FIVE NEW ISOPRENOID-SUBSTITUTED FLAVONOIDS, KANZONOLS F - J, FROM *GLYCYRRHIZA URALENSIS* [1]

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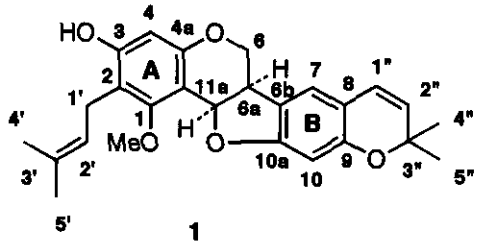
Abstract ---- A new isoprenoid-substituted pterocarpan derivative, kanzonol F, a new isoflavanone derivative, kanzonol G, and three new isoflavan derivatives, kanzonols H, I, J, were isolated from *Glycyrrhiza uralensis*. These structures were elucidated with spectroscopic and/or chemical methods.

Licorice, the roots and stolons of various species of *Glycyrrhiza* (Leguminosae), has been used for a long time as one of the most important crude drugs. The commercial Chinese licorice imported to Japan is generally classified to three kinds, *i.e.* the northeastern licorice (Touhoku Kanzoh in Japanese), the northwestern licorice (Seihoku Kanzoh in Japanese), and Xinjiang licorice (licorice from Xinjiang Uegur Autonomous Region of China, Shinkyo Kanzoh in Japanese). In the earlier papers, we reported the structures of isoprenoid-substituted flavonoids from the northwestern licorice[2-4] and Xinjiang licorice.[5] In the continuous research of commercial Chinese licorice, we examined the northeastern licorice (*G. uralensis*) imported from China. In this paper, we report five new isoprenoid-substituted flavonoids, named kanzonols F (**1**), G (**2**), H (**3**), I (**4**), and J (**5**), along with four known compounds, 1-methoxyficifolinol (**6**),[6] licoricidin (**7**),[2] licorisoflavan A (**8**),[7,8] and glyasperin D (**9**),[7,8] from the licorice.

Kanzonol F (**1**), $C_{26}H_{28}O_5$, $[\alpha]_D$ -119°, was negative to methanolic ferric chloride test. The uv spectrum of **1** resembles the spectra of pterocarpan derivatives, such as 1-methoxyficifolinol (**6**).[6] The ^{1}H nmr spectrum of **1** showed characteristic signals of pterocarpan, *i.e.* δ 3.45 (m, H-6a), 3.58 (t, H-6), 4.19 (ddd, H-6), and 5.62 (br d, H-11a), along with signals of protons of a prenyl group, protons of a 2,2-dimethylpyran ring, protons of a methoxyl group, and three singlet aromatic protons. These spectral data suggested that the compound (**1**) was monocyclized compound of 1-methoxyficifolinol (**6**). The presence of the methoxyl group at 1-position was



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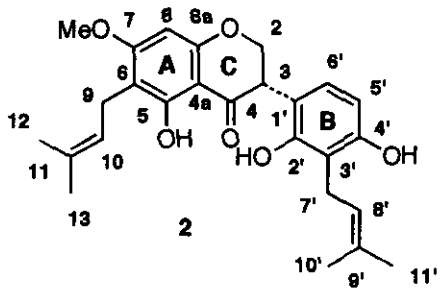

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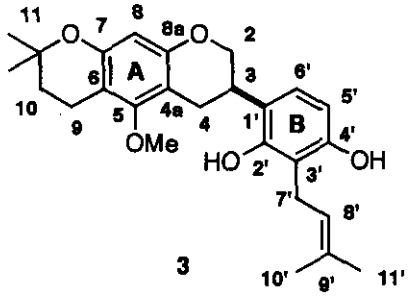

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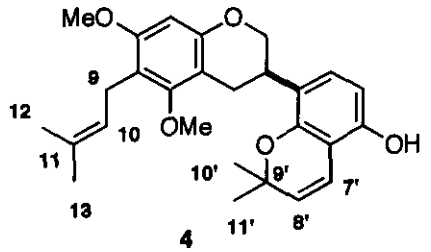

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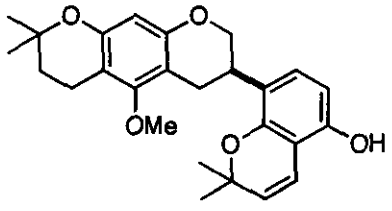

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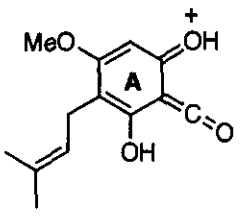

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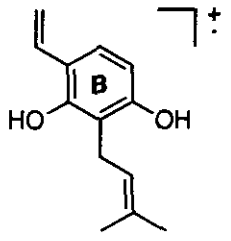

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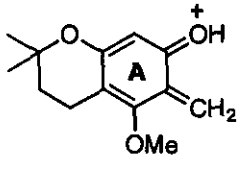

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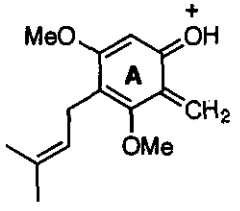
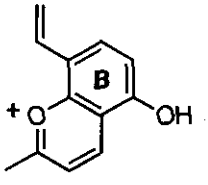


4a



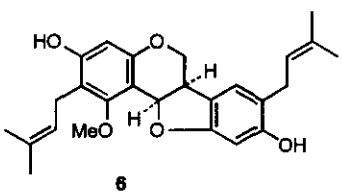
4b

Figure 1

Table 1. ^{13}C nmr data of **1** - **3**, **5** -**7**, **10** and **11** in acetone-d_6

C	**1**	**6**[c]	C	**2**[d]	**10**	**11**	**3**[d]	**5**	**7**
1	161.04	161.03	2	71.31	71.31		70.68	70.32	70.54
2	116.34*a*	116.18	3	46.91	47.38		32.24	32.37	32.17
3	158.50	158.37	4	199.12	199.23		27.12	27.10	27.29
4	100.11	100.05	4a	103.31	104.10		108.94	108.40	108.40
4a	156.06	156.00	5	161.42	161.34		157.69	157.63	158.31
6	66.95	67.07	6	110.14	109.85		107.70	107.68	114.40
6a	39.88	40.14	7	166.56	165.95		155.43	154.97	155.44
6b	120.72	119.05	8	91.70	91.51		100.90	100.82	99.83
7	122.91*b*	125.91	8a	162.87	162.94		155.04	154.48	154.43
8	115.45*a*	120.64	9	21.62	21.62		17.78	17.69	23.32
9	155.28	156.34	10	123.39	123.53		33.23	33.15	125.29
10	99.47	98.27	11	131.43	131.26		74.48	74.39	130.31
10a	161.48	159.64	12	17.81	17.80		26.93	26.49	17.85
11a	76.77	76.39	13	25.86	25.86		26.93	26.77	25.85
11b	107.11	107.33	1'	115.41		115.45	120.12	121.01	120.82
1'	23.40	23.30	2'	154.80		154.89	154.26	152.84	154.13
2'	124.70	124.76	3'	117.04		117.03	116.44	110.37	116.32
3'	130.96	130.89	4'	156.52		156.43	155.48	153.15	155.32
4'	17.98	17.97	5'	108.50		108.44	108.40	108.73	108.33
5'	25.85	25.85	6'	127.20		126.91	125.25	127.90	125.13
1"	122.72*b*	28.75	7'	23.29		23.27	23.42	118.09	23.32
2"	128.12	124.50	8'	123.78		123.69	124.03	129.26	123.93
3"	76.95	131.77	9'	131.78		131.61	131.92	76.48	131.82
4"	28.04	17.82	10'	17.97		17.95	18.07	27.86	17.95
5"	28.20	25.94	11'	25.89		25.88	25.99	27.94	25.28
OMe	63.07	63.02	OMe	56.51			59.84	59.75	60.57

a-b: The assignments may be interchanged. *c*: The assignments were confirmed with ^{13}C -^{1}H-COSY spectrum. *d*: The assignments were confirmed with HMBC spectrum.



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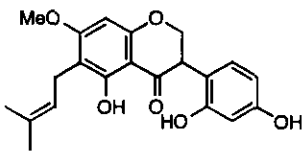

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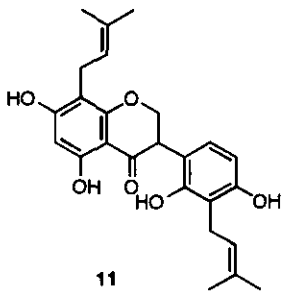

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Figure 2

determined by nuclear Overhauser effect (nOe) measurement of **1** as follow: The enhancement of the C-11a-H signal was observed by 6% when the methoxyl protons (δ 3.92) were irradiated. The presence of the 2,2-dimethylpyran ring on the B ring was also confirmed by nOe experiment as follow: The enhancement of the olefinic proton signal of the pyran ring (H-1") was observed by 13% when H-7 (δ 7.02) was irradiated. These data suggested that the structure of kanzonol F is formula (**1**). Further, the ^{13}C nmr spectrum of **1** (Table 1) supported the structure. The chemical shifts of the carbon atoms of the A ring of **1** were similar to those of relevant atoms of **6**. The C-1 signal of the prenyl group of **1** (C-1') was observed at δ 23.4. This result suggests that the both *ortho*-positions to the prenyl group were substituted by the oxygenated substituents.[9]

The compound (**1**) is laevorotatory pterocarpan which have the 6a*R*, 11a*R* absolute configuration.[10]

Thus, the structure of kanzonol F is characterized as formula (**1**).

Kanzonol G (**2**), $C_{26}H_{30}O_6$, $[\alpha]_D$ -13°, was negative to methanolic ferric chloride test. The uv spectrum showed that the compound (**2**) was either an isoflavanone or a flavanone derivative. The ^1H nmr spectrum exhibited the signals of an isoflavanone skeleton in which the methylene protons at C-2 position appeared at δ 4.62 (dd) and 4.72 (dd), and the methine proton at C-3 position appeared at δ 4.21 (dd). The ^1H nmr spectrum also showed the signals of the following protons: protons of two prenyl groups, protons of a methoxyl group, a singlet aromatic proton (A ring), AX type aromatic protons (B ring), and a hydrogen-bonded hydroxyl proton (5-OH). The mass spectrum of **2** shows the characteristic fragment ion at *m/z* 235 (**2a**, A ring). The presence of the methoxyl group at 7-position was confirmed by nOe measurement as follow: The enhancement of the signal of the aromatic proton on A ring [δ 6.16 (s)] was observed by 23% when the methoxyl protons (δ 3.91) were irradiated. In the ^{13}C nmr spectrum of **2** (Table 1), the chemical shifts of the carbon atoms of the A and B rings were similar to those of relevant atoms of the A ring of glyasperin B (**10**)[7] and the B ring of 3'-(γ,γ-dimethylallyl)-kievitone (**11**), respectively. All the above evidence suggest that the compound (**2**) is 3',6-diprenyl-7-methoxy-2',4',5-trihydroxyisoflavanone or 3',8-diprenyl-7-methoxy-2',4',5-trihydroxyisoflavanone. The position of the prenyl group on the A ring was determined by measurement of heteronuclear multiple bond correlation (HMBC) spectrum of **2**. The proton signal of the hydrogen-bonded hydroxyl group (δ 12.22) shows long-range correlations to both C-4a (δ 103.31) and C-6 (δ 110.14) in the spectrum. Therefore, the prenyl group exists at C-6 position.

The absolute configuration of **2** was assigned to be 3*S* by its CD spectrum in which the negative Cotton effect was exhibited at 333 nm.[10]

Thus, the structure of kanzonol G is characterized as formula (**2**).

Kanzonol H (**3**), $C_{26}H_{32}O_5$, $[\alpha]_D$ +5°, gave a brown color with methanolic ferric chloride test. The uv spectrum

Table 2. ^{1}H nmr data of **3** - **5** and **16** in acetone-d_6

	3	**4**	**5**	**16**
H-2(A)	4.18 (1H, ddd)	4.20 (1H, ddd)	4.18 (1H, ddd)	4.22 (1H, ddd)
H-2(B)	3.93 (1H, t)	4.01 (1H, t)	3.98 (1H, t)	4.00 (1H, t)
H-3	3.40 (1H, m)	3.37 (1H, m)	3.32 (1H, m)	3.42 (1H, m)
H-4(A)	2.92 (1H, ddd)	2.90 (1H, ddd)	2.93 (1H, dd)	2.93 (1H, ddd)
H-4(B)	2.75 (1H, dd)	------ *a*	2.80 (1H, dd)	2.79 (1H, dd)
H-8	6.00 (1H, s)	6.23 (1H, s)	6.00 (1H, s)	6.23 (1H, s)
H-9(A)	2.68 (2H, t)	3.24 (1H, br dd)	2.68 (2H, t)	3.22 (1H, br dd)
H-9(B)		3.26 (1H, br dd)		3.28 (1H, br dd)
H-10	1.75 (2H, t)	5.17 (1H, br t)	1.75 (2H, t)	5.18 (1H, br t)
Me-11	1.28 (6H, s)	1.64 (3H, br s)	1.28 (3H, s)	1.64 (3H, br d)
		1.75 (3H, br s)	1.29 (3H, s)	1.74 (3H, br s)
H-5'	6.45 (1H, d)	6.41 (1H, d)	6.41 (1H, d)	6.34 (1H, br d)
H-6'	6.83 (1H, d)	6.89 (1H, d)	6.89 (1H, d)	6.94 (1H, d)
H-7'	3.45 (2H, br d)	6.71 (1H, d)	6.71 (1H, d)	6.79 (1H, dd)
H-8'	5.26 (1H, br t)	5.67 (1H, d)	5.66 (1H, d)	5.70 (1H, d)
Me-9'	1.66 (3H, br d)	1.42 (3H, s)	1.42 (3H, s)	1.38 (6H, s)
	1.77 (3H, br s)	1.44 (3H, s)	1.43 (3H, s)	
OMe	3.72 (3H, s)	3.70 (3H, s)	3.72 (3H, s)	3.69 (3H, s)
		3.77 (3H, s)		3.77 (3H, s)

a : The signal was overlapped with the signal of water in the solvent.

Coupling constants; (H-2 - H-4), **3-5**, **16**: $J_{2A\text{-}2B} = J_{2B\text{-}3} = 10$ Hz, $J_{2A\text{-}3} = 3$ Hz, $J_{4A\text{-}4B} = 16$ Hz, $J_{4A\text{-}3} = 5$ Hz, $J_{2A\text{-}4A} = 2$ Hz, $J_{4B\text{-}3} = 11$ Hz.

(H-9, H-10), **3-5**, **16**: $J_{9\text{-}10} = 7$ Hz; (H-5', H-6'), **3-5**: $J_{5'\text{-}6'} = 8$ Hz, **16**: $J_{5'\text{-}6'} = 8.5$ Hz.

(H-7', H-8'), **3**: $J_{7'\text{-}8'} = 7$ Hz, **4**, **5**, **16**: $J_{7'\text{-}8'} = 10$ Hz.

(others), **3**: $J_{Me\text{-}9'\text{-}7'} = 1$ Hz, **4**, **16**: $J_{9A\text{-}9B} = 14$ Hz, **16**: $J_{5'\text{-}7'} = 0.7$ Hz, $J_{Me\text{-}11\text{-}9} = 1$ Hz.

of **3** showed that the compound (**3**) was either an isoflavan derivative or a flavan derivative. The ^{1}H nmr spectrum (Table 2) showed characteristic signals of isoflavan, *i.e*. δ 2.75 (dd, H-4), 2.92 (ddd, H-4), 3.40 (m, H-3), 3.93 (t, H-2), and 4.18 (ddd, H-2), along with signals of protons of a 3,4-dihydro-2,2-dimethylpyran ring, a prenyl group, a singlet aromatic proton (A ring), AX type aromatic protons (B ring), protons of a methoxyl group, and two hydroxyl protons [δ 7.18, 8.12 (each 1H, br s)]. The mass spectrum of **3** shows the characteristic fragment ions at *m/z* 204 (**3a**, B ring) and 221 (**3b**, A ring). In the ^{13}C nmr spectrum of **3** (Table 1), the chemical shifts of the carbon atoms of the B ring were similar to those of relevant atoms of the B ring of licoricidin (**7**, Figure 3). These data suggested that the structure of kanzonol H is formula (**3**). The position of the methoxyl group was confirmed by nOe measurement as follow: The enhancements of the signals of C-4-H (both 3%) and methylene protons of 3,4-dihydro-2,2-dimethylpyran ring (C-9-H, 4%) were observed when the methoxyl protons were irradiated. The absolute configuration was assigned to be 3*R* by the CD spectrum of **3** (Table 3) in which the positive Cotton effect was exhibited at 287 nm.[10]

Thus, the structure of kanzonol H was characterized as formula (**3**).

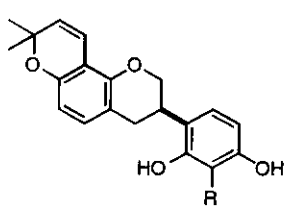
Kanzonol I (**4**), $C_{27}H_{32}O_5$, was negative to Gibbs test indicating the presence of a substituent at *para*-position to a phenolic hydroxyl group.[11] The uv spectrum of **4** resembles that of **3**. The ^{1}H nmr spectrum of **4** (Table 2) showed characteristic signals of isoflavan (C-2-H, C-3-H, and C-4-H), along with signals of protons of a prenyl group, protons of a 2,2-dimethylpyran ring, protons of two methoxyl groups, a singlet aromatic proton (A ring), AX type aromatic protons (B ring), and a hydroxyl proton [δ 8.50 (1H, br s)]. The mass spectrum of **4** shows the characteristic fragment ions at *m/z* 235 (**4a**, A ring) and 187 (**4b**, B ring). These data suggested that the structure of kanzonol I is formula (**4**). The absolute configuration at C-3 was established to be 3*R* as follow. The ORD spectrum of hispaglabridin A (**12**, Figure 3), which have 3*R* configuration, exhibits a positive Cotton effect at 289 nm. On the other hand, the ORD spectrum of hispaglabridin B (**13**), which have a 2,2-dimethylpyran ring on the B ring and 3*R* configuration, exhibits a negative Cotton effect at 292 nm.[11] The compounds (**12** and **13**) were also derived from glabridin (**14**).[11] The CD spectra of prenylated isoflavans (**7** - **9**, **14**, **15**), which have 3*R* configuration, exhibit a positive Cotton effect in the 286 - 289 nm region and a negative Cotton effect in the 272 - 275 nm region (Table 3). The CD spectrum of kanzonol I was different from the spectra of these prenylated isoflavans. Therefore, the compound (**4**) was derived from licorisoflavan A (**8**) with palladium chloride in methanolic solution. The compound (**4**) was obtained as optical active compound with this reaction [the optical purity is *ca.* 50% compared with the natural compound (**4**)], and the CD spectrum of the natural compound (**4**) was similar to that of the synthetic one (**4**) (Table 3).

Thus, the structure of kanzonol I was characterized as formula (**4**).

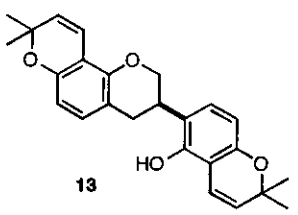
Table 3. CD spectral data of isoflavan derivatives

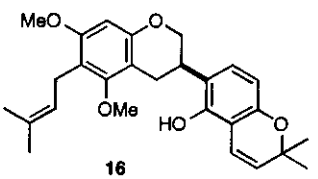
	nm [molecular ellipticity value, θ]
licoricidin (**7**)	237 [-4200], 255 [0], 272 [-1500], 280 [0], 288 [+2100], 296 [+212]
licorisoflavan A (**8**)	258 [+1100], 268 [0], 275 [-1400], 282 [0], 286 [+1900], 300 [+120], 350 [0]
glyasperin C (**14**)[7]	239 [-3200], 255 [-230], 275 [-2400], 283 [0], 289 [+1600], 300 [0]
glyasperin D (**9**)	239 [-4200], 256 [-380], 274 [-1900], 283 [0], 288 [+1100], 294 [0]
glyasperin I (**15**)[12]	242 [-1600], 254 [-220], 275 [-2000], 284 [0], 288 [+1100], 296 [0]
kanzonol H (**3**)	244 [-1000], 255 [-69], 273 [-1700], 281 [0], 287 [+2500], 300 [0]
kanzonol I (**4**) (natural)	240 [-4500], 257 [0], 270 [+840], 287 [+2500], 300[+700], 305 [+420], 325 [+420], 350 [0]
kanzonol I (**4**) (synthetic)	240 [-3300] 256 [0], 270 [+940], 285 [+1200], 300 [+470], 305 [+240], 325 [+120], 340 [0]
kanzonol J (**5**)	240 [-4600], 248 [0], 270 [+2700], 289 [+4600], 300 [+930], 305 [+520], 325 [+520], 340 [0]
compound (**16**)	240 [-6600], 255 [-2300], 270 [-3100], 280 [-3400], 290 [-1900], 300 [-470], 310 [0]
glyasperin G (**17**)[12]	242 [+670], 257 [+1200], 276 [+100], 288 [+270], 300 [0]
glyasperin H (**18**)[12]	247 [0], 255 [+130], 280 [+300], 290 [+200], 310 [+50], 340 [0]

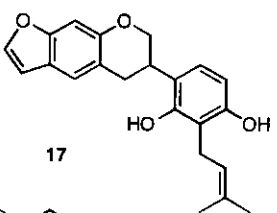
The molar concentrations of these solutions were as follows; **7**: 4.7×10^{-4} mol/l, **8**: 1.2×10^{-4}, **14**: 1.2×10^{-4}, **9**: 1.1×10^{-4}, **15**: 3.4×10^{-4}, **3**: $1,2 \times 10^{-4}$, **4** (natural): 1.8×10^{-4}, **4** (synthetic): 1.2×10^{-4}, **5**: 1.2×10^{-4}, **16**: 8.0×10^{-5}, **17**: 6.0×10^{-5}, **18**: 1.0×10^{-4}.

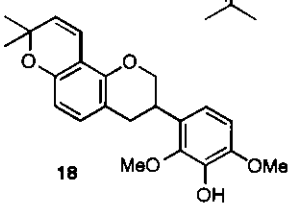


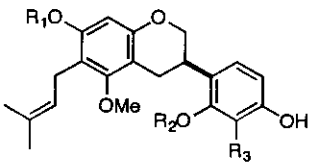
12: R=-$CH_2CH=C(Me)_2$
14: R=H











7: R_1=R_2=H, R_3=-$CH_2CH=C(Me)_2$
8: R_1=Me, R_2=H, R_3=-$CH_2CH=C(Me)_2$
9: R_1=Me, R_2=R_3=H
14: R_1=R_2=R_3=H
15: R_1=R_3=H, R_2=Me

Figure 3

It is noteworthy that the CD spectrum of compound (**16**), which was also obtained here by the cyclization of licorisoflavan A (**8**), was showed the negative Cotton effect at 280 nm (Table 3). The CD spectra of glyasperins G (**17**) and H (**18**) also differ from those of the prenylated isoflavans (**7** - **9**, **14**, **15**) (Table 3). We reported that these compound (**17**, **18**) have 3*R* absolute configuration.[12] Reinvestigation of the CD spectra of furanoisoflavan and pyranoisoflavan, such as **17** and **18**, is now in progress.

Kanzonol J (**5**), $C_{26}H_{30}O_5$, $[\alpha]_D$ +30°, was negative to both methanolic ferric chloride test and Gibbs test. The uv spectrum and ^{1}H nmr spectrum of **5** showed that the compound (**5**) is an isoflavan derivative. The ^{1}H nmr spectrum (Table 3) showed the signals of protons of a 3,4-dihydro-2,2-dimethylpyran ring, protons of a 2,2-dimethylpyran ring, protons of a methoxyl group, a singlet aromatic proton (A ring), AX type aromatic protons (B ring), and a hydroxyl proton [δ 8.46 (1H, br s)]. In the ^{13}C nmr spectrum of **5** (Table 1), the chemical shifts of the carbon atoms of the A ring were similar to those of kanzonol H (**3**). In the ^{1}H nmr spectrum of **5**, the chemical shifts of the protons of the B ring and the 2,2-dimethylpyran ring resemble those of relevant protons of **3**, but differ from **16** (Table 2). The mass spectrum of **5** shows the characteristic fragment ions at *m/z* 187 (**4b**, B ring) and 221 (**3b**, A ring). These data suggested that the structure of kanzonol J is formula (**5**). The position of the methoxyl group was also confirmed by nOe measurement (in $CDCl_3$) as follow: The enhancement of the signals of C-4-H were observed by 3%, respectively, when the methoxyl protons were irradiated. The enhancement of the signal of C-9-H was also observed by 4% when the methoxyl protons were irradiated. The CD spectrum of **5** (Table 3) was similar to that of **4**, therefore, the absolute configuration of **5** was assigned to be 3*R*.

Thus, the structure of kanzonol J was characterized as formula (**5**).

EXPERIMENTAL

Melting points were measured on Yazawa micromelting point apparatus (hot-stage type) and are uncorrected. The following instruments were used; ^{1}H and ^{13}C nmr spectra; JEOL JNM-EX-400 and JNM-α-500 NMR Spectrometers, uv spectra: Shimadzu UV-265 Spectrophotometer, mass spectra, JEOL JMS-D-300 (EI-ms) and JEOL JMS-DX-303 (HR-ms) Mass Spectrometers, optical rotations, JASCO DIP-4 instrument, and CD spectra : JASCO J-720 CD Spectrometer. The uv and CD spectra were measured in methanol. For tlc (silica gel) and preparative tlc (silica gel), Wakogel B-5FM and B-5F were used.

Plant Material

The northeastern licorice (lot. No.16905B) was purchased from Matuura Yakugyo Co., Nagoya, Japan. The licorice was identified to *Glycyrrhiza uralensis* by Dr. L. Zeng, Beijing Medical University.

Isolation of flavonoids from Glycyrrhiza uralensis Roots

The licorice (4.9 Kg) was extracted at room temperature with hexane (20 l, three times), benzene (20 l, x 3), and acetone (20 l, x 3), successively (each 3 days). Evaporation of the benzene and acetone solutions to dryness yielded 40 g and 150 g of the residues, respectively. The benzene extract (40 g) was chromatographed on silica gel (200 g) successively with benzene (Fr. 1 - 41), benzene-ether = 99:1 (Fr. 42 - 79), benzene-ether = 49:1 (Fr 80 - 99), and benzene-ether = 19:1 (Fr. 100 - 122) as the eluent (column A), each fraction (eluent volume 500 ml) being monitored by tlc. From the fraction 24 (0.1 g), **7** (52 mg) was obtained by recrystallization from benzene. The fraction 81 (0.1 g) was purified by preparative tlc (solvent system: hexane-acetone = 2:1, hexane-ethyl acetate = 2:1) to give **9** (2 mg). The fraction 3 (3 g) was rechromatographed on silica gel (80 g) with hexane-acetone (100:0 → 0:100) as the eluent (each volume 100 ml, column B). From the fraction 13 of column B (eluted with hexane-acetone = 22:3, 0.5 g), **8** (80 mg) was obtained by recrystallization from benzene. The fraction 14 of column B (eluted with hexane-acetone = 87: 13, 0.25 g) was purified by preparative tlc (hexane-ether = 2:1, hexane-ethyl acetate = 7:1) to give **2** (2 mg). The fractions 11 and 12 of column B (eluted with hexane-acetone = 9:1, 0.4 g) was rechromatographed on silica gel (50 g) with hexane-benzene (100:0 → 0:100) as the eluent (each volume 100 ml, column C). The fraction 11 of column C (eluted with benzene, 40 mg) was purified by preparative tlc (solvent system: hexane-acetone = 2:1, benzene-chloroform = 3:1, multiple development, × 3) to give **1** (1 mg) and **4** (2 mg). The fraction 6 of column A (2 g) was rechromatographed on silica gel (90 g) with hexane-acetone (100:0 → 0:100) as the eluent (each volume 100 ml, column D). The fraction 9 of column D (eluted with hexane-acetone = 9:1, 0.2 g) was purified by preparative tlc (benzene-ether = 5: 1, chloroform-ethyl acetate = 20:1) to give **5** (8 mg). The fraction 10 of column D (eluted with hexane-acetone = 9:1, 0.2 g) was purified by preparative tlc (benzene-ether = 5: 1) to give **3** (5 mg). The fraction 12 of column D (eluted with hexane-acetone = 9:1, 75 mg) was purified by preparative tlc (benzene-ether = 5: 1) to give **6** (17 mg).

Kanzonol F (1)

Compound (**1**) was obtained as an amorphous powder. $[\alpha]_D$ -119° (c = 0.035, MeOH). Gibbs test: negative. Uv λ_{max} nm (log ε): 230 (3.46), 283 (2.99), 312 (2.87). EI-ms (prove) 70 eV, *m/z* (rel. int.): 421 $[M+1]^+$ (23%), 420 $[M]^+$ (73), 405 (100),349 (16). HR-ms, *m/z* 420.1988 $[M]^+$ ($C_{26}H_{28}O_5$ requires: 420.1937). ^1H

Nmr (500 MHz, acetone-d_6): δ 1.37, 1.38 (each 3H, s, Me-3"), 1.66 (3H, br d, J = 1 Hz, Me-3'), 1.77 (3H, br s, Me-3'), 3.28, 3.36 (each 1H, br dd, J = 7, 14 Hz, H-1'), 3.45 (1H, m, H-6a), 3.58 (1H, t, J = 11 Hz, H-6), 3.92 (3H, s, OMe), 4.19 (1H, ddd, J = 0.7, 5, 11 Hz, H-6), 5.27 (1H, br t, J = 7 Hz, H-2'), 5.54 (1H, d, J = 10 Hz, H-2"), 5.62 (1H, br d, J = 6.5 Hz, H-11a), 6.22 (1H, s, H-10), 6.25 (1H, s, H-4), 6.34 (1H, d, J = 10 Hz, H-1"), 7.02 (1H, s, H-7). ^{13}C Nmr (125 MHz, acetone-d_6): see Table 1.

Kanzonol G (2)

Compound (**2**) was obtained as a pale yellow oil. $[\alpha]_D$ -13° (c = 0.042, MeOH). Uv λ_{max} nm (log ε): 207 (4.63), 291 (4.24), +AcONa: no shift. EI-ms, *m/z* : 439 $[M+1]^+$ (6), 438 $[M]^+$ (21), 383 (5), 382 (6), 381 (6), 329 (7), 235 (36), 179 (79). HR-ms, *m/z* 438.2042 $[M]^+$ ($C_{26}H_{30}O_6$ requires: 438.2042). ^{1}H Nmr (400 MHz, acetone-d_6): δ 1.62 (3H, br d, J = 1 Hz, Me-9'), 1.65 (3H, br d, J = 1 Hz, Me-11), 1.73 (3H, br s, Me-11), 1.76 (3H, br s, Me-9'), 3.21 (2H, br d, J = 7 Hz, H_2-9), 3.41 (2H, br d, J = 7 Hz, H_2-7'), 3.91 (3H, s, OMe), 4.21 (1H, dd, J = 5, 8 Hz, H-3), 4.62 (1H, dd, J = 5, 11 Hz, H-2), 4.72 (1H, dd, J = 8, 11 Hz, H-2), 5.15 (1H, br , J = 7 Hz, H-7'), 5.23 (1H, br t, J = 7 Hz, H-10), 6.16 (1H, s H-8), 6.43 (1H, d, J = 8 Hz, H-5'), 6.93 (1H, d, J = 8 Hz, H-6'), 12.22 (1H, s, OH-5). ^{13}C Nmr (100 MHz, acetone-d_6): see Table 1. CD (c = 7.8 × 10^{-5} mol/l), $[\theta]_{250}$ 0, $[\theta]_{268}$ -640, $[\theta]_{285}$ 0, $[\theta]_{293}$ +1900, $[\theta]_{315}$ 0, $[\theta]_{333}$ -800, $[\theta]_{350}$ 0.

Kanzonol H (3)

Compound (**3**) was obtained as fine prisms, mp 198 - 199℃ (from benzene). $[\alpha]_D$ +5° (c = 0.11, MeOH). Uv λ_{max} nm (log ε): 277 (sh 3.67), 283 (3.70), 310 (sh 2.00). EI-ms, *m/z* : 425 $[M+1]^+$ (7), 424 $[M]^+$ (24), 221 (100), 204 (4). HR-ms, *m/z* 424.2205 $[M]^+$ ($C_{26}H_{32}O_5$ requires: 424.2250). ^{1}H Nmr (400 MHz, acetone-d_6): see Table 2. ^{13}C Nmr (100 MHz, acetone-d_6): see Table 1.

Kanzonol I (4)

Compound (**4**) was obtained as colorless prisms, mp 180 - 185℃ (from benzene). Uv λ_{max} nm (log ε): 225 (4.17), 275 (3.64), 285 (sh 3.60), 310 (sh 2.98). EI-ms, *m/z* : 437 $[M+1]^+$ (31), 436 $[M]^+$ (100), 421 (40), 405 (15), 235 (77), 190 (51), 187 (60). HR-ms, *m/z* 436.2300 $[M]^+$ ($C_{27}H_{32}O_5$ requires: 436.2250). ^{1}H Nmr (400 MHz, $CDCl_3$): δ 1.42, 1.43 (each 3H, s, Me-9'), 1.67, 1.77 (each 3H, br s, Me-11), 2.88 (1H, dd, J = 11, 16 Hz, H-4), 2.97 (1H, ddd, J = 2, 5, 16 Hz, H-4), 3.44 (1H, m, H-3), 3.50 (2H, br d, J = 6 Hz, H_2-9), 3.72, 3.77 (each 3H, s, OMe), 4.02 (1H, t, J = 10 Hz, H-2), 4.28 (1H, ddd, J = 2, 3, 10 Hz, H-2), 5.62 (1H,

d, J = 10 Hz, H-8'), 6.25 (1H, s, H-8), 6.29 (1H, d, J = 8 Hz, H-5'), 6.64 (1H, d, J = 10 Hz, H-8'), 6.82 (1H, d, J = 8 Hz, H-6'), (400 MHz, acetone-d_6): see Table 2

Kanzonol J (5)

Compound (**5**) was obtained as pale yellow oil. $[\alpha]_D$ +30° (c = 0.059, MeOH). Uv λ_{max} nm (log ε): 275 (4.04), 288 (sh 4.00), 310 (sh 3.35). EI-ms, *m/z* : 423 $[M+1]^+$ (9), 422 $[M]^+$ (30), 421 (40), 407 (11), 221 (100), 187 (25). HR-ms, *m/z* 422.2066 $[M]^+$ ($C_{26}H_{30}O_5$ requires: 422.2093). ^{1}H Nmr (400 MHz, $CDCl_3$): δ 1.32, 1.34 (each 3H, s, Me-11),1.41, 1.42 (each 3H, s, Me-9'), 1.76 (2H, t, J = 7 Hz, H_2-10), 2.70 (2H, t, J = 7 Hz, H_2-9), 2.79 (1H, dd, J = 11, 16 Hz, H-4), 2.98 (1H, ddd, J = 2, 5, 16 Hz, H-4), 3.45 (1H, m, H-3), 3.74 (3H, s, OMe), 4.00 (1H, t, J = 10 Hz, H-2), 4.26 (1H, ddd, J = 2, 3, 10 Hz, H-2), 5.61 (1H, d, J = 10 Hz, H-8'), 6.18 (1H, s, H-8), 6.29 (1H, d, J = 8 Hz, H-5'), 6.64 (1H, d, J = 10 Hz, H-8'), 6.81 (1H, d, J = 8 Hz, H-6'), (400 MHz, acetone-d_6): see Table 2. ^{13}C Nmr (100 MHz, acetone-d_6): see Table 1.

Formation of Kanzonol I (4) and Compound (16) from Licorisoflavan A (8)

A mixture of **8** (25 mg) and palladium chloride (2 mg) in 90% aqueous methanol solution (1 ml) was kept at 30 ℃ for 25 h. The products were purified by preparative tlc (hexane-acetone=4:1, × 5, chloroform-benzene=3:1, × 3) to give **4** (2.5 mg) and **16** (7 mg). The product (**4**) was identified as kanzonol I (**4**) by co-tlc and ^{1}H nmr spectra.

Compound (16)

Compound (**16**) was obtained as pale yellow oil. $[\alpha]_D$ -27° (c = 0.003, MeOH). Gibbs test: positive (dark blue). Uv λ_{max} nm (log ε): 277 (4.08), 287 (sh 4.04), 310 (sh 3.41). EI-ms, *m/z* : 437 $[M+1]^+$ (27), 436 $[M]^+$ (91), 421 (63), 405 (3), 235 (80), 190 (14), 187 (100). HR-ms, *m/z* 436.2229 $[M]^+$ ($C_{27}H_{32}O_5$ requires: 436.2250). ^{1}H Nmr (400 MHz, acetone-d_6): see Table 2.

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