FIVE NEW ISOPRENOID-SUBSTITUTED FLAVONOIDS, KANZONOLS M - P AND R, FROM TWO *GLYCYRRHIZA* SPECIES[1]

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Abstract ——— Three new formylated isoflavan derivatives, kanzonols M, N, and O, and a new prenylated pterocarpan derivative, kanzonol P, were isolated from *Glycyrrhiza uralensis* along with kanzonol Q (dihydroxanthoxyletin). A new prenylated isoflavan derivative, kanzonol R, was isolated from *G. glabra*. These structures were elucidated on the basis of spectrometric evidence.

Licorice has been used for a long time as one of the most important crude drug.[2] In earlier paper, we reported the structures of isoprenoid-substituted flavonoids from Chinese licorice.[3] In our continuous research on Chinese licorice, we isolated isoprenoid-substituted flavonoids, kanzonols F - L, from *Glycyrrhiza uralensis*.[4,5] In this paper, we report three new isoprenoid-substituted isoflavans, kanzonols M (**1**), N (**2**), and O (**3**) which have a formyl group at C-8, and a new prenylated pterocarpan, kanzonol P (**4**), from this species. The dihydropyranocoumarin, kanzonol Q (**5**, dihydroxanthoxyletin[6]), was also isolated for the first time as a natural product from the plant. We also report here the isolation and the structure of a prenylated isoflavan, kanzonol R (**6**), from *G. glabra*.

Kanzonol M (**1**), $C_{23}H_{26}O_6$, was negative to the methanolic ferric chloride test on tlc plate. The uv spectrum showed that the compound was either an isoflavan or a flavan derivative. The ^{1}H nmr spectrum of **1** (Table 1) exhibited characteristic signals for isoflavan skeleton (C-2-H × 2, C-3-H, C-4-H × 2). The ^{1}H nmr spectrum also showed signals for protons of a 3-methyl-2-butenyl (prenyl) group, protons of two methoxyl groups, a singlet aromatic proton (A ring), *ortho*-coupled aromatic protons (AX-type, B ring), a hydroxyl proton, a proton of formyl group (δ 10.07), and a hydrogen-bonded hydroxyl proton (δ 12.40). The ^{13}C nmr spectrum of **1** (Table 2) also showed the presence of the formyl group [δ 192.53 (d, J = 181 Hz)]. In the ^{13}C nmr spectrum, five oxygenated aromatic carbon atoms appeared between δ 153.83 and 166.66 indicating that these carbons located at *meta*-position(s) each other.[7] The mass spectrum of **1** showed characteristic fragment ions at *m/z* 181 (**1a**, A ring) and 218 (**1b**, B ring). The positions of the methoxyl groups were suggested by the following nOe measurements. The enhancement of the singlet signal at δ 6.10 was observed by 18% when the methoxyl protons at δ 3.91 were irradiated. The enhancement of the doublet signal at δ 6.55 was observed by 18% when the other methoxyl protons (δ 3.80) were irradiated. The above all data indicated that the structure of kanzonol M is formula (**1**) or (**1'**). The structure of the compound was determined by measurement of heteronuclear multiple bonded correlation (HMBC) spectrum of **1**. The signals of C-4-H showed long-range correlation to C-5 (δ 166.66) which was also correlated by the methoxyl proton signal (δ 3.91) and C-6-H signal (Table 2). Thus, the structure of kanzonol M was characterized as formula (**1**) except the stereochemistry at the C-3 position.

Kanzonol N (**2**), $C_{22}H_{24}O_6$, $[\alpha]_D$ - 9°, was positive to the methanolic ferric chloride test on tlc plate. The uv and ^{1}H nmr spectra showed that the compound was an isoflavan derivative. The ^{1}H nmr spectrum of **2** (Table 1) exhibited characteristic signals for isoflavan skeleton (C-2-H × 2, C-3-H, and C-4-H × 2) along with signals of following protons: protons of a prenyl group, protons of a methoxyl group, a singlet aromatic proton (A ring), *ortho*-coupled aromatic protons (AX-type, B ring), two hydroxyl protons, a proton of formyl group (δ 10.05), and a hydrogen-bonded hydroxyl proton (δ 12.38). The mass spectrum of **2** showed characteristic fragment ions at *m/z* 181 (**1a**, A ring) and 204 (**2a**, B ring). The ^{13}C nmr spectrum of **2** was analyzed by comparison with the spectra of isoflavan derivatives as shown in Table 2. The chemical shifts of the carbon atoms of the A and B rings of **2** were similar to those of the relevant atoms of the A ring of kanzonol M (**1**) and the B ring of licoricidin (**7**),[4] respectively. The position of the methoxyl group (C-5) was confirmed by the nOe measurement: the enhancement of the C-6-H signal [δ 6.09 (s)] was observed by 11% when the methoxyl protons were irradiated. Thus, the structure of kanzonol N was characterized as formula (**2**) except the stereochemistry at the C-3 position.

Kanzonol O (**3**), $C_{22}H_{22}O_6$, $[\alpha]_D$ - 10°, was positive to the methanolic ferric chloride test on tlc plate. The uv and ^{1}H nmr spectra showed that the compound was an isoflavan derivative. The ^{1}H nmr spectrum of **3** (Table 1) exhibited characteristic signals for isoflavan skeleton (C-2-H × 2, C-3-H, and C-4-H × 2) along with signals for the following protons: protons of a 2,2-dimethylpyran ring, protons of a methoxyl group, a singlet aromatic proton (A ring), *ortho*-coupled aromatic protons (AX-type, B ring), a hydroxyl proton, a proton of formyl group (δ 10.06), and a hydrogen-bonded hydroxyl proton (δ 12.40). The mass spectrum of **3** showed characteristic fragment ions at *m/z* 181 (**1a**, A ring), 187 (**3a**, B ring), and 202 (**3b**, B ring). In the ^{13}C nmr spectrum of **3** (Table 2), the chemical shifts of the carbon atoms of the A and B rings of **3** were similar to those of the relevant atoms of the A ring of **1** and the B ring of kanzonol J (**8**),[4] respectively. The above all data suggested that the structure of kanzonol O is formula (**3**). The structure was confirmed by the nOe measurements as follows. The

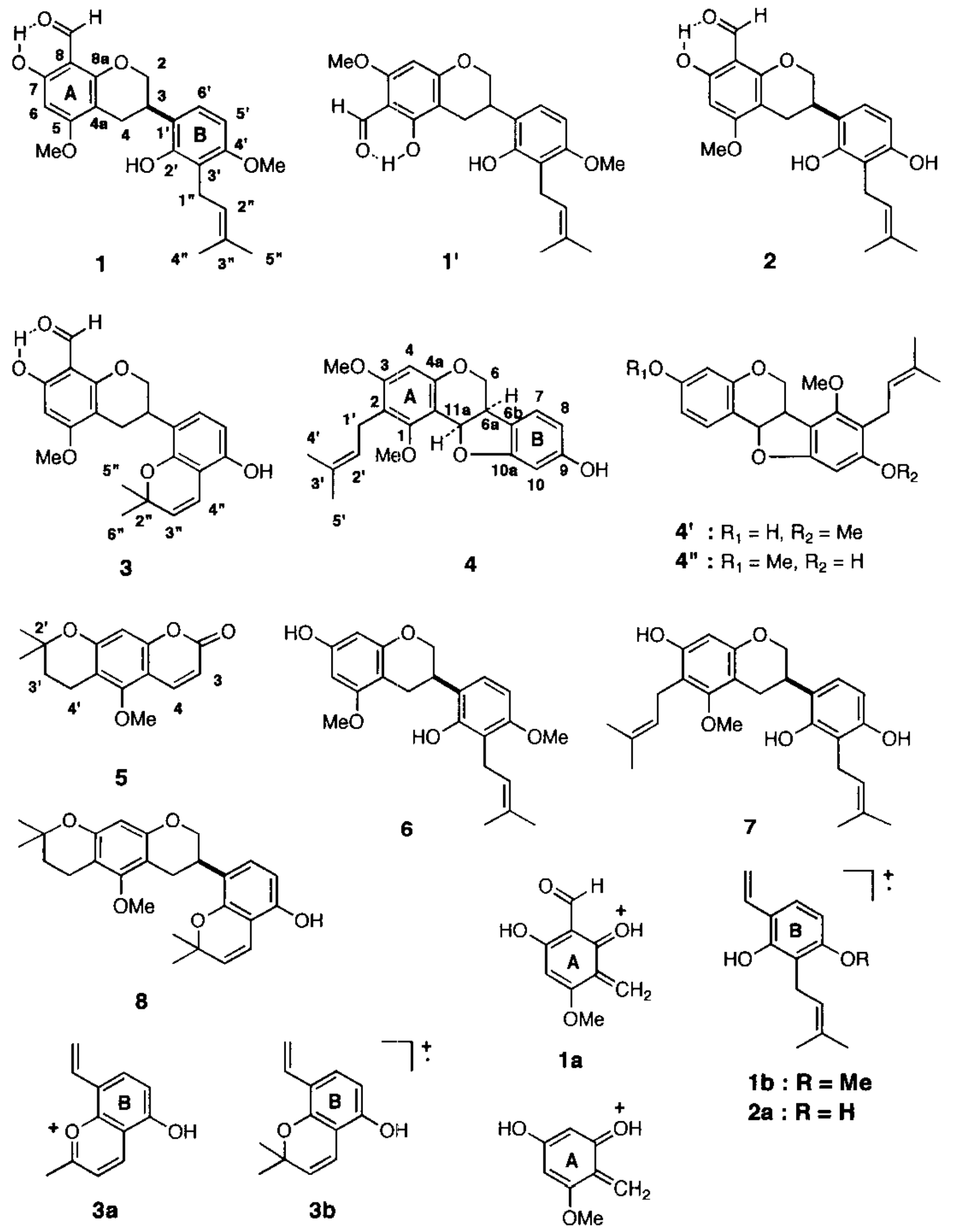

Figure 1.

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

	1	**2**
H-2	4.14 (t, J =10 Hz)	4.10 (t, J =10 Hz)
	4.40 (ddd, J =2, 3.5, and 10 Hz)	4.39 (ddd, J =2, 3.5, and 10 Hz)
H-3	3.52 (m)	3.51 (m)
H-4	2.63 (dd, J =10.5 and 15.5 Hz)	2.59 (dd, J =11 and 16 Hz)
	2.84 (ddd, J =2, 5, and 15.5 Hz)	2.81 (ddd, J =2, 5, and 16 Hz)
H-6	6.10 (s)	6.09 (s)
H-5'	6.55 (d, J =8.5 Hz)	6.46 (d, J =8 Hz)
H-6'	7.00 (d, J =8.5 Hz)	6.84 (d, J =8 Hz)
H_2-1"	3.43 (br d, J =7 Hz)	3.45 (br d, J =7 Hz)
H-2"	5.28 (br t, J =7.Hz)	5.24 (br t, J =7 Hz)
H-3"	......	......
H-4"	......	......
Me	1.65 (br d, J =1Hz)	1.65 (br d, J =1 Hz)
Me	1.77 (br d, J =0.7 Hz)	1.76 (br s)
OMe-5	3.91 (s)	3.91 (s)
OMe-4'	3.80 (s)	......
OH-2'	7.34 (s)	7.29 (br s)
OH-4'	.....	8.32 (br s)
OH-7	12.40 (s)	12.38 (s)
CHO	10.07 (s)	10.05 (s)

	3	**6**
H-2	4.15 (t, J =10 Hz)	3.93 (t, J = 10 Hz)
	4.35 (ddd, J =2, 3.5, and 10 Hz)	4.17 (ddd, J = 2, 3, and 10 Hz)
H-3	3.45 (m)	3.40 (m)
H-4	2.65 (dd, J =11 and 16 Hz)	2.57 (dd, J = 11 and 16 Hz)
	2.78 (ddd, J =2, 5.5, and 16 Hz)	2.82 (ddd, J = 2, 5, and 16 Hz)
H-6	6.09 (s)	6.04 (d, J = 2 Hz)
H-8	......	5.94 (d, J = 2 Hz)
H-5'	6.42 (d, J =8 Hz)	6.51 (d, J = 8 Hz)
H-6'	6.90 (d, J = 8 Hz)	6.95 (d, J = 8 Hz)
H_2-1"	......	3.41 (br d, J = 7 Hz)
H-2"	......	5.17 (br t, J = 7 Hz
H-3"	5.66 (d, J = 10 Hz)	......
H-4"	6.71 (d, J =10 Hz)	... ..
Me	1.42 (s)	1.64 (br d, J = 1Hz)
Me	1.44 (s)	1.75 (br d, J = 1 Hz)
OMe-5	3.91 (s)	3.74 (s)
OMe-4'	.....	3.77 (s)
OH-4'	8.54 (s)	.....
OH-2'	.....	7.26 (s)
OH-7	12.40 (s)	8.16 (s)
CHO	10.06 (s)	......

Table 2. ^{13}C nmr data of **1** - **3** and **6** - **8** in acetone-d_6

C	**1**	C-H *via* $^{2\text{-}4}J$ ^{a}	**2**	**7**	**3**	**8**	**6**
2	71.03	H-4×2, H-3	71.42		71.02 (Tm)^b		70.58
3	32.58	H-2×2, H-4×2, H-6'	31.85		31.66 (Dm)		32.29
4	25.66	H-2×2, H-3	26.17		25.40 (Tm)		26.70
4a	103.58	H-2×2, H-3	103.93		103.63 (Sm)		103.47
5	166.66	OMe (δ 3.91), H-4×2, H-6	166.96		166.80 (Sm)		159.80*
6	92.05	OH (δ 12.40), CHO	92.26		92.17 (Dd)		92.43
7	165.29	CHO, OH (δ 12.40), H-6	165.56		165.40 (Sm)		158.02*
8	106.18	H-6, CHO, OH (δ 12.40)	106.47		105.99 (Sddd)		96.57
8a	158.45	H-4×2, H-2×2	158.76		158.58 (Sm)		156.57*
1'	121.68	H-4×2, H-2×2	120.38	120.82	120.30 (Sm)	121.01	122.74
2'	153.83	H-6', OH (δ 7.34), H-1"×2, H-3	154.52	154.13	153.15 (Sm)	152.84	153.96
3'	117.76	H-1"×2, H-5', OH (δ 7.34)	116.70	116.32	110.55 (Sm)	110.37	117.87
4'	158.05	H-6', H-5', OMe (δ 3.80), H-1"×2	155.87	155.32	153.15 (Sm)	153.15	158.02
5'	104.07	......	108.70	108.33	108.64 (D)	108.73	104.02
6'	125.51	H-3	125.60	125.29	128.15 (Dd)	127.90	125.57
1"	23.16	H-2"	23.57	23.23	.....	.....	23.38
2"	123.64	H-1"x2, Me×2	124.10	123.93	76.72 (Sm)	76.48	123.97
3"	132.03	H-1"x2, Me×2	132.32	131.82	129.45 (Dm)	129.26	132.01
4"	17.92	H-2", Me (δ 1.65)	18.25	17.95	118.18 (D)	118.09	18.09
5"	25.89	H-2", Me (δ 1.77)	26.00	25.88	27.92 (Qm)	27.86	26.06
6"	....		....		28.09 (Qm)	27.94	. .
OMe	55.94		56.86		56.72 (Q)		55.82
	56.59						56.10
CHO	192.53	H-6, OH (12.40)	192.83		192.68 (D)		....

a: The correlations between protons and carbon signals in HMBC spectrum. *b*: Capital letters refer to the coupling pattern resulting from directly bonded proton(s) and lowercase letters to long-range ^{13}C-^{1}H coupling.
*: The assignment may be interchanged.

enhancement of the C-6-H signal [δ 6.09 (s)] was observed by 19% when the methoxyl protons were irradiated. The enhancement of the C-5'-H signal [δ 6.42 (d)] was observed by 8% when the hydroxyl proton at δ 8.54 was irradiated. Thus the structure of kanzonol O was characterized as formula (**3**) except the stereochemistry at the C-3 position.

Kanzonol P (**4**), $C_{22}H_{24}O_5$, $[\alpha]_D$ - 58°, was positive to the methanolic ferric chloride test on tlc plate. The ^{1}H nmr spectrum (in acetone d_6) exhibited characteristic signals for pterocarpan skeleton [δ 3.56 (t, C-6-H), 3.42 (m, C-6a-H), 4.20 (ddd, C-6-H), and 5.60 (br d, C-11a-H)]. The ^{1}H nmr spectrum of **4** also showed the following protons: protons of a prenyl group, protons of two methoxyl groups, singlet aromatic proton, AXYtype aromatic protons, and a hydroxyl proton. In the ^{13}C nmr spectrum of **4**, five oxygenated aromatic carbons appeared between δ 156.70 and 162.06 indicating that these carbon atoms located at *meta*-position(s) each other.[7] The above data suggested that the structure of the compound is formula (**4**) or (**4'**) or (**4"**). The structure of kanzonol P was elucidated by the nOe experiments (in $CDCl_3$) as shown in Figure 2. The compound was laevorotatory pterocarpan which has 6a*R*, 11a*R* absolute configuration.[8] Thus the structure of kanzonol P was characterized as formula (**4**).

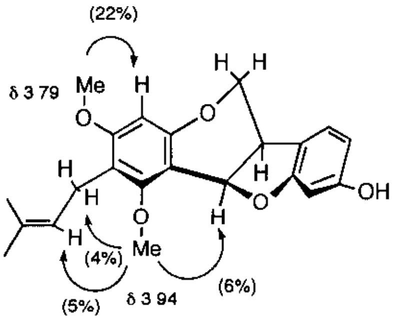

Figure 2. NOe values of kanzonol P (**4**)

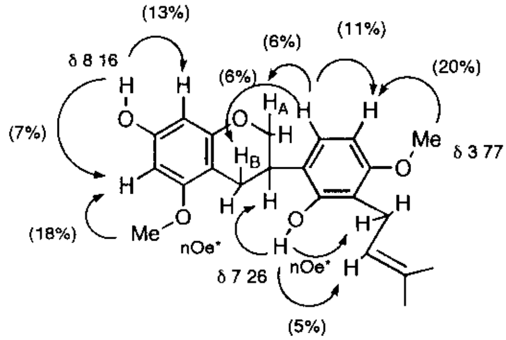

Figure 3. NOe values of kanzonol R (**6**)
* A part of the C-3-H signal was overlapped with C-1"-H_2 signal
H_A δ 3 93, H_B δ 2 57

Kanzonol R (**6**), $C_{22}H_{26}O_5$, $[\alpha]_D$ - 25°, was positive to the methanolic ferric chloride test on tlc plate. The uv and ^1H nmr spectra showed that the compound was an isoflavan derivative. The ^1H nmr spectrum of **6** (Table 1) exhibited characteristic signals for isoflavan skeleton (C-2-H × 2, C-3-H, and C-4-H × 2) along with signals for the following protons: protons of a prenyl group, protons of two methoxyl groups, *meta*-coupled aromatic protons (AB type, A ring), *ortho*-coupled aromatic protons (AX type, B ring), two hydroxyl protons. The mass spectrum of **6** gave characteristic fragment ions at *m/z* 153 (**6a**, A ring) and 218 (**1b**, B ring). The ^{13}C nmr spectrum of **6** (Table 2) was analyzed by comparison with that of **1** in which the chemical shifts of A-ring carbons of the corresponding desformyl compound were calculated by use of the substituent effect of formyl group.[9] The above data suggested that kanzonol R (**6**) is desformylkanzonol M. The structure of **6** was confirmed by the nOe measurements (in acetone-d_6) as shown in Figure 3. The absolute configuration of **6** was assigned to be 3*R* by its CD spectrum in which the positive Cotton effects were exhibited at 273 and 278 nm.[10] Thus, the structure of kanzonol R was characterized as formula (**6**).

The absolute configuration of kanzonols M - O (**1** - **3**) could not be determined by their CD spectra because these compounds were isolated for the first time as isoflavan derivative having a formyl group, and suitable reference compounds were not found. Therefore, kanzonol M (**1**) was derived from kanzonol R (**6**) by the formylation.[11] The CD spectrum of the natural compound (**1**) and the synthetic one (**1**) showed the same curve except molecular ellipticity values ($[\theta]$), and the spectrum of kanzonol N (**2**) was similar to that of **1**. Thus, the absolute configuration of **1** and **2** was assigned to be 3*R*.

On the other hand, the CD spectrum of kanzonol O (**3**) was different from the spectra of **1** and **2**. The uv spectrum of **3** showed the maximum at 292 nm, and the CD spectrum of **3** showed a positive Cotton effect at 277 nm and a negative Cotton effect at 298 nm (the $[\theta]$ at 288 nm was zero). These spectra suggested that these maxima on the CD spectrum were due to Davydov-split Cotton effect which was arisen by chiral exciton coupling between A and B ring chromophores.[12] Although, the absolute configuration could not be determined by the exciton chirality method because the directions of the electron transition moments of these rings could not be established.[13] The study of the stereochemistry of the compound (**3**) is now in progress.

EXPERIMENTAL

Melting points were measured on a Yazawa micro-melting point apparatus (hot-stage type) and are uncorrected. The following instruments were used; ^{1}H and ^{13}C nmr spectra; JEOL JNM-EX-400 NMR Spectrometer, uv spectra: Shimadzu UV-265 Spectrophotometer, mass spectra, JEOL JMS-D-300 (EI-ms), JMS-DX-303, and JMS-SX-102A (HR-ms) Mass Spectrometers, optical rotations, JASCO DIP-4 instrument, and CD spectra: JASCO J-720 CD Spectrometer. For tlc (silica gel) and preparative tlc (silica gel), Wakogel B-5FM and B-5F were used. The uv and CD spectra were measured in methanol unless noted otherwise.

Isolation of kanzonols M - Q (1 - 5) from the roots of Glycyrrhiza uralensis

The plant materials, extract, and fractions of column chromatography on silica gel were used as described in the previous paper.[4] 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 an eluent (column A), each fraction (eluent volume 500 ml) being monitored by tlc. The fraction 3 (3 g) was rechromatographed on silica gel (80 g) with hexane-acetone (100:0 → 0:100) as an eluent (each volume 100 ml, column B). The fraction 9 of the column B (eluted with hexane-acetone=23:2, 0.15 g) was purified by preparative tlc [hexane-acetone=4:1, multiple developments (×3), chloroform-hexane=1:1] to give kanzonol M (**1**, 3 mg). The fraction 6 of the column A (2 g) was rechromatographed on silica gel (90 g) with hexane-acetone (100:0 → 0:100) as an eluent (each volume 100 ml, column C). The fraction 8 of the column C (hexane-acetone=9:1, 0.08 g) was purified by preparative tlc (benzene-ether=5:1, benzene-acetone=8:1) to give kanzonol Q (**5**, dihydroxanthoxyletin, 0.1 mg). The fraction 9 of the column C (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 kanzonol J (**8**, 8 mg)[4] and kanzonol P (**2**, 4 mg). The fraction 4 of the column A (benzene, 1.8 g) was rechromatographed on silica gel (150 g) with hexane-acetone (100:0 → 0:100) as an eluent (each volume 100 ml, column D). The fraction 12 of the column D (hexane-acetone=7:3, 0.4 g) was purified by preparative tlc [hexane-ethyl acetate=4:1 (×2), benzene-ether=20:1] to give kanzonol N (**2**, 2 mg) and kanzonol O (**3**, 2 mg).

Isolation of kanzonol R (6) from Glycyrrhiza glabra

The plant materials, extract, and fractions of column chromatography on silica gel were used as described in the previous paper.[14] The licorice (400 g) was extracted at room temperature with hexane (1 l, three times) and then with benzene (1 l, x 3) (each 3 days). Evaporation of the hexane and benzene solutions to dryness yielded 1.1 g and 4.4 g of the residues, respectively. The benzene extract (4.4 g) was chromatographed on silica gel (100 g) successively with benzene (Fr. 1 -6), benzene-ether = 99:1 (Fr. 7 - 10), benzene-ether = 49:1 (Fr. 11 and 12) as an eluent (column A), each fraction (eluent volume 500 ml) being monitored by tlc. The fraction 9 (0.4 g) was rechromatographed on silica gel (10 g) with hexane-chloroform as an eluent (each 100 ml, column B). The fraction 10 of the column B (eluted with hexane-chloroform=2:3, 60 mg) was purified by preparative tlc (benzene-acetone=4:1, hexane-ethyl acetate=3:1, chloroform-acetone=14:1) to give kanzonol R (**6**, 4 mg).

Kanzonol M (1)

Compound (**1**) was obtained as pale yellow prisms from benzene-acetone, mp 109-116°C, $[\alpha]_D$ 0° (c = 0.02, MeOH). Uv λ_{max} (EtOH) nm (log ε): 296 (4.24), 345 (sh 2.91), (EtOH+$AlCl_3$): 314 (4.04),388 (sh 3.21), λ_{max} (MeOH) nm: 211, 225 (sh), 295, 340 (sh). EI-ms, m/z : 399 $[M+1]^+$ (7%), 398 $[M]^+$ (28), 381 (3), 343 (3), 218 (58), 217 (100), 205 (15), 181 (24), 163 (43), 162 (36). HR-ms, m/z 398.1718 $[M]^+$ ($C_{23}H_{26}O_6$ requires: 398.1729). ^1H Nmr: see Table1, ^{13}C Nmr: see Table 2. CD (c = 1.1×10^{-4} mol/l), $[\theta]_{250}$ 0, $[\theta]_{275}$ - 570, $[\theta]_{289}$ + 7000, $[\theta]_{304}$ 0, $[\theta]_{314}$ - 2700, $[\theta]_{347}$ 0, $[\theta]_{360}$ + 380.

Kanzonol N (2)

Compound (**2**) was obtained as an amorphous powder, $[\alpha]_D$ - 9° (c = 0.0094, MeOH). Uv λ_{max} nm (log ε): 216 (4.69), 291 (4.34), 350 (sh 3.56). EI-ms, m/z : 385 $[M+1]^+$ (9), 384 $[M]^+$ (35), 367 (12), 235 (44), 205 (9), 204 (1), 181 (6), 179 (100). HR-ms, m/z 384.1564 $[M]^+$ ($C_{22}H_{24}O_6$ requires: 384.1573), 204.1143 [2a] ($C_{13}H_{16}O_2$ requires 204.1150). ^1H Nmr: see Table1, ^{13}C Nmr: see Table 2. CD (c = 9.0×10^{-5} mol/l), $[\theta]_{252}$ 0, $[\theta]_{288}$ + 6400, $[\theta]_{300}$ 0, $[\theta]_{310}$ - 4700, $[\theta]_{348}$ 0, $[\theta]_{358}$ + 840, $[\theta]_{380}$ 0.

Kanzonol O (3)

Compound (**3**) was obtained as an amorphous powder, $[\alpha]_D$ - 10° (c = 0.010, MeOH). Uv λ_{max} nm (log ε): 225 (4.97), 292 (4.75), 342 (sh 3.92), (MeOH+$AlCl_3$): 278 (sh 4.41), 314 (4.83), 391 (3.88). EI-ms, m/z : 383 $[M+1]^+$ (10), 382 $[M]^+$ (39), 367 (92), 221 (21), 202 (25), 201 (33), 187 (100), 179 (6). HR-ms, m/z 382.1397 $[M]^+$ ($C_{22}H_{22}O_6$ requires: 382.1416). ^1H Nmr: see Table1, ^{13}C Nmr: see Table 2. CD (c = 2.6×10^{-5} mol/l), $[\theta]_{240}$ 0, $[\theta]_{277}$ + 620, $[\theta]_{288}$ 0, $[\theta]_{298}$ - 800, $[\theta]_{344}$ 0, $[\theta]_{355}$ + 40.

Kanzonol P (4)

Compound (**4**) was obtained as an amorphous powder, $[\alpha]_D$ - 58° (c = 0.0114, MeOH). Uv λ_{max} nm (log ε): 284 (4.18). EI-ms, m/z : 367 $[M+1]^+$ (25), 368 $[M]^+$ (100), 353 (47). HR-ms, m/z 368.1573 $[M]^+$ ($C_{22}H_{24}O_5$ requires: 368.1624). ^{1}H Nmr (400 MHz, acetone-d_6): δ 1.64, 1.76 (each 3H, br d, J = 1 Hz, Me), 3.24 (1H, br dd, J = 7 and 14 Hz, H-1'), 3.32 (1H, br dd, J = 7 and 14 Hz, H-1'), 3.42 (1H, m, H-6a), 3.56 (1H, t, J = 11 Hz, H-6), 3.80, 3.91 (each 3H, s, OMe), 4.20 (1H, ddd, J = 0.7, 5, and 11 Hz, H-6),5.17 (1H, br t, J = 7 Hz, H-2'), 5.60 (1H, br d, J = 7 Hz, H-11a), 6.30 (1H, s, H-4), 6.30 (1H, d, J = 2 Hz, H-10), 6.36 (1H, dd, J = 2 and 8 Hz, H-8), 7.14 (1H, d, J = 8 Hz, H-7), 8.30 (1H, s, OH). ^{13}C Nmr (100 MHz, acetone-d_6): δ 18.18 (C-4'), 23.57 (C-1'), 26.09 (C-5'), 40.12 (C-6a), 56.29 (OMe), 63.41 (OMe), 67.37 (C-6), 76.74 (C-11a), 96.84 (C-4), 98.86 (C-10), 108.52 (C-8), 108.17 (C-11b), 117.60 (C-2), 119.46 (C-6b), 124.83 (C-2'), 126.07 (C-7), 131.31 (C-3'), 156.70 (C-4a), 159.83 (C-9), 160.76 (C-10a), 160.94 (C-1), 162.06 (C-3).

Kanzonol Q (5, Dihydroxanthoxyletin[6] *)*

Compound (**5**) was obtained as pale yellow needles from benzene, mp 108.5 - 114 °C . Uv λ_{max} nm (log ε): 258 (4.87), 287 (5.11), 328 (5.27). EI-ms, m/z : 261 $[M+1]^+$ (8), 260 $[M]^+$ (40), 245 (6), 205 (100), 147 (13).. HR-ms, m/z 260.1076 $[M]^+$ ($C_{15}H_{16}O_4$ requires: 260.1127). ^{1}H Nmr (400 MHz, $CDCl_3$): δ 1.37 (6H, s Me), 1.83 (2H, t, J = 7 Hz, H_2-4'), 2.79 (2H,t, J = 7 Hz, H_2-3'), 3.86 (3H, s, OMe), 6.19 (1H, d, J = 9.5 Hz, H-3), 7.85 (1H, dd, J = 0.5 and 9.5 Hz, H-4), 6.56 (1H, br s, H-8). ^{13}C Nmr (100 MHz, acetone-d_6): δ 17.62 (C-4'), 26.94 (C-5' and C-6'), 32.39 (C-3'), 62.50 (OMe), 76.57 (C-2'), 100.96 (C-8), 112.76 (C-3), 139.60 (C-4). The ^{1}H nmr data of the natural compound was agreement with that of the synthetic compound (**5**) reported by Lassak and Pinhey.[15]

Kanzonol R (6)

Compound (**6**) was obtained as a crystalline granule from benzene-acetone, mp 69 - 72°C, $[\alpha]_D$ - 25° (c = 0.04, MeOH). Uv λ_{max} nm (log ε): 214 (4.76), 272 (3.91), 280 (sh 3.87), 295 (sh 3.65). EI-ms, m/z : 371 $[M+1]^+$ (15), 370 $[M]^+$ (55), 218 (100), 175 (23), 163 (63), 153 (65). HR-ms, m/z 370.1797 $[M]^+$ ($C_{22}H_{26}O_5$ requires: 370.1780). ^{1}H Nmr: see Table 1, ^{13}C Nmr: see Table 2. CD (c = 1.2 × 10^{-4} mol/l), $[\theta]_{247}$ 0, $[\theta]_{256}$ + 1500, $[\theta]_{273}$ +1200, $[\theta]_{278}$ + 1200, $[\theta]_{285}$ 0, $[\theta]_{294}$ - 940, $[\theta]_{315}$ - 900.

Formation of kanzonol M (1) from kanzonol R (6)

A mixture of **6** (2.2 mg, 5.9 μmol), dry aluminum chloride (1.0 mg, 7.5 μmol), ethyl orthoformate (0.1 ml, 676 μmol), and dry benzene (1.0 ml) was stirred at room temperature for 30 min after which 5% hydrochloric acid (3 ml) was added to it. The products were extracted with ethyl ether and washed with water, dried and evaporated to dryness. The residue was purified by preparative tlc (n-hexane-acetone=3:1, × 2) to give 8-formylkanzonol R

(**1**, 0.04 mg, 1.7%). The other formylated compounds were not obtained as pure form. The product (**1**) was identified as kanzonol M (**1**) by ^1H nmr and mass spectra and tlc analysis. **1**: CD ($c = 5.0 \times 10^{-5}$ mol/l), $[\theta]_{274}$ 0, $[\theta]_{290}$ +5400, $[\theta]_{304}$ 0, $[\theta]_{315}$ -2800, $[\theta]_{350}$ 0, $[\theta]_{359}$ +200.

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