Phytochemistry, Vol. 30, No. 4, pp. 1245 1250, 1991
Printed in Great Britain.

0031-9422/91 $3.00+0.00
© 1991 Pergamon Press plc

SIX PRENYLATED PHENOLS FROM *GLYCYRRHIZA URALENSIS**

TOSHIO FUKAI, QING-HUA WANG† and TARO NOMURA‡

Faculty of Pharmaceutical Sciences, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274, Japan

(*Received* 3 *September* 1990)

Key Word Index—*Glycyrrhiza uralensis*; Leguminosae; licorice; prenylated flavone; prenylated dihydrostilbene; prenylated dihydrophenanthrene; gancaonins Q–V.

Abstract—A new prenylated flavone, gancaonin Q, and three new prenylated dihydrostilbenes, gancaonins R, S and T, along with two new prenylated dihydrophenanthrenes, gancaonins U and V were isolated from the aerial parts of *Glycyrrhiza uralensis*. The structures of gancaonins Q–V were elucidated by spectroscopic methods.

INTRODUCTION

We reported earlier the structures of isoprenoid-substituted flavonoids from Xibei licorice (*Glycyrrhiza* species, Seihoku Kanzo in Japanese), the aerial parts of *G. uralensis* Fisch. et DC., and the aerial parts and roots of *G. pallidiflora* Maxim. [1–5]. In continuation of the investigation, we studied the phenolic constituents of the aerial parts of *G. uralensis*, and describe here the characterization of six new prenylated phenolic compounds, gancaonins Q–V (**1**–**6**).

RESULTS AND DISCUSSION

Gancaonin Q (**1**), pale yellow needles, mp 212–214°, $C_{25}H_{26}O_5$, gave a dark green colour with methanolic ferric chloride and was positive to the Gibbs test. The UV spectrum of **1** resembled the spectra of flavone derivatives [6]. The ^{1}H NMR spectrum showed the signals of the following: two 3,3-dimethylallyl (prenyl) group protons, ABC type aromatic protons, olefinic and/or aromatic proton(s) [δ6.60 (1H, *br s*), 6.61 (1H, *s*)], a hydrogen-bonded hydroxyl and two hydroxyl protons. The ^{13}C NMR spectrum of **1** was analysed (Table 1) by comparing the spectrum with those of gancaonin O (**7**) [5] and kuwanon S (**8**) [7]. In the spectrum of **1**, the chemical shifts of carbon atoms of the A and C rings were in agreement with those of the relevant carbon atoms of **7**, while the chemical shifts of B ring carbon atoms were consistent with those of the relevant carbon atoms of **8**. Thus, the structure of gancaonin Q is **1**.

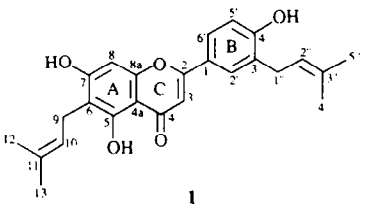
Gancaonin R (**2**), needles, mp 142–144°, $C_{24}H_{30}O_4$, also gave a dark green colour with methanolic ferric chloride. Treatment of **2** with dimethyl sulphate gave a tetramethyl ether (**2a**). The ^{1}H NMR spectrum of **2** showed the following: protons in two prenyl groups [δ1.65, 1.75 (each 6H, *br s*), 3.35 (4H, *br d*, $J=6$ Hz), 5.12 (2H, *br t*, $J=6$ Hz)], two pairs of benzylmethylene protons, ABC type aromatic protons and an aromatic proton. The ^{1}H NMR spectra of **2a** showed proton signals of the two prenyl groups: δ1.66 (6H, *br d*, $J=1$ Hz), 1.76 (6H, *br d*, $J=0.7$ Hz), 3.35 (4H, *br d*, $J=7$ Hz), 5.10 (2H, *br t*, $J=7$ Hz). The above ^{1}H NMR spectra revealed that **2** is a dihydrostilbene derivative having two equivalent prenyl groups in its structure. The ^{13}C NMR spectrum of **2** was analysed by using gated decoupling with NOE (Table 2). Comparison between the ^{13}C NMR spectrum of **2a** and that of the model compound, 2,2-dimethyl-6-(3′,4′-dimethoxyphenethyl) chromene (**9**) [8], showed the chemical shifts of the B ring carbon atoms of **2a** to be in agreement with those of the relevant carbon atoms of **9**. In the ^{13}C NMR spectra of **2** and **2a**, the carbon atoms at C-2 and C-6 were observed as equivalent, as well as the carbon atoms at C-3 and C-5. These results suggest that the A ring of **2** is a 3,5-dihydroxy-2,6-diprenyl phenyl, or a 3,5-diprenyl-2,6-dihydroxyl, structure. The former structure is supported by the following: in the ^{13}C NMR spectrum of **2**, the C1 signal of the prenyl group was observed at δ25.6, suggesting that one of the *ortho*-positions to the prenyl group is substituted by an alkyl or alkenyl group, the other by an oxygenated substituent [9]. Furthermore in the ^{13}C NMR spectrum of **2a**, the methoxy carbon atoms of the A ring were observed at δ55.86. This result suggests that an *ortho*-position to the methoxyl groups has no substituent [10]. Thus, the structure of gancaonin R is **2**.

Gancaonin S (**3**), needles, mp 115–116°, $C_{24}H_{30}O_4$, gave a tetramethyl ether (**3a**) by treatment with dimethyl sulphate. The ^{1}H NMR spectrum of **3** showed signals of the following: protons in two prenyl groups, two pairs of benzylmethylene protons, ABC type aromatic protons and an aromatic proton. The ^{13}C NMR spectrum of **3** was analysed by using gated decoupling with NOE and by comparison with the spectra of **2** and **9** (Table 2). In the ^{13}C NMR spectrum of **3**, the chemical shifts of the B ring carbon atoms were in agreement with those of the relevant atoms of **2**, and the oxygenated carbon atoms in the A ring were observed at δ154.10 and 154.24. This result suggests that the B ring is a 3′,4′-dihydroxyphenyl

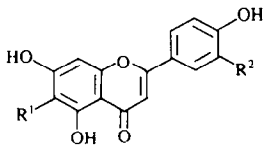
*Part 6 in the series 'Phenolic Constituents of *Glycyrrhiza* Species'. For Part 5 see ref. [1].

†Present address: Heilongjiang Institute of Drug Control, Harbin, China.

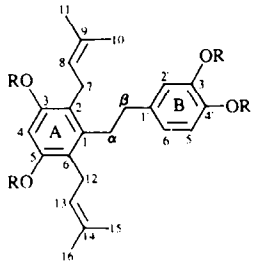
‡Author to whom correspondence should be addressed.



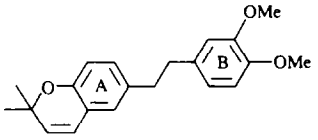
1



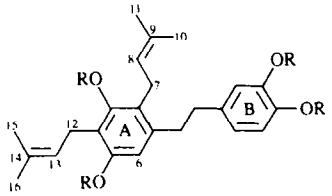
7 R^1=prenyl, R^2=OH
8 R^1=H, R^2=geranyl



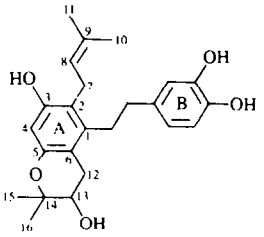
2 R=H
2a R=Me



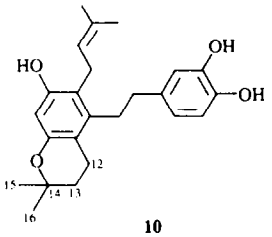
9



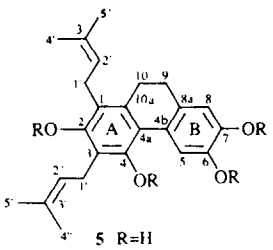
3 R=H
3a R=Me



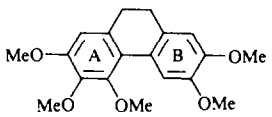
4



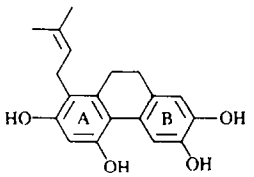
10



5 R=H
5a R=Me



11



6

structure, and that the two oxygenated carbon atoms in the A ring are located at *meta*-positions to each other [11]. The C1 signal of one of the two prenyl groups in the A ring was observed at δ25.53. This result suggests that one of the *ortho*-positions to the prenyl group is substituted by an alkyl or alkenyl group, the other by an oxygenated substituent [9]. The C-1 signal of the other prenyl group was observed at δ23.20. This result suggests that the di*ortho*-positions to the prenyl group are substituted by the oxygenated substituents [9]. Thus, the structure of gancaonin S is **3**.

Gancaonin T (**4**), was an amorphous powder, $C_{24}H_{30}O_5$, $[\alpha]_D$ 0°. The ^{1}H NMR spectrum of **4** showed signals of the following (in acetone-d_6): protons in a

Table 1. ^{13}C NMR data of compounds **1**, **7** and **8** (acetone-d_6, 100 MHz)

C	1*	7	8
2	165.09	164.88	165.4
3	103.98	104.22	104.0
4	183.14	183.13	—
4a	105.22	105.29	·
5	160.24	160.23	—
6	112.33	112.38	—
7	162.42	162.42	—
8	94.07	94.10	-
8a	156.58	156.39	—
9	22.02	22.03	·
10	123.27[a]	123.26	—
11	131.59	131.61	—
12	17.91	17.90	·
13	25.88[b]	25.87	—
1′	123.45	—	123.2
2′	128.85	—	128.8
3′	129.91	—	129.9†
4′	159.53	—	159.6†
5′	116.34	·	116.3
6′	126.57	·	126.6†
1″	29.05	—	28.9
2″	123.04[a]	—	122.9
3″	133.28	—	—
4″	17.91	—	-
5″	25.91[b]	—	—

*Data from complete decoupling and off-resonance decoupling spectra.

†Signals reassigned.

[a,b]Signals may be interchanged.

prenyl group, protons in a 2,2-dimethyl-3-hydroxypyrane ring [δ1.17, 1.32 (each 3H, *s*), 2.58 (1H, *dd*, $J=8$ and 16 Hz), 2.93 (1H, *dd*, $J=5$ and 16 Hz), 3.75 (1H, *td*, $J=5$ and 8 Hz); δ(in methanol-d_4) 1.17, 1.28 (each 3H, *s*), 2.51 (1H, *dd*, $J=8$ and 16 Hz), 2.83 (1H, *dd*, $J=6$ and 16 Hz), 3.69 (1H, *dd*, $J=6$ and 8 Hz)], two pairs of benzylmethylene protons, ABC type aromatic protons, an aromatic proton and a proton of hydroxyl group [δ4.15 (1H, *br d*, $J=5$ Hz, OH-13)]. The ^{13}C NMR spectrum of **4** was analysed using off-resonance decoupling and by comparison with the spectra of **2** and **3** (Table 2). From the ^1H and ^{13}C NMR spectra of **4**, it is obvious that the B ring is a 3′,4′-dihydroxyphenyl structure. In the ^{13}C NMR spectrum of **4**, the α-carbon atom was observed at much higher field than the β-carbon atom (Δ3.66 ppm). In the ^{13}C NMR spectrum of **2**, the α-carbon atom shifted to much higher field than the β-carbon atom (Δ4.48 ppm), while in the spectrum of **3** the α-carbon atom shifted to higher field (Δ1.55 ppm). These results suggest that the C-2 and C-6 positions in the A ring are substituted by the alkyl and/or alkenyl groups [12, 13]. This assumption was confirmed by the following evidence. The chemical shifts of the carbon atoms of the A ring of **4** were in agreement with the values of the relevant atoms of compound **10** which was derived from **2** (Table 2). Thus, the structure of gancaonin T is **4**.

Gancaonin U (**5**), needles, mp 72–74°, $C_{24}H_{28}O_4$, gave a tetramethyl ether (**5a**) by treatment with dimethyl sulphate. The UV spectrum of **5** resembled that of a 9,10-dihydrophenanthrene derivative [14]. The ^1H NMR spectrum of **5** showed signals of the following: protons in two prenyl groups, two pairs of benzylmethylene protons and two aromatic protons (each *s*). The locations of one of the prenyl groups and one of the aromatic protons were shown to be at the C-1 and C-8 positions, respectively, by a NOE experiment (Fig. 1). The structure of the B ring was supported by long-range selective proton decoupling (LSPD) and gated decoupling with NOE described in Table 3. Furthermore in the ^{13}C NMR spectrum of **5a**, the chemical shifts of the B ring carbon atoms were in agreement with those of the relevant carbon atoms of icariside A_1 monomethyl ether (**11**) [15]. The structure of the A ring is supported by the following: the C-1 signal of one of the two prenyl groups was observed at δ25.50. This suggests that one of the *ortho*-positions to the prenyl group is substituted by an alkyl or alkenyl group, the other by an oxygenated substituent [9]. The C-1 signal of the other prenyl group was observed at δ23.10. This result suggests that the di*ortho*-positions to the prenyl group were substituted by oxygenated substituents [9]. Thus, the structure of gancaonin U is **5**.

Gancaonin V (**6**), needles, mp 170–173°, $C_{19}H_{20}O_4$, was suggested to be a 9,10-dihydrophenanthrene derivative by its UV spectrum [14]. The ^1H NMR spectrum of **6** showed signals of the following: protons in a prenyl group, two pairs of benzylmethylene protons and three aromatic protons [δ6.43, 6.67, 7.90 (each 1H, *s*)]. The locations of the prenyl group and one of the aromatic protons were supported by NOE (Fig. 1). The structure of the B ring was supported by comparison of the ^1H and ^{13}C NMR spectra of **6** with those of **5**. In the ^{13}C NMR spectrum of **6**, the oxygenated carbon atoms of the A ring were observed at δ153.53 and 154.46. From this result, the oxygenated carbon atoms are thus located at positions *meta* to each other [11]. Thus, the structure of gancaonin V is **6**.

EXPERIMENTAL

Mps: uncorr. General procedures followed and instruments used are described in our previous paper [16]. Plant materials, extraction and chromatography with Amberlite XAD-2 are as reported in preceding papers [3, 5].

Isolation of gancaonin Q (**1**), *R* (**2**), *S* (**3**), *T* (**4**), *U* (**5**) *and V* (**6**). The C_6H_6 eluted fr. (25 g) on Amberlite XAD-2 CC [5] was rechromatographed on silica gel (200 g) successively with *n*-hexane–C_6H_6 (1:1) (frs 1–6), C_6H_6 (frs 7–20), C_6H_6–Me_2CO (1:1) (frs 21, 22), Me_2CO (frs 23–25), each fr. (eluted vol. 500 ml) being monitored by TLC. Frs 12, 13 (0.7 g) were fractionated by Sephadex LH-20 chromatography (25 × 2 cm) with MeOH, successively, by prep. TLC (silica gel, *n*-hexane–EtOAc, 3:2) and by HPLC (*n*-hexane–EtOAc, 5:2; column: Senshu Pak SSC-Silica 4251-N, 25 × 1 cm, detector: UV, 280 nm) to give gancaonin S (**3**, 18 mg). Fr. 14 (0.4 g) was fractionated by Sephadex LH-20 chromatography with MeOH and then by HPLC (*n*-hexane–EtOAc, 4:1) to give gancaonin U (**5**, 70 mg). Fr. 16 (0.4 g) was fractionated by HPLC (*n*-hexane–EtOAc, 3:1) and then by prep. TLC ($CHCl_3$–Me_2CO, 5:1) to give gancaonin Q (**1**, 9 mg). Frs 19, 20 (0.5 g) were fractionated by HPLC (*n*-hexane–EtOAc, 2:1) to give gancaonin R (**2**, 85 mg) and gancaonin V (**6**, 11 mg). Fr. 24 (0.1 g) was fractionated by prep. TLC ($CHCl_3$–Me_2CO, 2:1) to give gancaonin T (**4**, 8 mg).

Table 2. ^{13}C NMR data of compounds **2–4** and related compounds (100 MHz)

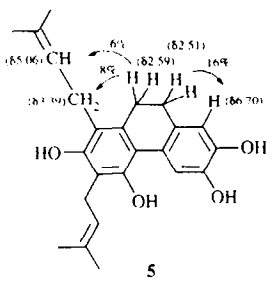
C	**2** (acetone-d_6)	**3** (acetone-d_6)	**2a*** ($CDCl_3$)	**3a*** ($CDCl_3$)	**9** ($CDCl_3$)	**4** (acetone-d_6)	**10** (acetone-d_6)
1	141.19 *br S*†	139.39	140.33	139.36		140.68	140.55
2	118. 55 *br S*	118.46	120.22	121.35		119.61	119.24
3	154.42 *Std* ($^2J = {}^3J = 4$ Hz)	154.24	156.61	156.57[a]		155.13	154.98
4	101.59 *D* ($^1J = 154$ Hz)	113.57	94.39	125.50		102.42	102.67
5	154.42	154.10	156.61	157.34		152.67	153.64
6	118.55	109.08	120.22	108.15		110.84	111.38
7	25.60 *Td* ($^1J = 123$, $^2J = 4$ Hz)	25.53	25.72	25.21		25.45	25.48
8	126.18 *Dm* ($^1J = 152$ Hz)	125.19	124.60	124.70		125.90	126.02
9	129.99 (*Sm*)	131.08[a]	130.32	130.74[b]		130.02	130.01
10	18.14 *Qm* ($^1J = 124$ Hz)	18.04[b]	18.03	18.05		18.14	18.14
11	25.83 *Qm* ($^1J = 124$ Hz)	25.86[c]	25.09	25.75[c]		25.85	25.86
12	25.60	23.20	25.72	23 37		‡	20.47
13	126.18	124.17	124.60	123.71		70.83	34.04
14	129.99	131.54[a]	130.32	130.83[b]		76.67	73.44
15	18.14	17.89[b]	18.03	17.85		19.99	26.94
16	25.83	25.79[c]	25.09	25.64[c]		26.21	26.94
α	32.80 *Tm* ($^1J = ca$ 125 Hz)	36.16	31.89	35.41	37.1	32.58	32.47
β	37.28 *Tm* ($^1J = ca$ 125 Hz)	37.71	36.74	37.25	37.6	36.24	36.34
1′	135.14 *br S*	134.79	135.27	134.76	134.4	134.86	134.98
2′	116.08 *Dm* ($^1J = 154$ Hz)	116.14	112.08	112.12	111.9	116.12	116.19
3′	145.81 *Sddd* ($^2J = 4$, $^3J = 7$, $^4J = 1$ Hz)	145.56	149.09	148.87	148.7	145.83	145.84
4′	143.96 *Sddd* ($^2J = 3$, $^3J = 7$ and 10 Hz)	143.73	147.56	147.41	147.1	144.04	144.05
5′	116.02 *D* ($^1J = 156$ Hz)	115.92	111.77	111.46	111.2	116.02	116.04
6′	120.18 *Dtd* ($^1J = 154$, $^3J = 5$ and 7 Hz)	120.31	121.08	120.32	120.3	120.21	120.29
OMe	--	--	55.86 (2C)	55.67		--	--
			55.91	55.83			
			56.10	56.03			
				61.53			

*Data from complete decoupling spectrum.

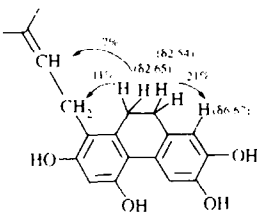
†Capital letters refer to pattern resulting from directly bonded proton(s), lower case letters to long-range ^{13}C–^1H coupling.

‡Measured in methanol-d_4: δ30.1.

[a–c]Assignment may be interchanged in each column.



5



6

Fig. 1. NOE values of compounds **5** and **6** in acetone-d_6.

Gancaonin Q (**1**). Recrystallized from Me_2CO–*n*-hexane to give pale yellow needles, mp 212–214°. $FeCl_3$ test: dark green. Gibbs test: positive. UV λ_{max}^{MeOH} nm (log ε): 215 (4.50), 274 (4.16), 305 (sh 4.03), 338 (4.28); $\lambda_{max}^{MeOH+AlCl_3}$: 212 (4.51), 285 (4.14), 300 (sh 4.13), 361 (4.30), 390 (sh 4.11); $\lambda_{max}^{MeOH+NaOAc}$: 276 (4.23), 303 (4.05), 315 (4.05), 348 (4.13). EIMS (probe) 70 eV, *m/z* (rel. int.): 407 $[M+1]^+$ (23%), 406 $[M]^+$ (78), 391 (13), 363 (100), 352 (24), 351 (98), 307 (13), 165 (8). HRMS, *m/z* 406.1769 $[M]^+$ ($C_{25}H_{26}O_5$ requires: 406.1780). ^1H NMR (400 MHz, Me_2CO-d_6): δ1.65 (3H, *br d*, $J = 1$ Hz, Me-11), 1.75 (3H, *br d*, $J = 1$ Hz, Me-3″), 1.76 (3H, *br s*, Me-3″), 1.78 (3H, *br s*, Me-11), 3.35 (2H, *br d*, $J = 7$ Hz, H_2-9), 3.41 (2H, *br d*, $J = 7$ Hz, H_2-1″), 5.28 (1H, *br t*, $J = 7$ Hz, H-10), 5.40 (1H, *br t*, $J = 7$ Hz, H-2″), 6.60 (1H, *br s*, H-8), 6.61 (1H, *s*, H-3), 7.02 (1H, *d*, $J = 8$ Hz, H-5′), 7.75 (1H, *dd*, $J = 2$ and 8 Hz, H-6′),

Table 3. ^{13}C NMR data of compounds **5**, **6** and related compounds (100 MHz)

C	**5*** (chloroform-*d*–methanol-d_4, 4:1)	**5** (acetone-d_6)	**6**† (acetone-d_6)	**5a**‡ (chloroform-*d*)	**11**§ (chloroform-*d*)
1	115.89 *Sm*	117.30	117.86	123.96	
2	151.81 *Sm*	152.22	154.46	155.86[a]	
3	113.11 *Sm*	115.51	102.56	126.98	
4	149.51 *Sm*	150.81	153.53	154.93[a]	
4a	117.69 *Sm*	119.06	115.46	125.48	
4b	125.42 *Std* (^3J = 3 and 8 Hz)	126.37	126.69	123.96	125.2
5	113.19 *D* (^1J = 156 Hz)	115.43	116.53	111.23	111.1[a]
6	142.38 *Sdd* (^2J = 4, ^3J = 7 Hz)	143.70[a]	143.40[a]	147.38[b]	147.3[b]
7	142.57 *Sdd* (^2J = 4, ^3J = 7 Hz)	143.60[a]	143.28[a]	147.56[b]	147.4[b]
8	114.85 *Dt* (^1J = 161, ^3J = 3 Hz)	115.14	114.62	110.30	111.0[a]
8a	131.15 *Sm*	132.41	130.47	128.22	130.4
9	29.19 *Tm* (^1J = 128 Hz)	29.83	29.77	29.12	29.4
10	26.52 *Tm* (^1J = *ca* 128 Hz)	27.32	27.31	26.17	30.6
10a	136.56 *Sm*	136.84	139.95	137.55	
1′	25.50 *Td* (^1J = 125, ^2J = 4 Hz)	25.90	25.25	25.79[c]	
2′	123.02[a] *Dm* (^1J = *ca* 154 Hz)	124.74[b]	125.07	124.41[d]	
3′	132.82[b] *Sm*	130.82[c]	130.00	130.91[e]	
4′	17.95[c] *Qm* (^1J = *ca* 125 Hz)	18.00	17.98	18.07[f]	
5′	25.80[d] *Qm* (^1J = *ca* 125 Hz)	25.80	25.83	25.73[c]	
1″	23.10 *Td* (^1J = 126, ^2J = 4 Hz)	23.73		23.92	
2″	122.44[a] *Dm* (^1J = *ca* 152 Hz)	124.13[b]		123.52[d]	
3″	134.49[d] *Sm*	131.20[c]		131.50[e]	
4″	17.86[c] *Qm* (^1J = *ca* 124 Hz)	18.00		17.98[f]	
5″	25.72[d] *Qm* (^1J = *ca* 123 Hz)	25.80		25.62[c]	
OMe	—	--		55.78	
				56.18	
				60.37	
				61.59	

*LSPD experiment with irradiation of C-8 proton (δ6.75); C-4b [*Std*→*St* (^3J = 3 Hz)], C-6 [*Sdd*→*Sd* (^2J = 4 Hz)], C-7 [*Sdd*→*Sd* (^3J = 7 Hz)], C-9 [*Tm*→*Tt* (^2J = 5 Hz)], irradiation of C-9 protons (δ 2.64): C-4b [*Std*→*Sd*, ^3J = 8 Hz)], C-8 (*Dt*→*D*), C-10a [*Sm*→*Stt* (^2J = ^3J = 4 Hz)].

†Data from complete decoupling and off-resonance decoupling spectra.

‡Data from complete decoupling spectra.

§Signals reassigned.

[a–f]Assignment may be interchanged in each column.

7.80 (1H, *d*, *J* = 2 Hz, H-2′), 9.45 (2H, *br*, OH × 2) 13.31 (1H, *s*, OH-5).

Gancaonin R (**2**). Recrystallized from Me_2CO–*n*-hexane to give needles, mp 142–144°. $FeCl_3$ test: dark green. UV λ_{max}^{MeOH} nm (log ε): 210 (4.67), 230 (sh 4.16), 285 (3.82). EIMS, *m/z* (rel. int.): 383 [M + 1]$^+$ (27%), 382 [M]$^+$ (100), 327 (20), 325 (25), 313 (16), 271 (25), 269 (12), 259 (18), 257 (20), 245 (37), 203 (32), 161 (30), 137 (9), 123 (55), 69 (40). HRMS, *m/z* 382.2141 [M]$^+$ ($C_{24}H_{30}O_4$ requires: 382.2145). ^1H NMR (400 MHz, Me_2CO-d_6): δ1.65 (6H, *br s*, Me-9 and Me-14), 1.75 (6H, *br s*, Me-9 and Me-14), 2.63, 2.78 (each 2H, *m*, H_2-α or H_2-β), 3.35 (4H, *br d*, *J* = 6 Hz, H_2-7 and H_2-12), 5.12 (2H, *br t*, *J* = 6 Hz, H-8 and H-13), 6.38 (1H, *s*, H-4), 6.61 (1H, *dd*, *J* = 2 and 8 Hz, H-6′), 6.78 (1H, *d*, *J* = 2 Hz, H-2′), 6.78 (1H, *d*, *J* = 8 Hz, H-5′), 7.72 (4H, *br*, OH × 4).

Gancaonin R tetramethyl ether (**2a**). A mixt. of gancaonin R (**2**, 40 mg), Me_2SO_4 (1 ml) and dry K_2CO_3 (4 g) in Me_2CO (10 ml) was refluxed for 2 hr. The reaction product was purified by prep. TLC (*n*-hexane–EtOAc, 4:1) to give the tetraMe ether (**2a**, 25 mg), **2a** was recrystallized from Me_2CO to give prisms, mp 78–80°. EIMS, *m/z* (rel. int.): 439 [M + 1]$^+$ (26%), 438 [M]$^+$ (86), 382 (15), 381 (28), 369 (30), 325 (19), 313 (26), 287 (12), 273 (33), 231 (28), 189 (19), 165 (7), 151 (100). ^1H NMR (400 MHz, $CDCl_3$): δ1.66 (6H, *br d*, *J* = 1 Hz, Me-9 and Me-14), 1.76 (6H, *br d*, *J* = 0.7 Hz, Me-9 and Me-14), 2.72, 2.87 (each 2H, *m*, H_2-α or H_2-β), 3.35 (4H, *br d*, *J* = 7 Hz, H_2-7 and H_2-12), 3.82 (6H, *s*, OMe × 2), 3.85, 3.86 (each 3H, *s*, OMe), 5.10 (2H, *br t*, *J* = 7 Hz, H-8 and H-13), 6.42 (1H, *s*, H-4), 6.72 (1H, *d*, *J* = 2 Hz, H-2′), 6.77 (1H, *dd*, *J* = 2 and 8 Hz, H-6′), 6.81 (1H, *d*, *J* = 8 Hz, H-5′).

Formation of compound **10** *from gancaonin R* (**2**). A mixt. of gancaonin R (**2**, 210 mg), 35% HCl (4 ml) and MeOH (8 ml) was kept at room temp. for 20 min. The reaction product was purified by prep. TLC ($CHCl_3$–Me_2CO, 3:1) and then by HPLC (*n*-hexane–EtOAc, 3:1) to give **10** (25 mg) as an amorphous powder. EIMS, *m/z* (rel. int.): 383 [M + 1]$^+$ (27%), 382 [M]$^+$ (100), 328 (11), 327 (50), 325 (10), 271 (17) 259 (41), 245 (27), 204 (15), 203 (13), 161 (15), 137 (9), 123 (28), 69 (18). ^1H NMR (400 MHz, Me_2CO-d_6): δ1.25 (6H, *s*, Me_2-14), 1.65 (3H, *br d*, *J* = 1 Hz, Me-9), 1.73 (2H, *t*, *J* = 7 Hz, H_2-13), 1.76 (3H, *br s*, Me-9), 2.59 (2H, *m*, H_2-α or H_2-β), 2.66 (2H, *t*, *J* = 7 Hz, H_2-12), 2.76 (2H, *m*, H_2-α or H_2-β), 3.36 (2H, *br d*, *J* = 6.5 Hz, H-7), 5.13 (1H, *br t*, *J* = 6.5 Hz, H-8), 6.20 (1H, *s*, H-4), 6.59 (1H, *dd*, *J* = 2 and 8 Hz, H-6′), 6.75 (1H, *d*, *J* = 2 Hz, H-2′), 6.75 (1H, *d*, *J* = 8 Hz, H-5′).

Gancaonin S (**3**). Recrystallized from C_6H_6 to give needles, mp 115–116°. $FeCl_3$ test: dark green. UV λ_{max}^{MeOH} nm (log ε): 206 (4.56), 228 (sh 3.95), 283 (3.53). EIMS, *m/z* (rel. int.): 383 [M + 1]$^+$ (27%), 382 [M]$^+$ (100), 327 (33), 326 (30), 325 (28), 311 (18), 283

(8), 271 (29), 259 (21), 257 (12), 245 (22), 204 (36), 203 (70), 189 (31), 161 (39), 137 (6), 123 (71), 69 (21). HRMS, *m/z* 382.2117 $[M]^+$ ($C_{24}H_{30}O_4$ requires: 382.2145). ^{1}H NMR (400 MHz, Me_2CO-d_6): δ 1.66 (6H, *br s*, Me-9 and Me-14), 1.75, 1.77 (each 3H, *br s*, Me-9 or Me-14), 2.66, 2.72 (each 2H, *m*, H_2-α or H_2-β), 3.34 (2H, *br d*, J = 6.5 Hz, H_2-7), 3.40 (2H, *br d*, J = 7 Hz, H_2-12), 5.09 (1H, *br t*, J = 6.5 Hz, H-8), 5.25 (1H, *br t*, J = 7 Hz, H-13), 6.34 (1H, *s*, H-6), 6.55 (1H, *dd*, J = 2 and 8 Hz, H-6'), 6.73 (1H, *d*, J = 2 Hz, H-2'), 6.75 (1H, *d*, J = 8 Hz, H-5'), 7.69 (4H, *br*, OH × 4).

Gancaonin S tetramethyl ether (**3a**). A mixt. of gancaonin S (**3**, 20 mg), Me_2SO_4 (0.5 ml) and dry K_2CO_3 (2 g) in Me_2CO (8 ml) was refluxed for 2 hr. The reaction product was purified by prep. TLC (*n*-hexane–EtOAc, 4:1) to give the tetraMe ether (**3a**, 15 mg) as an amorphous powder. EIMS, *m/z* (rel. int.): 439 $[M+1]^+$ (31%), 438 $[M]^+$ (96), 383 (20), 382 (26), 381 (34), 327 (11), 287 (21), 273 (25), 231 (21), 217 (17), 189 (10), 165 (10), 151 (100). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.67 (6H, *br s*, Me-9 and Me-14), 1.75, 1.77 (each 3H, *br s*, Me-9 or Me-14), 2.82 (4H, *br s*, H_2-α and H_2-β), 3.31, 3.34 (each 2H, *br d*, J = 7 Hz, H_2-7 or H_2-12), 3.68, 3.76, 3.83, 3.86 (each 3H, *s*, OMe), 6.48 (1H, *s*, H-6), 6.63 (1H, *d*, J = 2 Hz, H-2'), 6.74 (1H, *dd*, J = 2 and 8 Hz, H-6'), 6.81 (1H, *d*, J = 8 Hz, H-5').

Gancaonin T (**4**). Amorphous powder. $FeCl_3$ test: dark green. $[\alpha]_D^{20}$ 0° (MeOH; *c* 0.08). UV λ_{max}^{MeOH} nm (log ε): 209 (4.96), 230 (sh 4.46), 285 (4.12). EIMS, *m/z* (rel. int.): 399 $[M+1]^+$ (27%), 398 $[M]^+$ (100), 341 (28), 275 (18), 271 (25), 261 (47), 257 (16), 203 (24), 189 (11), 161 (25), 137 (17), 123 (55), 69 (14). HRMS, *m/z* 398.2160 $[M]^+$ ($C_{24}H_{30}O_5$ requires: 398.2094). ^{1}H NMR (400 MHz, Me_2CO-d_6): δ 1.17, 1.32 (each 3H, *s*, Me-14), 1.65 (3H, *br d*, J = 1 Hz, Me-9), 1.76 (3H, *br s*, Me-9), 2.58 (1H, *dd*, J = 8 and 16 Hz, H-12, overlapping with the signal at 2.59), 2.59, 2.75 (each 2H, *m*, H_2-α or H_2-β), 2.93 (1H, *dd*, J = 5 and 16 Hz, H-12), 3.35 (2H, *br d*, J = 6 Hz, H_2-7), 3.75 (1H, *td*, J = 5 and 8 Hz, H-13), 4.15 (1H, *br d*, J = 5 Hz, OH-13), 5.13 (1H, *br t*, J = 6 Hz, H-8), 6.22 (1H, *s*, H-4), 6.59 (1H, *dd*, J = 2 and 8 Hz, H-6'), 6.75 (1H, *d*, J = 2 Hz, H-2'), 6.75 (1H, *d*, J = 8 Hz, H-5'), 7.70 (2H, *br s*, OH × 2), 8.00 (1H, *br s*, OH). ^{1}H NMR (400 MHz, CD_3OD): δ 1.17, 1.28 (each 3H, *s*, Me-14), 1.65, 1.75 (each 3H, *br s*, Me-9), 2.51 (1H, *dd*, J = 8 and 16 Hz, H-12), 2.58, 2.74 (each 2H, *br t*, J = 8 Hz, H_2-α or H_2-β), 2.83 (1H, *dd*, J = 6 and 16 Hz, H-12), 3.69 (1H, *dd*, J = 6 and 8 Hz, H-13), 5.07 (1H, *br t*, J = 6 Hz, H-8), 6.14 (1H, *s*, H-4), 6.51 (1H, *dd*, J = 2 and 8 Hz, H-6'), 6.63 (1H, *d*, J = 2 Hz, H-2'), 6.67 (1H, *d*, J = 8 Hz, H-5'). The signal of H_2-7 overlapped with that of the solvent.

Gancaonin U (**5**). Recrystallized from *n*-hexane–Et_2O to give needles, mp 72–74°. $FeCl_3$ test: green. UV λ_{max}^{MeOH} nm (log ε): 220 (4.45), 268 (sh 3.91), 277 (3.97), 305 (3.95), 312 (sh 3.93). EIMS, *m/z* (rel. int.): 381 $[M+1]^+$ (27%), 380 $[M]^+$ (100), 325 (17), 324 (26), 309 (28), 281 (11), 269 (43), 268 (72). HRMS, *m/z*: 380.1987 $[M]^+$ ($C_{24}H_{28}O_4$ requires: 380.1987). ^{1}H NMR (400 MHz, Me_2CO-d_6): δ 1.65 (3H, *br d*, J = 1 Hz, Me-3'), 1.68 (3H, *br d*, J = 1 Hz, Me-3''), 1.76 (3H, *br d*, J = 1 Hz, Me-3'), 1.81 (3H, *br d*, J = 1 Hz, Me-3''), 2.51 (2H, *m*, H_2-9), 2.59 (2H, *m*, H_2-10), 3.39 (2H, *br d*, J = 6.5 Hz, H_2-1'), 3.51 (2H, *br d*, J = 7 Hz, H_2-1''), 5.06 (1H, *br t*, J = 6.5 Hz, H-2'), 5.25 (1H, *br t*, J = 7 Hz, H-2''), 6.70 (1H, *s*, H-8), 6.77 (2H, *br*, OH × 2), 7.59 (2H, *br*, OH × 2), 7.65 (1H, *s*, H-5).

Gancaonin U tetramethyl ether (**5a**). A mixt. of gancaonin U (**5**, 10 mg), Me_2SO_4 (0.5 ml) and dry K_2CO_3 (2 g) in Me_2CO (8 ml) was refluxed for 2 hr. The reaction product was purified by prep. TLC (*n*-hexane–EtOAc, 4:1) to give the tetraMe ether (**5a**, 6 mg), **5a** was recrystallized from MeOH to give needles, mp 96–98°. EIMS, *m/z* (rel. int.): 437 $[M+1]^+$ (31%), 436 $[M]^+$ (100), 421 (4), 365 (4), 349 (4), 337 (4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68 (3H, *br s*, Me-3'), 1.70 (3H, *br s*, Me-3''), 1.78 (3H, *br s*, Me-3'), 1.82 (3H, *br s*, Me-3''), 2.67 (4H, *br s*, H_2-9 and H_2-10), 3.41 (2H, *br d*, J = 6.5 Hz, H_2-1'), 3.44 (2H, *br d*, J = 6.5 Hz, H_2-1''), 3.50, 3.72, 3.91, 3.92 (each 3H, *s*, OMe), 5.07 (1H, *br t*, J = 6.5 Hz, H-2'), 5.28 (1H, *br t*, J = 6.5 Hz, H-2''), 6.75 (1H, *s*, H-8), 8.01 (1H, *s*, H-5).

Gancaonin V (**6**). Recrystallized from *n*-hexane–Me_2CO to give needles, mp 170–173°. $FeCl_3$ test: dark green. UV λ_{max}^{MeOH} nm (log ε): 221 (4.26), 267 (sh 3.72), 275 (3.79), 306 (3.81), 315 (3.79). EIMS, *m/z* (rel. int.): 313 $[M+1]^+$ (21%), 312 $[M]^+$ (100), 257 (95), 256 (41), 255 (12), 239 (6), 227 (10). HRMS, *m/z* 312.1366 $[M]^+$ ($C_{19}H_{20}O_4$ requires: 312.1361). ^{1}H NMR (400 MHz, Me_2CO-d_6): δ 1.64 (3H, *br s*, Me-3'), 1.76 (3H, *br d*, J = 1 Hz, Me-3''), 2.54 (2H, *m*, H_2-9), 2.65 (2H, *m*, H_2-10), 3.35 (2H, *br d*, J = 7 Hz, H_2-1'), 5.09 (1H, *br t*, J = 7 Hz, H_2-2'), 6.43 (1H, *s*, H-3), 6.67 (1H, *s*, H-8), 7.90 (1H, *s*, H-5), 7.49, 7.55, 8.06, 8.11 (each 1H, *br s*, OH).

REFERENCES

1. Fukai, T., Wang, Q.-H., Inami, R. and Nomura, T. (1990) *Heterocycles* **31**, 643.
2. Fukai, T., Toyono, M. and Nomura, T. (1988) *Heterocycles* **27**, 2309.
3. Fukai, T., Wang, Q.-H. and Nomura, T. (1989) *Heterocycles* **29**, 1369.
4. Fukai, T., Wang, Q.-H., Kitagawa, T., Kusano, K., Nomura, T. and Iitaka, Y. (1989) *Heterocycles* **29**, 1761.
5. Fukai, T., Wang, Q.-H., Takayama, M. and Nomura, T. (1990) *Heterocycles* **31**, 373.
6. Mabry, T. J., Markham, K. R. and Thomas, M. B. (1970) in *The Systematic Identification of Flavonoids*, Chap. 5. Springer, New York.
7. Fukai, T., Hano, Y., Hirakura, K., Nomura, T. and Uzawa, J. (1985) *Chem. Pharm. Bull.* **33**, 4288.
8. Tanaka, N., Wada, H., Murakami, T., Sahashi, N. and Ohmoto, T. (1986) *Chem. Pharm. Bull.* **34**, 3727.
9. Fukai, T. and Nomura, T. (1989) *Heterocycles* **29**, 2379.
10. Dhami, K. S. and Stothers, J. B. (1966) *Can. J. Chem.* **44**, 2855.
11. Markham, K. R., Chari, V. M. and Mabry, T. J. (1982) in *The Flavonoids: Advances in Research* (Harborne, J. B. and Mabry, T. J., eds), p. 21. Chapman & Hall, New York.
12. Woolfenden, W. R. and Grant, D. M. (1966) *J. Am. Chem. Soc.* **88**, 1496.
13. Pearson, H. (1975) *J. Chem. Soc., Chem. Commun.* 912.
14. Letcher, R. M. and Nhamo, L. R. M. (1972) *J. Chem. Soc., Perkin Trans 1* 2941.
15. Miyase, T., Ueno, A., Takizawa, N., Kobayashi, H. and Karasawa, H. (1987) *Chem. Pharm. Bull.* **35**, 1109.
16. Fukai, T. and Nomura, T. (1988) *Phytochemistry* **27**, 259.