Pergamon

PII: S0031-9422(97)00564-5

Phytochemistry, Vol. 47, No. 2, pp. 273–280, 1998

Printed in Great Britain
0031-9422/98 $19.00+0.00

ISOPRENYLATED FLAVANONES FROM *MORUS CATHAYANA**

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(*Received* 17 *April* 1997)

Key Word Index—*Morus cathayana*; Moraceae; mulberry tree; root bark; prenylated flavanone; sanggenols F–K.

Abstract—Three new 2-prenyl-3-hydroxyflavanones, sanggenols F, G and I, having an ether linkage between C-3 and C-2′ and a prenyl (geranyl) side chain, were isolated along with sanggenol J, regarded as a Diels-Alder type adduct between dehydrosanggenol F (diene) and a chalcone (dienophile) from the root bark of *Morus cathayana*. A new 2-farnesyl-3-hydroxyflavanone, sanggenol H, with an ether linkage between C-3 and C-2′, and a new 3-hydroxyflavanone, sanggenol K, were also isolated from the bark. Their structures were elucidated by spectroscopic methods. © 1997 Elsevier Science Ltd

INTRODUCTION

The Mulberry tree is an economically important plant because its leaves are indispensable food for silkworms. Its root bark, "sang-bai-pi", is used in traditional Chinese medicine as an antiphlogistic, diuretic and expectorant, and in traditional Sino–Japanese medicine in Japan. The root bark of the Chinese mulberry tree is used in Japan but its origin in Japanese markets is uncertain. Many phenolic compounds have been isolated from *Morus* species, e.g., the antihypertensive compounds kuwanons G and H which are also bombesin receptor antagonists [1–3]. However, the phenolic constituents of the Chinese i.e., sanggenons A–E§, herb are quite different from those of identified *Morus* species (*M. alba*, *M. bombycis*, *M. lhou*, *M. australis*) [1]. Previously sanggenons A, C, M and O were isolated from *M. mongolica* collected in Liaoning Province of China [4]. Hence 'Sang-bai-pi' in Japanese markets was considered as *M. mongolica* [1]. A HPLC chromatogram of the herb resembles most closely that of *M. mongolica* collected in China (Beijing, Liaoning Province, Shandong Province), however one of the main phenolic compounds of 'Sag-bai-pi', sanggenon C (an antihypertensive compound), was not detected in *M. mongolica* [5]. Recently, we examined one of the Chinese mulberry trees, *Morus cathayana*, and isolated sanggenons A (**7**), C (**8**), D (**9**), L (**10**) and M (**11**) together with six new prenylated flavonoids, sanggenols A–E, and mulberrofuran V from the root bark of the plant [6]. These sanggenons were not detected in Indonesian *M. cathayana* by HPLC analysis [5]. More recently the structures of the sanggenons were revised to **7**–**11** as shown in Fig. 1 [7]. On further examination of the root bark of *M. cathayana* collected in China, we isolated five new flavonoids, sanggenols F (**1**), G (**2**), H (**3**), I (**4**) and J (**5**), having prenyl (geranyl) groups and same skeleton as sanggenons A–E and soroceins D–G isolated from *Sorocea bonplandii* and *S. ilicifolia* [8, 9] together with a new 2*R*,3*R*-3-hydroxyflavanone with prenyl and geranyl groups, sanggenol K (**6**), and a known flavonoid, sorocein F (**12**).

RESULTS AND DISCUSSION

Sanggenol F (**1**), $C_{25}H_{26}O_7$, $[\alpha]_D+82°$, showed a positive reaction to the methanolic ferric chloride test on a TLC plate. Its UV spectrum exhibited maxima at 206, 235 (sh), 290 (sh), 307 and 350 (sh) and was similar to that of sorocein F (**12**) [9]. The ^{1}H NMR spectrum of **1** showed the signals of an aromatic proton (A ring), AXY type aromatic protons (B ring), three hydroxyl protons, a hydrogen-bonded hydroxyl proton and the protons of two prenyl groups. The chemical shifts and coupling constants of methylene protons of one of the prenyl groups, δ 2.76 (*br dd*, $J = 6$ and 15 Hz) and 3.11 (*br dd*, $J = 9$ and 15 Hz), indicated that this prenyl group was attached to position 2 of a flavanone. This was also shown by the NOE between C-6′-H and one of the methylene protons at δ 3.11 (4%). Hence, the position of the ali-

* Part 29 in the series 'Constituents of the Moraceae Plants' and Part 2 in the series 'Components of the Root Bark of *Morus cathayana*'. For part 28 see reference 6.

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§ Chinese term 'Sang-gen' means root of mulberry tree.

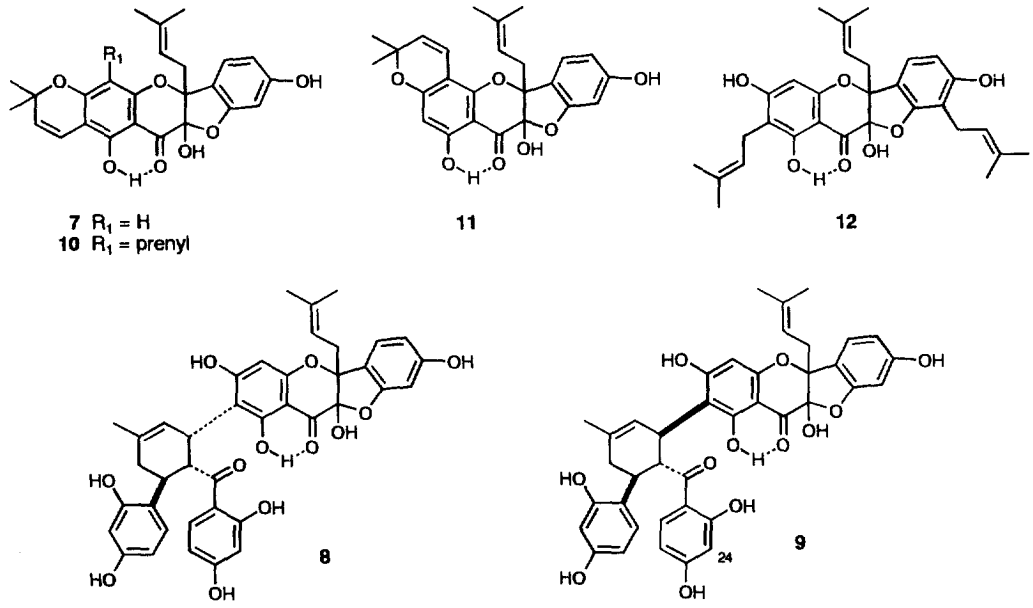


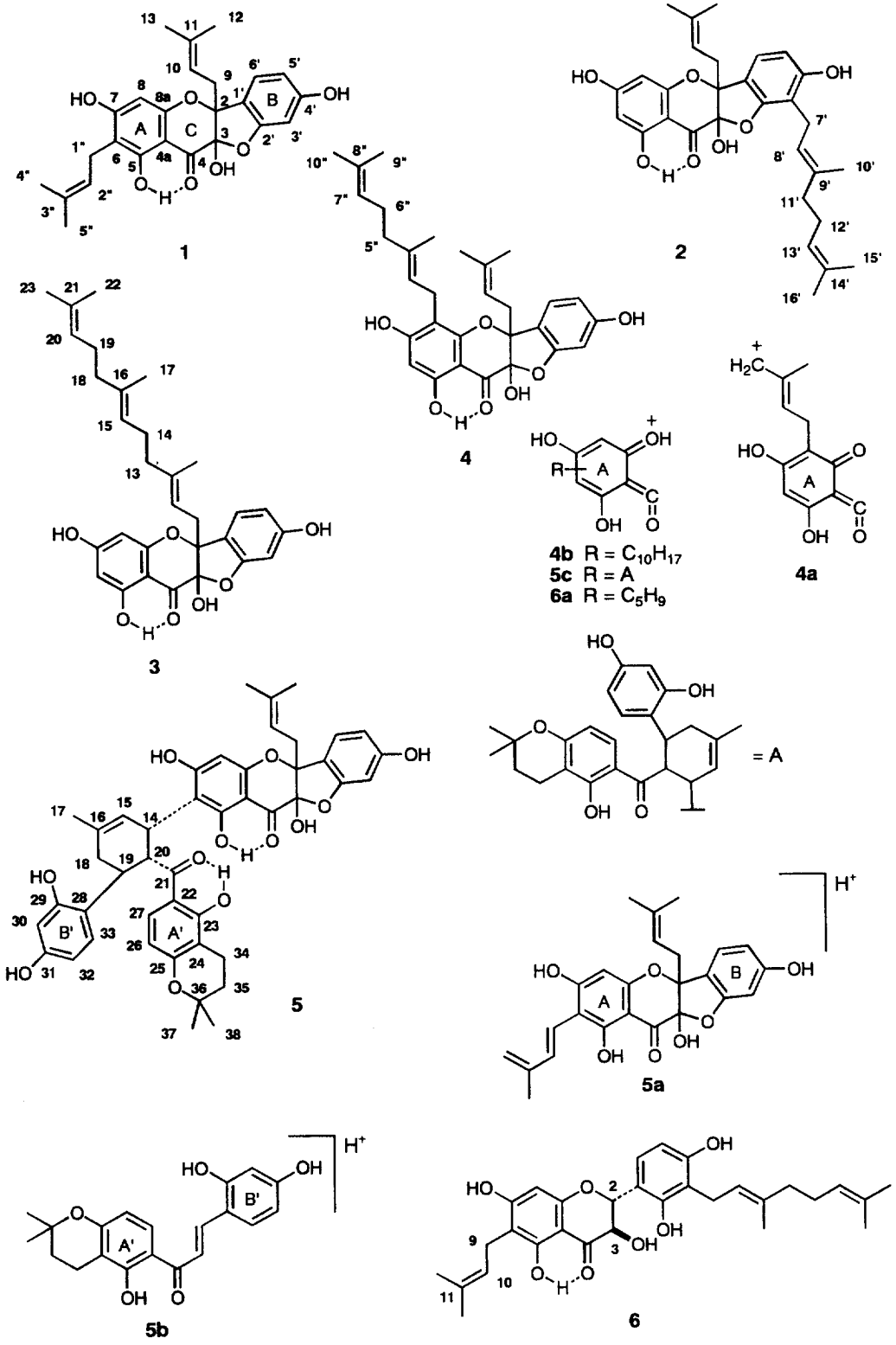
Fig. 1. Structures of known flavonoids isolated from *M. cathayana*.

phatic hydroxyl group was at C-3. The presence of a 3-hydroxyl group was also shown by the observation of three cross-peaks between the hydroxyl proton (δ 7.08) and C-2 (quaternary carbon), C-3 (hemiketal carbon) and C-4 (carbonyl carbon) in the HMBC spectrum of **1**. The other prenyl group was located at the 6-position because cross-peaks between the methylene proton signal at δ 3.21 (2H, *br d*, $J = 7$ Hz) and C-5, C-6 and C-7 were observed in the spectrum of **1** (Table 1 and Fig. 2). Thus, the structure of sanggenol F is 3′-desprenylsorocein F (**1**).

Sanggenol G (**2**), $C_{30}H_{34}O_7$, $[\alpha]_D + 53°$, showed a positive reaction to the methanolic ferric chloride test on a TLC plate. Its ^{1}H NMR spectrum showed the signals of AB type aromatic protons (A ring), *ortho*-coupled aromatic protons (AX type, B ring), three hydroxyl protons, a hydrogen-bonded hydroxyl proton and protons of a prenyl group and a geranyl group. All carbon and proton signals were assigned by comparison with the corresponding signals of similar compounds, such as sanggenon A (**7**), sorocein F (**12**), etc. [1, 8, 9], and the HMBC spectrum of **2** (Table 1). Three cross-peaks between the benzylic methylene protons of the geranyl group, δ 3.26 (2H, *br d*, $J = 7$ Hz), and C-2′, C-3′ and C-4′ in the HMBC spectrum (Table 1 and Fig. 2) placed this group at C-3′. The presence of 2-prenyl and 3-hydroxyl groups was also confirmed by the HMBC spectrum as described for **1**. Thus, the structure of sanggenol G is elucidated as **2** except for the stereochemistry at C-2 and C-3.

Sanggenol H (**3**), $C_{30}H_{34}O_7$, $[\alpha]_D - 46°$, showed a positive reaction to the methanolic ferric chloride test on a TLC plate. Its UV spectrum was similar to that of **2**. The ^{1}H NMR spectrum of **3** showed the signals of *meta*-coupled aromatic protons (A ring), AXY type aromatic protons (B ring), three hydroxyl protons, a hydrogen-bonded hydroxyl proton and the protons of a farnesyl group. The position of the farnesyl group was deduced to be the 2-position from the HMBC and NOESY spectra of **3** as follows: cross-peaks between the methylene proton(s) of C-9 [δ 2.80 (*br dd*, $J = 7$ and 15 Hz), 3.19 (*br dd*, $J = 9$ and 15 Hz)] and C-2, C-3 and C-1′ were observed in the HMBC spectrum (Table 2 and Fig. 2) and a cross-peak between one of the methylene protons (δ 3.19, H-9) and H-6′ along with a NOE between H-8 and one of methyl groups (δ 1.65, Me-11) was observed in the NOESY spectrum. The presence of the 3-hydroxyl group was shown by the observation of three cross-peaks between the hydroxyl proton (δ 7.08) and C-2, C-3 and C-4 in the HMBC spectrum. Thus, the structure of sanggenol H is determined as **3** except for the stereochemistry at C-2 and C-3. This is the second flavonoid having a farnesyl group to be isolated from natural sources [10].

Sanggenol I (**4**), $C_{30}H_{34}O_7$, was isolated as a minor flavonoid. Its UV spectrum resembled to that of **1**. The ^{1}H NMR spectrum of **4** showed the signals of an aromatic proton (A ring), AXY type aromatic protons (B ring), a hydrogen-bonded hydroxyl proton and the protons of a prenyl group and a geranyl group. The above data indicated that the compound was an isomer of sanggenol G (**2**). The EI mass spectrum of **4** gave characteristic fragment ions at *m/z* 219 (**4a**) and 289 (**4b**) indicating the presence of geranyl group on the A ring. The existence of a 2-prenyl group was deduced from the ^{1}H-^{1}H COSY spectrum of **4**: The C-3″ methyl protons of the geranyl group, characterized by a cross-peak between the signal and the H_2-5″, were correlated to the benzylic methylene protons at δ 3.16 and 3.24 (each, *br dd*, $J = 7$ and 14 Hz) but not to the C-9 methylene protons [δ 2.85 (*br dd*, $J = 7$ and 15



Hz), 3.06 (*br dd*, $J = 9$ and 15 Hz)]. The protons of C-9 were correlated to the methyl group(s) at δ 1.57 and/or 1.58. The remaining methyl signals at δ 1.52 and 1.59 were correlated with H-7″ and the signal at δ 1.59 was correlated to H_2-6″. Thus, the geranyl group was located on the A ring and the prenyl group was at the 2-position. Recently, we reported a new method of structure determination of 6- and 8-prenyl (geranyl)flavonoids based on the chemical shift of the 5-OH group. The method predicts the chemical shifts

Table 1. ^{13}C NMR data of sanggenols F (**1**) and G (**2**) in Me_2CO-d_6

C	1	Long-range correlation	2	Long-range correlation
2	91.8	3-OH, H_2-9, H-6′	92.7	3-OH, H_2-9, H-6′
3	102.6	3-OH, H-9 (δ 3.11)	102.1	3-OH, H-9 (δ 3.12)
4	188.3	3-OH	188.6	H-8
4a	100.2	5-OH, H-8	100.2	5-OH, H-6, H-8
5	162.6	H_2-1″, 5-OH	165.8	5-OH, H-6
6	109.1	H_2-1″, H-8, 5-OH	96.7	5-OH, H-8
7	166.7	H_2-1″, H-8	169.0	H-6, H-8
8	95.3	—	95.6	H-6
8a	161.5	H-8	163.9	H-8
9	32.0	H-10	32.2	H-10
10	118.7	H_2-9, H_3-12, H_3-13	118.7	H_2-9, H_3-12, H_3-13
11	136.5	H_2-9, H_3-12, H_3-13	136.6	H_2-9, H_3-12, H_3-13
12	18.1	H-10, H_3-13 (δ 1.50)	18.1	H-10, H_3-13
13	25.8*	H-10, H_3-12 (δ 1.60)	25.9	H-10, H_3-12
1′	121.4	H-3′, H-5′, H-9 (δ 3.11)	121.0	H-5′, H_2-9
2′	161.3	H-3′, H-6′	159.3	H-6′, H_2-7′
3′	99.5	H-5′	113.0	H-5′, H_2-7′, H-8′
4′	161.2	H-3′, H-5′, H-6′	158.5	H-5′, H-6′, H_2-7′
5′	109.7	H-3′	109.5	—
6′	125.6	—	122.4	—
7′			23.2	H-8′
8′			122.8	H_2-7′, H_2-11′, H_3-10′
9′			135.6	H_2-7′, H_2-11′, H_2-12′, H_3-10′
10′			16.2	H-8′, H_2-11′
11′			40.4	H-8′, H_2-12′, H_3-10′
12′			27.3	H-13′, H_2-11′
13′			125.1	H_2-11′, H_2-12′, H_3-15′, H_3-16′
14′			131.6	H_2-11′, H_3-15′, H_3-16′
15′			17.6	H-13′, H_3-16′
16′			25.7	H-13′, H_3-15′
1″	21.5	H-2″		
2″	123.3	H_2-1″, H_3-4″, H_3-5″		
3″	131.4	H_2-1″, H_3-4″, H_3-5″		
4″	17.8	H-2″, H_3-5″ (δ 1.61)		
5″	25.8*	H-2″, H_3-4″ (δ 1.72)		

* The signals were observed at δ 25.79 and 25.84.

of the flavonoids by calculation with a model compound and the substituent parameters [11, 12]. The calculated value for the 8-geranylated flavanone (**4**) was δ 11.58–11.61 and the 6-geranyl isomer (**4′**) was δ 11.92–11.94; the model compound used was sanggenol H (**3**, δ 11.64 in acetone-d_6), and the parameters of geranylation at C-6 and C-8 were +0.28–+0.30 ppm and −0.03–−0.06 ppm, respectively. The 5-OH signal of sanggenol I (δ 11.61) was in agreement with the calculated value for 8-geranylflavanone (**4**) but not 6-geranyl isomer (**4′**). Thus, the structure of sanggenol I was characterized as **4**, except for the stereochemistry at C-2 and C-3.

Sanggenol J (**5**), $[\alpha]_D$ +98°, molecular formula $C_{45}H_{44}O_{12}$ (FAB MS and, ^1H and ^{13}C NMR) was isolated as an amorphous powder. Its UV spectrum was similar to those of sanggenons E (24-prenylsanggenon D) and P (24-prenylsanggenon C, sorocein H) regarded as naturally occurring Diels–Alder type adducts of dehydrosanggenol F (diene, dehydroprenylflavanone) and a prenylchalcone (dienophile) [8, 13]. The FAB mass spectrum gave characteristic fragment ion peaks of a Diels–Alder type adduct at *m/z* 437 (**5a**) and 341 (**5b**) along with an ion peak at *m/z* 559 (**5c**). The ^1H NMR spectrum showed the signals of an aromatic proton (A ring), two sets of AXY type aromatic protons (B and B′ rings), *ortho*-coupled aromatic protons (A′ ring), five hydroxyl protons, two hydrogen-bonded hydroxyl protons, the protons of a prenyl group, a 3,4-dihydro-2,2-dimethylpyran ring and a trisubstituted 1-methylcyclohexene ring. The presence of 2-prenyl and 3-hydroxyl groups were deduced from the HMBC and NOESY spectra of **5** as described for **1** and **3** (Table 2 and Fig. 2). In the HMBC spectrum, the 5-OH signal correlated with the signal at δ 109.1 (C-6) indicating the presence of a substituent at C-6 by its chemical shift [1, 13]. The attachment of the methylcyclohexene ring at C-6 was also confirmed by the NOESY spectrum: A cross-peak between 5-OH (δ 12.94) and H-14 was observed as well as between 7-OH (δ 9.09) and H-15. A cross-peak between H-33 and C-19 was

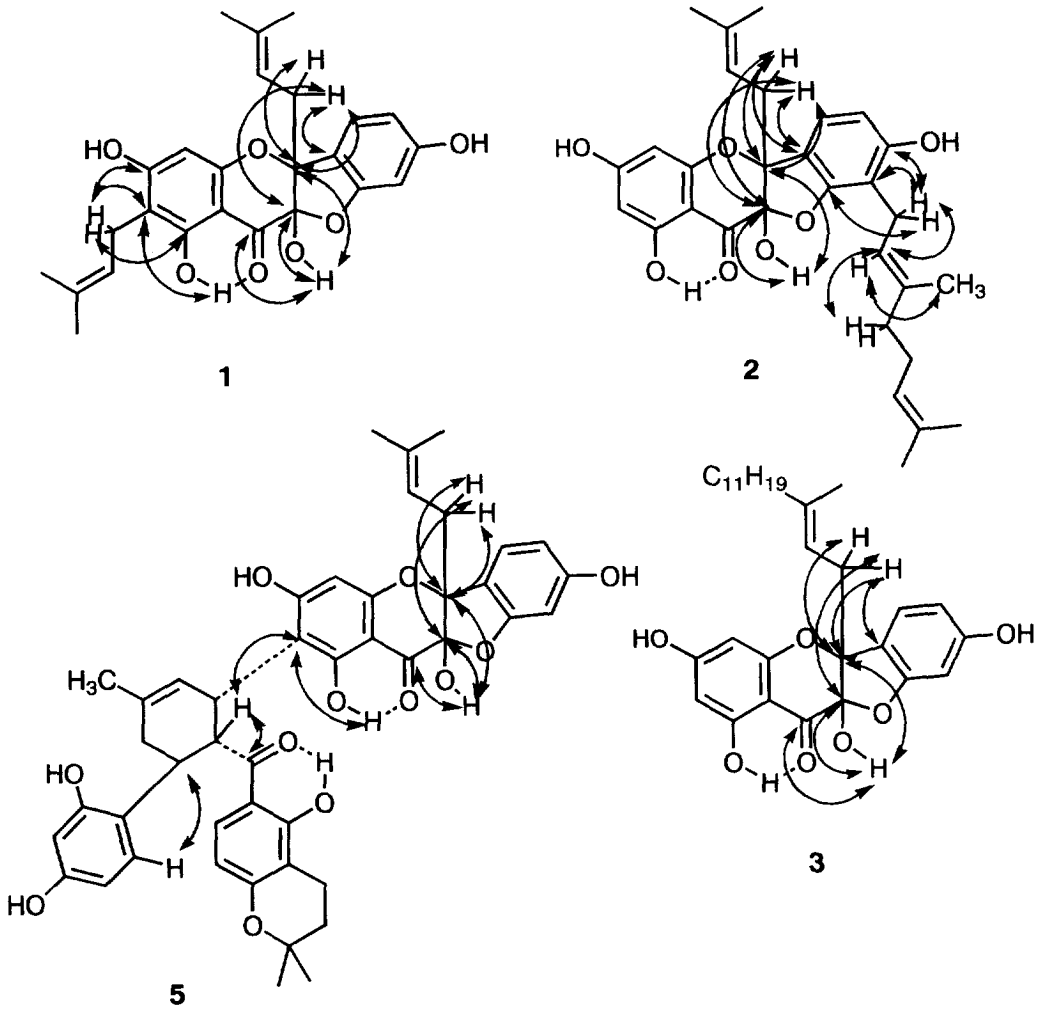


Fig. 2. Long-range coupling correlations in HMBC spectra based on the structure determinations of **1**–**3** and **5**.

observed as well as between H-20 and C-21 (δ 209.1) in the HMBC spectrum. Thus, the B′ ring was located at C-19 and the benzoyl group (A′ ring) was at C-20. The 3,4-dihydro-2,2-dimethylpyran ring was located on the A′ ring based on the observation of three cross-peaks between H_2-34 and C-23, H_2-35 and C-24, H_2-34 and C-25, respectively, in the HMBC spectrum and a NOE between H_2-34 and 23-OH in the NOESY spectrum. The coupling constants of the proton signals of the methylcyclohexene ring ($J_{14-20} = {}_{19-20} = J_{19-18A} = J_{19-18B} = 5.5$ Hz, $J_{18A-18B} = 16$ Hz) resembled to those of sanggenons C (**8**) and P but not sanggenons D (**9**) and E [13]. Thus, the relative configuration of the three substituents on the methylcyclohexene ring was the same as sanggenons C (**8**) and P. The CD spectrum of **5** was similar to that of **8**. Hence, the absolute configuration of **5** was the same as that of **8**, i.e., 14*S*,19*S*,20*R*-sanggenon [1], but the stereochemistry at C-2 and C-3 is still unknown as is the case with the other sanggenons. Thus, the structure of sanggenol J was **5**. The study of the stereochemistry at C-2 and C-3 of sanggenon type flavanones, 2-prenyl-3-hydroxyflavanones with an ether linkage between C-3 and C-2′, is now progress.

Sanggenol K (**6**), $C_{30}H_{36}O_7$ (*m/z* 508 $[M]^+$), $[\alpha]_D + 80°$, was isolated as a minor flavonoid. The UV spectrum exhibited maxima at 208, 230 (sh), 295 and 340 (sh) nm and was similar to that of prenylated (geranylated) 3-hydroxyflavanones, such as sanggenols C (2*R*,3*R*-3′-geranyl-8-prenyl-3,4′,5,7-tetrahydroxyflavanone) and E (2*R*,3*R*-5′,8-diprenyl-3′-geranyl-2′,3,4′,5,7-pentahydroxyflavone), etc. [6]. The ^{1}H NMR spectrum of **6** showed the signals of the C ring [δ 4.26 (*br*, 3-OH), 4.72 (*br d*, $J = 12$ Hz, C-3-H), 5.45 (*d*, $J = 12$ Hz, C-2-H)], an aromatic proton (A ring), *ortho*-coupled aromatic protons (AX type, B ring), a hydrogen-bonded hydroxyl proton, the protons of a prenyl group and a geranyl group. The EI mass spectrum of **6** gave characteristic fragment ion at *m/z* 221 (**6a**). The data indicated that the compound was an isomer of sanggenol D (2*R*,3*R*-3′geranyl-5′-prenyl-2′,3,4′,5,7-pentahydroxyflavone) which has the prenyl group located at the A ring and the geranyl group at the B ring. This was confirmed by the NOESY spec-

Table 2. ^{13}C NMR data of sanggenols H (**3**) and J (**5**)

C	3	Long-range correlation	5	Long-range correlation
2	92.3	3-OH, H-6′, H_2-9	91.9	3-OH, H_2-9, H-6′
3	102.4	3-OH, H-9 (δ 3.19)	102.4	3-OH, H-9 (δ 3.08)
4	188.2	3-OH	188.3	3-OH, H-8
4a	100.1	H-6, H-8, 5-OH	99.9	5-OH, H-8
5	165.8	H-6, 5-OH	163.8	5-OH
6	96.8	H-8, 5-OH	109.1	5-OH, H-8, H-20
7	169.1	H-6, H-8	167.6	H-8
8	95.6	H-6	96.6	7-OH
8a	164.1	H-8	161.9*	H-8
9	32.0	H-10	32.1	—
10	118.2	H_2-9, H_3-12, H_2-14	118.5	H_2-9, H_3-12, H_3-13
11	140.7	H_2-9, H_3-12, H_2-13, H_2-14	136.7	H_2-9, H_3-12, H_3-13
12	16.6	H-10, H_2-13	18.1	H-10, H_3-13
13	40.7	H-10, H_3-12, H_2-14	25.9	H-10, H_3-12
14	27.1	H_2-13, H-15	32.3	H-19, H-20
15	125.2	H_2-13, H_2-14	122.8	H-20, H_3-17
16	135.6	H_3-17, H_2-18, H_2-19	135.0	H-19, H_3-17
17	16.0	H_2-18	23.7	H-15
18	40.4	H-15, H_3-17, H_2-19, H-20	33.4 (33.8)†	H_3-17 (H-19, H-20, H_3-17)
19	27.4	H_2-18, H-20	35.8	H-20, H-33
20	125.0	H_2-18, H_2-19, H_3-22, H_3-23	47.9	H-15, H-19
21	131.6	H_2-19, H_3-22, H_3-23	209.1	H-20, H-27
22	17.7	H_3-23 (δ 1.64), H-20	113.1	H-26, 23-OH
23	25.8	H_3-22 (δ 1.57), H-20	164.1	H-27, H_2-34, 23-OH
1′	121.4	H-3′, H-5′, H-9 (δ 3.19)	121.3	H-3′, H-5′
2′	161.3*	4′-OH	161.1	H-6′
3′	99.5	H-5′, H-6′, 4′-OH	99.4	4′-OH, H-5′
4′	161.3*	4′-OH	161.1	H-3′, H-6′, 4′-OH
5′	109.8	H-3′, 4′-OH	109.7	H-3′, 4′-OH
6′	125.5	—	125.6	—
24			109.6	H_2-34, H_2-35, H-26, 23-OH
25			161.9*	H-26, H-27, H_2-34
26			109.7	—
27			131.3	29-OH
29			156.4	H-19, H-30, H-33
30			103.7	H-32, 31-OH
31			157.8	H-30, H-33, H-32, 31-OH
32			107.6	31-OH
33			128.9	H-19
34			16.8	H_2-35
35			32.2	H_2-34, H_3-37, H_3-38
36			76.8	H_2-34, H_2-35, H_3-37, H_3-38
37, 38			26.8	H_3-37 (H_3-38)

* These signals of C-2′ and C-4′ of **3** were observed at δ 161.26 and 161.32 and C-8a and C-25 were observed at δ 161.89 and 161.87 of **5**.

† The signal in parenthesis was observed as a cross-peak in the HMBC spectrum. This signal may be due to a conformational isomer.

trum of **6**. Thus the benzylic methylene protons at ring A (δ 3.25, H_2-9) were correlated to the olefinic proton at δ 5.22 (H-10) and H-10 was correlated to the methyl protons of the prenyl group (δ 1.63, Me-11). The benzylic methylene protons at the 3′-position (δ 3.43, H_2-7′) was correlated to the methyl protons of the geranyl group (δ 1.77 correlated to the methylene protons of C-11′).* The calculated chemical shift of the 5-OH of the 6-prenylflavanone **6** was δ 12.00–12.03 and that of the 8-prenyl isomer δ 11.66–11.70; the model compound used was 3′-geranyl-2′,4′,5,7-tetrahydroxyflavanone (sanggenol A, δ 12.19 in acetone-d_6) and the parameters of hydroxylation at C-3 of the flavanone were −0.46–−0.47 ppm in acetone-d_6, and of prenylation at C-6 and C-8 were +0.28–+0.30 ppm and −0.03–−0.06 ppm, respectively [6,

* The benzylic methylene protons of the prenyl (geranyl) group on ring A of flavanones appear between δ 3.18–3.33 in acetone-d_6 and those of ring B (3′-prenyl group of 2′,4′-dihydroxyflavanones) appear between δ 3.42–3.48 [7, 15].

12]. The chemical shift of the 5-OH group of **6** (δ 11.96) was close to the calculated value of 5-OH for the 6-prenyl isomer but not the 8-prenyl isomer. Hence, the structure of sanggenol K was postulated to be 3′-geranyl-6-prenyl-2′,3,4′,5,7-pentahydroxyflavanone. The absolute configuration of **6** was assigned to be 2*R*,3*R* by its CD spectrum, in which the negative and positive Cotton effects were exhibited at 296 and 327 nm, respectively [14]. From the above results, the structure of sanggenol K was elucidated as **6**.

EXPERIMENTAL

General procedures and instruments used were as described in our previous paper [6].

Isolation of flavonoids. The plant materials, their identification, extraction, and fractionation using CC on silica gel were as reported in the previous paper [6]. The flavonoids reported here were isolated from frs collected from column A [6]. Frs 20–21 eluted with C_6H_6–Me_2CO (99:1) were purified by prep. TLC (silica gel) using $CHCl_3$–Et_2O (4:1), C_6H_6–MeOH (10:1), then C_6H_6–EtOAc (3:1) to give sorocein F (**12**, 4 mg). Frs 22–24 were purified by prep. TLC in C_6H_6–Me_2CO (10:1), C_6H_6–MeOH (10:1), $CHCl_3$–MeOH (10:1), then *n*-hexane–Me_2CO (1:1) to give sanggenol G (**2**, 4 mg). Sanggenol K (**6**, 0.3 mg) was isolated from frs 27–30 by prep. TLC in *n*-hexane–Et_2O (1:2), C_6H_6–MeOH (10:1), then by HPLC; Senshu Pak SSC-silica 4251-N, 4 × 25 cm, *n*-hexane–EtOAc = 4:1. Frs 37–41 eluted with C_6H_6–Me_2CO (49:1) were purified by prep. TLC using C_6H_6–Me_2CO (4:1), $CHCl_3$–MeOH (20:1), *n*-hexane–EtOAc (1:1), *n*-hexane–Me_2CO (4:1) to give sanggenol F (**1**, 3 mg). Sanggenols H (**3**, 4 mg) and I (**4**, 0.5 mg) were isolated from frs 49–54 eluted by C_6H_6–Me_2CO (97:3) by prep. TLC in *n*-hexane–EtOAc (4:1), *n*-hexane–Me_2CO (7:1), then by the HPLC. Frs 75–83 eluted with C_6H_6–Me_2CO (93:7, 470 mg) were rechromatographed on silica gel CC eluted with *n*-hexane–EtOAc (3:2) to give frs 1′–20′: each fr. 300 ml (column B). Frs 5′–6′ were purified by prep. TLC using *n*-hexane–EtOAc (1:1) to give sanggenol J (**5**, 9 mg).

Sanggenol F (**1**). Amorphous powder, $[\alpha]_D^{24}+82°$ (*c* 0.135). $FeCl_3$ test: olive. UV λ_{max}^{MeOH} nm (log ε): 206 (4.56), 235 (sh 4.13), 290 (sh 4.02), 307 (4.10), 350 (sh 3.41); EI-MS (probe) 70 eV *m/z* (rel. int.): 439 $[M+H]^+$ (7), 438 $[M]^+$ (25), 377 (6), 370 $[M-68]^+$ (11), 369 (10), 313 (15), 310 (12), 221 (98), 217 (10), 213 (11), 188 (10), 165 (100), 162 (32); HR-MS *m/z*: 438.1668 $[M]^+$ ($C_{25}H_{26}O_7$ requires: 438.1678); ^1H NMR (400 MHz, Me_2CO-d_6): δ 1.50, 1.60 (each 3H, *br s*, 11-Me), 1.61, 1.72 (each 3H, *br d*, *J* = 1 Hz, 3″-Me), 2.76 (1H, *br dd*, *J* = 6 and 15 Hz, H-9), 3.11 (1H, *br dd*, *J* = 9 and 15 Hz, H-9), 3.21 (2H, *br d*, *J* = 7 Hz, H_2-1″), 5.17 (1H, *tm*, *J* = 7 Hz, H-10), 5.22 (1H, *tm*, *J* = 7 Hz, H-2″), 5.91 (1H, *s*, H-8), 6.38 (1H, *d*, *J* = 2 Hz, H-3′), 6.50 (1H, *dd*, *J* = 2 and 8 Hz, H-5′), 7.08 (1H, *br s*, 3-OH), 7.34 (1H, *d*, *J* = 8 Hz, H-6′), 8.56 (1H, *br s*, 4′-OH), 9.58 (1H, *br*, 7-OH), 11.90 (1H, *s*, 5-OH); CD (*c* 27 ppm, MeOH): $[\theta]_{218}+17\,000$, $[\theta]_{235}$ 0, $[\theta]_{240}-4400$, $[\theta]_{245}$ 0, $[\theta]_{249}+4300$, $[\theta]_{264}$ 0, $[\theta]_{273}-4000$, $[\theta]_{281}$ 0, $[\theta]_{291}+7200$, $[\theta]_{315}+2300$, $[\theta]_{338}+4000$, $[\theta]_{450}$ 0.

Sanggenol G (**2**). Amorphous powder, $[\alpha]_D^{24}+53°$ (*c* 0.29, MeOH). $FeCl_3$ test: light brown. UV λ_{max}^{MeOH} nm (log ε): 210 (4.57), 230 (sh 4.28), 275 (infl. 3.89), 290 (4.02), 340 (sh 3.62); EI-MS *m/z*: 507 $[M+H]^+$ (1), 506 $[M]^+$ (3), 438 (22), 437 (47), 409 (11), 369 (10), 353 (8), 315 (23), 285 (16), 219 (21), 153 (100), 123 (21), 122 (10), 69 (74); HR-MS *m/z*: 506.2282 $[M]^+$ ($C_{30}H_{34}O_7$ required: 506.2304); ^1H NMR (500 MHz, Me_2CO-d_6): δ 1.50 (6H, *br s*, 11- and 14′-Me), 1.57 (3H, *br d*, *J* = 1 Hz, 14′-Me), 1.61 (3H, *br s*, 11-Me), 1.70 (3H, *br s*, 9′-Me), 1.90 (2H, *br t*, *J* = 7 Hz, H_2-11′), 2.00 (2H, *td*, *J* = 7 and 7 Hz, H_2-12′), 2.76 (1H, *br dd*, *J* = 6 and 15 Hz, H-9), 3.12 (1H, *br dd*, *J* = 8 and 15 Hz, H-9), 3.26 (2H, *br d*, *J* = 7 Hz, H_2-7′), 5.03 (1H, *tm*, *J* = 7 Hz, H-13′), 5.23 (1H, *tm*, *J* = 7 Hz, H-10), 5.26 (1H, *tm*, *J* = 7 Hz, H-8′), 5.81 (1H, *d*, *J* = 2 Hz, H-8), 5.92 (1H, *d*, *J* = 2 Hz, H-6), 6.54 (1H, *d*, *J* = 8 Hz, H-5′), 7.09 (1H, *br s*, 3-OH), 7.18 (1H, *d*, *J* = 8 Hz, H-6′), 8.62 (1H, *br s*, 4′-OH), 9.95 (1H, *br*, 7-OH), 11.69 (1H, *s*, 5-OH); CD (*c* 39 ppm, MeOH): $[\theta]_{236}+18\,000$, $[\theta]_{247}$ 0, $[\theta]_{254}+4600$, $[\theta]_{263}$ 0, $[\theta]_{275}-8000$, $[\theta]_{284}$ 0, $[\theta]_{293}+9100$, $[\theta]_{314}+3100$, $[\theta]_{334}+6400$, $[\theta]_{415}$ 0.

Sanggenol H (**3**). Amorphous powder, $[\alpha]_D^{24}-46°$ (*c* 0.367, MeOH). $FeCl_3$ test: light brown. UV λ_{max}^{MeOH} nm (log ε): 205 (4.50), 230 (sh 4.12), 282 (sh 3.89), 303 (3.94), 350 (sh 3.32); EI-MS *m/z*: 507 $[M+H]^+$ (11), 506 $[M]^+$ (31), 437 (25), 383 (20), 370 (22), 355 (19), 353 $[M-153]^+$ (16), 315 (57), 302 (100), 285 (64), 153 (100), 134 (15), 123 (10), 69 (14); HR-MS *m/z*: 506.2294 $[M]^+$ ($C_{30}H_{34}O_7$ requires: 506.2304); ^1H NMR (500 MHz, Me_2CO-d_6): δ 1.55 (3H, *br s*, 16-Me), 1.57 (3H, *br s*, 21-Me), 1.64 (3H, *br d*, *J* = 1 Hz, 21-Me), 1.65 (3H, *br s*, 11-Me), 1.82 (2H, *m*, H_2-13), 1.84 (2H, *m*, H_2-14), 1.94 (2H, *br t*, *J* = 8 Hz, H_2-18), 2.05 (H_2-19; detected by NOESY spectrum), 2.80 (1H, *br dd*, *J* = 7 and 15 Hz, H-9), 3.19 (1H, *br dd*, *J* = 9 and 15 Hz, H-9), 5.03 (1H, *br t*, *J* = 7 Hz, H-15), 5.08 (1H, *tqq*-like, *J* = 1 and 7 Hz, H-20), 5.24 (1H, *tm*, *J* = 8 Hz, H-10), 5.81 (1H, *d*, *J* = 2 Hz, H-8), 5.92 (1H, *d*, *J* = 2 Hz, H-6), 6.40 (1H, *d*, *J* = 2 Hz, H-3′), 6.53 (1H, *dd*, *J* = 2 and 8 Hz, H-5′), 7.08 (1H, *s*, 3-OH), 7.38 (1H, *d*, *J* = 8 Hz, H-6′), 8.75 (1H, *s*, 4′-OH), 9.91 (1H, *br*, 7-OH), 11.64 (1H, *s*, 5-OH); CD (*c* 22 ppm, MeOH): $[\theta]_{230}$ 0, $[\theta]_{238}+5400$, $[\theta]_{248}$ 0, $[\theta]_{253}-690$, $[\theta]_{260}$ 0, $[\theta]_{271}+1500$, $[\theta]_{288}$ 0, $[\theta]_{290}-4900$, $[\theta]_{381}-960$, $[\theta]_{457}-2300$, $[\theta]_{533}$ 0.

Sanggenol I (**4**). Amorphous powder. UV λ_{max}^{MeOH} nm: 208, 230 (sh), 290, 306, 360 (sh); EI-MS *m/z*: 506 $[M]^+$ (2), 488 (1), 437 (1), 394 (6), 383 (5), 342 (6), 289 (**4b**, 18), 219 (**4a**, 37), 218 (10), 165 (100); HR-MS *m/z*: 506.2285 $[M]^+$ ($C_{30}H_{34}O_7$ required: 506.2304); ^1H NMR (500 MHz, Me_2CO-d_6): δ 1.52, 1.59 (each 3H, *br s*, 8″-Me), 1.57, 1.58 (each 3H, *br s*, 11-Me), 1.69 (3H, *br s*, 3″-Me), 1.88 (2H, *br t*, *J* = 7 Hz, H_2-5″),

1.98 (2H, *m*, H_2-6″), 2.85 (1H, *br dd*, $J = 7$ and 1.5 Hz, H-9), 3.06 (1H, *br dd*, $J = 9$ and 15 Hz, H-9), 3.16, 3.24 (each 1H, *br dd*, $J = 7$ and 14 Hz, H-1″), 5.02 (1H, *tm*, $J = 7$ Hz, H-7″), 5.10 (1H, *tm*, $J = 7$ Hz, H-2″), 5.30 (1H, *br t*, $J = 7$ Hz, H-10), 6.02 (1H, *s*, H-6), 6.36 (1H, *d*, $J = 2$ Hz, H-3′), 6.50 (1H, *dd*, $J = 2$ and 8 Hz, H-5′), 7.34 (1H, *d*, $J = 8$ Hz, H-6′), 11.61 (1H, *s*, 5-OH).

Sanggenol J (**5**). Amorphous powder, $[\alpha]_D^{24} + 98°$ (*c* 0.927, MeOH). UV λ_{max}^{MeOH} nm (log ε): 210 (5.01), 235 (infl. 4.78), 289 (4.64), 300 (sh 4.63); FAB-MS *m/z*: 799 $[M+Na]^+$, 777 $[M+H]^+$, 707, 571, 559, 503, 501, 437, 421, 407, 369, 353, 314, 219; ^{1}H NMR (500 MHz, Me_2CO-d_6); δ 1.27, 1.29 (each 3H, *s*, 36-Me), 1.51, 1.59 (each 3H, *br s*, 11-Me), 1.76 (2H, *t*, $J = 7$ Hz, H_2-35), 1.87 (3H, *br s*, 16-Me), 2.24 (1H, *br d*, $J = 16$ Hz, H-18), 2.43 (1H, *br d*, $J = 16$ Hz, H-18), 2.51 (2H, *t*, $J = 7$ Hz, H_2-34), 2.72 (1H, *br dd*, $J = 6$ and 14.5 Hz, H-9), 3.08 (1H, *br dd*, $J = 8$ and 14.5 Hz, H-9), 3.83 (1H, *td*, $J = 5.5$ and 5.5 Hz, H-19), 4.54 (1H, *t*, $J = 5.5$ Hz, H-20), 4.08 (1H, *br*, H-14), 5.19 (1H, *br t*, $J = 7$ Hz, H-10), 5.54 (1H, *br s*, H-15), 5.73 (1H, *s*, H-8), 6.20 (*d*, $J = 9$ Hz, H-26), 6.28 (1H, *dd*, $J = 2$ and 8 Hz, H-32), 6.29 (1H, *d*, $J = 2$ Hz, H-3′), 6.46 (1H, *d*, $J = 2$ Hz, H-30), 6.47 (1H, *dd*, $J = 2$ and 8 Hz, H-5′), 6.93 (1H, *d*, $J = 8$ Hz, H-33), 6.98 (1H, *s*, 3-OH), 7.30 (1H, *d*, $J = 8$ Hz, H-6′), 8.04 (1H, *s*, 31-OH), 8.21 (1H, *d*, $J = 9$ Hz, H-27), 8.56 (1H, *s*, 29-OH), 8.64 (1H, *s*, 4′-OH), 9.09 (1H, *s*, 7-OH), 12.04 (1H, *s*, 5-OH), 12.89 (1H, *s*, 23-OH); CD (*c* 28 ppm, MeOH): $[\theta]_{252} + 24\,900$, $[\theta]_{276} + 3800$ (valley), $[\theta]_{301} + 43\,500$, $[\theta]_{325}$ 0, $[\theta]_{334} - 16\,800$, $[\theta]_{362}$ 0, $[\theta]_{374} + 1400$, $[\theta]_{384}$ 0, $[\theta]_{459} - 9300$, $[\theta]_{356}$ 0.

Sanggenol K (**6**). Amorphous powder, $[\alpha]_D^{24} + 80°$ (*c* 0.01, MeOH). UV λ_{max}^{MeOH} nm (log ε): 208 (4.52), 230 (sh 4.28), 295 (4.04), 340 (sh 319); EI-MS *m/z*: 508 $[M]^+$ (4), 506 (23), 490 (22), 438 (32), 383 (26), 286 (17), 273 (19), 270 (5), 221 (**6a**, 68), 1.65 (96), 69 (100); ^{1}H NMR (400 MHz, Me_2CO-d_6): δ 1.55, 1.61 (each 3H, *br s*, 14′-Me), 1.63, 1.74 (each 3H, *br s*, 11-Me), 1.77 (3H, *br s*, 9′-Me), 1.95 (2H, *br t*, $J = 6$ Hz, H_2-11′), 3.25 (2H, *br d*, $J = 7$ Hz, H_2-9), 3.43 (2H, *br d*, $J = 7$ Hz, H_2-7′), 4.26 (1H, *br*, 3-OH), 4.72 (1H, *br d*, $J = 12$ Hz, H-3), 5.08 (1H, *tm*, $J = 7$ Hz, H-13′), 5.22 (1H, *tm*, $J = 7$ Hz, H-10), 5.29 (1H, *tm*, $J = 7$ Hz, H-8′), 5.45 (1H, *d*, $J = 12$ Hz, H-2), 6.03 (1H, *s*, H-8), 6.52 (1H, *d*, $J = 8.5$ Hz, H-5′), 7.18 (1H, *d*, $J = 8.5$ Hz, H-6′), 7.41, 8.36 (each 1H, *br*, OH), 11.96 (1H, *s*, 5-OH); CD (*c* 40 ppm, MeOH); $[\theta]_{228} + 16\,500$, $[\theta]_{249} + 4600$ (valley), $[\theta]_{259} + 5200$, $[\theta]_{285}$ 0, $[\theta]_{296} - 4600$, $[\theta]_{308}$ 0, $[\theta]_{327} + 4000$.

REFERENCES

1. Nomura, T., in *Fortschritte der Chemie organischer Naturstoffe*, Vol. 53, ed. W. Herz, H. Grisebach, G. W. Kirby and Ch. Tamm. Springer, Wien, 1988, p. 87.
2. Nomura, T. and Hano, Y., *Natural Products Reports*, 1994, **11**, 205.
3. Mihara, S., Hara, M., Nakamura, M., Sakurawi, K., Tokura, K., Fujimoto, M., Fukai, T. and Nomura, T., *Biochemistry and Biophysics Research Communications*, 1995, **213**, 594.
4. Sun, J.-Y., Hano, Y. and Nomura, T., *Heterocycles*, 1989, **29**, 195.
5. Nunome, S., Okada, M., Hano, Y., Fukai, T., Nomura, T. and Mitsuhashi, H., *Natural Medicines*, 1994, **48**, 71.
6. Fukai, T., Pei, Y.-H., Nomura, T., Xu, C.-Q., Wu, L.-J. and Chen, Y.-J., *Heterocycles*, 1996, **43**, 425.
7. Hano, Y., Kanzaki, R., Fukai, T. and Nomura, T., *Heterocycles*, 1997, **45**, 867.
8. Messana, I., Ferrari, F., Delle Monache, F., Yunes, R. A. and Gacs-Baitz, E., *Heterocycles*, 1994, **38**, 1287.
9. Ferrari, F. and Messana, I., *Phytochemistry*, 1995, **38**, 251.
10. Barron, D. and Ibrahim, R. K., *Phytochemistry*, 1996, **43**, 921.
11. Fukai, T., Nishizawa, J. and Nomura, T., *Phytochemistry*, 1994, **36**, 225.
12. Nomura, T. and Fukai, T., in *Fortschritte der Chemie organischer Naturstoffe*, ed. W. Herz, G. W. Kirby, R. E. Moore, W. Steglich and Ch. Tamm. in press.
13. Hano, Y., Kohno, H., Suzuki, S. and Nomura, T., *Heterocycles*, 1996, **24**, 2285.
14. Gafflied, W., *Tetrahedron*, 1979, **26**, 4093.
15. Fukai, T. and Nomura, T., *Heterocycles*, 1993, **36**, 329.