 8.7)	120.3	7.00(*d*, 9.0)	120.3
4″	7.09(*d*, 8.7)	122.9	7.10(*d*, 9.0)	122.8
5″		150.8		150.7
6″		122.9		122.8
7″		72.9		72.8
8″	1.46*s*	26.2	1.38*s*	25.6
1‴		111.5		111.5
2‴		158.3		158.3
3‴		115.2		115.0
4‴	7.73(*d*, 8.7)	132.0	7.68(*d*, 8.7)	131.8
5‴	6.57(*d*, 8.7)	111.0	6.43(*d*, 8.7)	111.3
6‴		158.,4		158.3
7‴		204.6		204.8
8‴	2.67*s*	26.3	2.66*s*	26.2
OH	15.59		15.59	
	15.53		15.53	
	8.73		8.93	
	8.21		8.25	
	6.80		7.37	

EXPERIMENTAL

General. Mp are uncorr. ^1H and ^{13}C, NOE, NOESY, HMQC and HMBC spectra were run on Bruker AC-300 and AMX 400 spectrometers.

Plant materials. Roots of *C. taiwanianum* Yamazaki were collected in Cha-Yi, Taiwan, in May 1993. A voucher specimen is deposited at the Herbarium of the Department of Botany, National Taiwan University, Taipei, Taiwan.

Extraction and isolation. Roots (5 kg) were extracted with EtOH at 50°. The EtOH extract were partitioned between EtOAc and *n*-BuOH, successively. Both frs were subjected to repeated sepn and purification on silica gel and reverse-phase gel CC and afforded nine pregnane oligoglycosides, 4-hydroxyacetophenone, 3,4-dihydroxyacetophenone, β-amyrin, β-sitosteryl glucosides, two acetophenone glucosides [5], cynandione A (**1**) (3.65 g), cynanchone A (**2**) (315 mg), cynandione B (**3**) (55 mg) and cynandione C (**4**) (30 mg).

Partial hydrolysis of cynanchone A (**8**). Cynandiones *B* (**9**) and *C* (**4**). The three compounds (5 mg) of each and $TsOH \cdot H_2O$ (5 mg) were dissolved in 2 ml of Me_2CO and stirred at room temp. for 2 days. Each reaction mixt. was purified by silica gel cc and gave mainly cynandione A (**1**) (3 mg).

Methylation of cynanchone A (**2**). A mixture of **2** (10 mg), MeI (0.5 ml), K_2CO_3 (20 mg) and 2 ml Me_2CO was stirred overnight under reflux. After solvent was evapd, 10ml of H_2O was poured onto the residue and the mixt. extracted with Et_2O (30 ml). The extract was

purified by silica gel CC to yield **5** (2 mg), **6** (1.5 mg) and **7** (1 mg).

Compound **5**. Amorphous. IR ν_{max}^{KBr} cm^{-1}: 3040, 1670, 1595, 1570, 1560, 1500, 1250, 1200, 1080, 1060, 1030. EIMS (70 eV) *m/z*: 358 $[M]^+$. ^1H NMR ($CDCl_3$): δ 1.58 (3H, *s*, H-8), 2.64 (3H, *s*, H-8′), 3.21, 3.42, 3.82 and 3.84 (each 3H, *s*, OMe), 6.80 and 7.66 (each 1H, *d*, $J = 8.6$ Hz, H-5′ and H-4′), 6.92 and 6.95 (each 1H, *d*, $J = 9.0$ Hz, H-4 and H-5).

Compound **6**. Amorphous. IR ν_{max}^{KBr} cm^{-1}: 3250, 1635, 1600, 1595, 1505, 1245, 1055, 1040, 1020, 865. EIMS (70 eV) *m/z*: 344 $[M]^+$. ^1H NMR ($CDCl_3$): δ 1.53 (3H, *s*, H-8), 2.60 (3H, *s*, H-8′), 3.23, 3.83, and 3.88 (each 3H, *s*, OMe), 6.60 and 7.66 (each 1H, *d*, $J = 8.6$ Hz, H-5′ and H-4′), 6.90 and 7.0 (each 1H, *d*, $J = 9.0$ Hz, H-4 and H-5).

Compound **7**. Mp 106–107°. IR ν_{max}^{KBr} cm^{-1}: 3420, 3200, 1705, 1660, 1600, 1590, 1270, 1240, 1050, 1010, 855. EIMS (70 eV) *m/z*: 330 $[M]^+$. ^1H NMR ($CDCl_3$): δ 2.35 (3H, *s*, H-8), 2.54 (3H, *s*, H-8′), 3.68 and 3.82 (each 3H, *s*, OMe), 6.76 and 7.87 (each 1H, *d*, $J = 8.6$ Hz, H-5′ and H-4′), 6.99 (2H, *s*, H-4 and H-5), 5.81 and 12.98 (each 1H, *br s*, OH).

Compound **8**. (Obtained from **5** in $CDCl_3$.) Amorphous. IR ν_{max}^{KBr} cm^{-1}: 3400, 1705, 1660, 1600, 1590, 1270, 1050, 1030, 1010, 825. EIMS (70 eV) *m/z*: 344 $[M]^+$. ^1H NMR ($CDCl_3$): δ 2.35 (3H, *s*, H-8), 2.55 (3H, *s*, H-8′), 3.46, 3.70 and 3.83 (each 3H, *s*, OMe), 6.76 and 7.67 (each 1H, *d*, $J = 8.6$ Hz, H-5′ and H-4′), 6.99 (2H, *s*, H-4 and H-5), 5.60 (1H, *br s*, OH).

Reaction of cynandione A (**1**) *in methanol.* Cynandione A (**1**) (50 mg) and SiO_2 (10 mg) were added to 5 ml of MeOH. The reaction mixt. was stirred at room temp. for 7 days. After filtration, the filtrate was evapd *in vacuo* and the residue analyzed by HPLC on a RP-18 column to give four products, **1**–**4**.

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