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UNUSUAL BIFLAVONOIDS IN THE FARINOSE EXUDATE OF *PENTAGRAMMA TRIANGULARIS*

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Key Word Index—*Pentagramma triangularis*; Adiantaceae; farinose exudate, biflavonoid.

Abstract—Three new and unusual biflavonoids, composed of a flavonol and a dihydrochalcone nucleus through a methylene group, were isolated from the farinose exudate of *Pentagramma triangularis* in addition to a herbacetin dimethyl ester. These structures were determined by means of spectroscopic analysis. Copyright © 1997 Published by Elsevier Science Ltd

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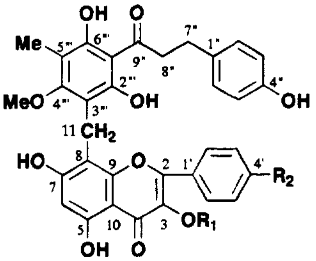
INTRODUCTION

In the continuing studies of the chemistry of farinose exudate found in some ferns, we have isolated two unusual biflavonoids (**5** and **6**) which are composed of a flavonol and a dihydrochalcone nucleus through a methylene group from the frond exudate of *Pentagramma triangularis* [1]. The genus *Pentagramma* has recently been separated from *Pityrogramma* on the basis of morphological characters and flavonoid chemistry [2]. Further investigation of flavonoid constituents in the exudate of *P. triangularis* resulted in the isolation of three new biflavonoids and herbacetin dimethyl ether. In this paper, the isolation and structural elucidation of these compounds as well as the behaviour of a chelated hydroxyl proton and methoxyl signals in the biflavonoid skeleton observed in the ^{1}H NMR spectrum are discussed.

RESULTS AND DISCUSSION

The farinose exudate of *Pentagramma triangularis* collected at Oregon State was rinsed with acetone. After concentration, the acetone extract was repeatedly purified by silica gel CC, Sephadex LH-20, preparative TLC and recrystallization to give four compounds (**1**–**4**) along with kaempferol and *p*-methoxybenzoic acid.

Compound **1**, obtained as a yellow powder, gave a positive reaction to the FeCl$_3$ test on TLC. In the negative ion FABMS, the $[M-H]^-$ was observed at *m/z* 613 which corresponds to $C_{34}H_{30}O_{11}$. The IR and UV spectrum showed that **1** had a kaempferol-like skeleton. In the ^{1}H NMR spectrum, two sets of *ortho*-coupled two-proton doublets were observed at δ 7.11, 8.31 ($J = 9$ Hz) and at δ 6.74, 7.06 ($J = 8$ Hz) attributed to two *para*-substituted benzene rings. An NOE was found at the protons (δ 7.11) when a methoxyl group at δ 3.91 was irradiated. A weak fragment ion appeared at *m/z* 300 that was regarded as **1′** in the EIMS (Fig. 1). These results indicate that **1** had a kaempferol 4′-methyl ester as a flavonol part as in **5**. The ^{1}H NMR spectrum also showed the presence of a set of triplets due to two methylenes at δ 2.87 and 3.41 (each $J = 8$ Hz), two singlets based on a methyl-



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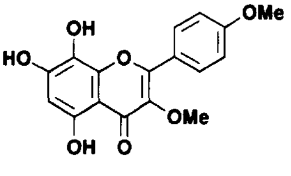
2 : R$_1$ = Me, R$_2$ = OMe
3 : R$_1$ = Me, R$_2$ = H



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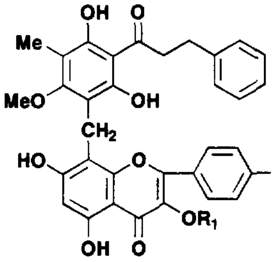


5 : R$_1$ = H, R$_2$ = OMe
6 : R$_1$ = Me, R$_2$ = H

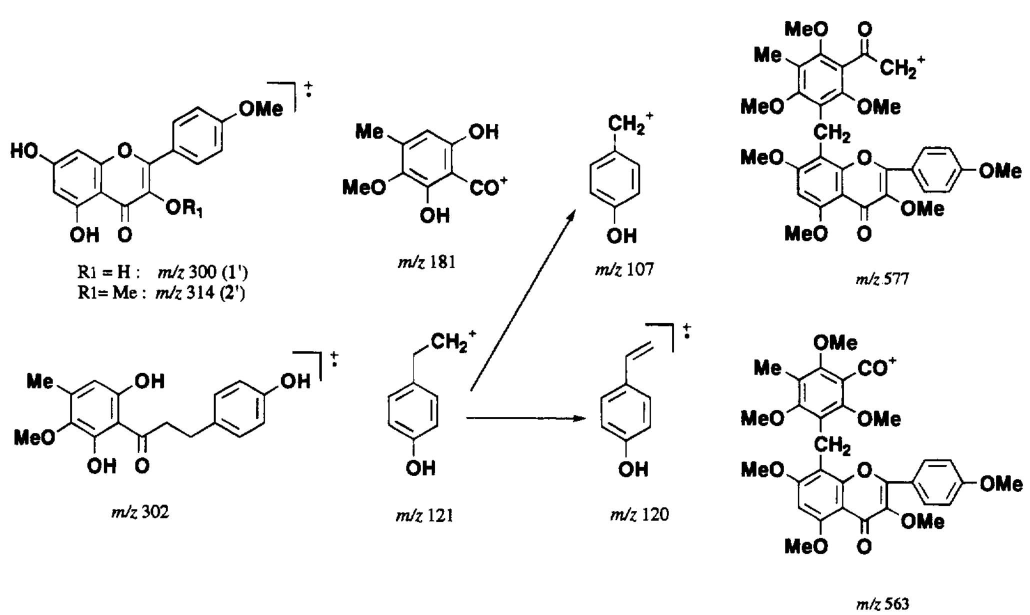
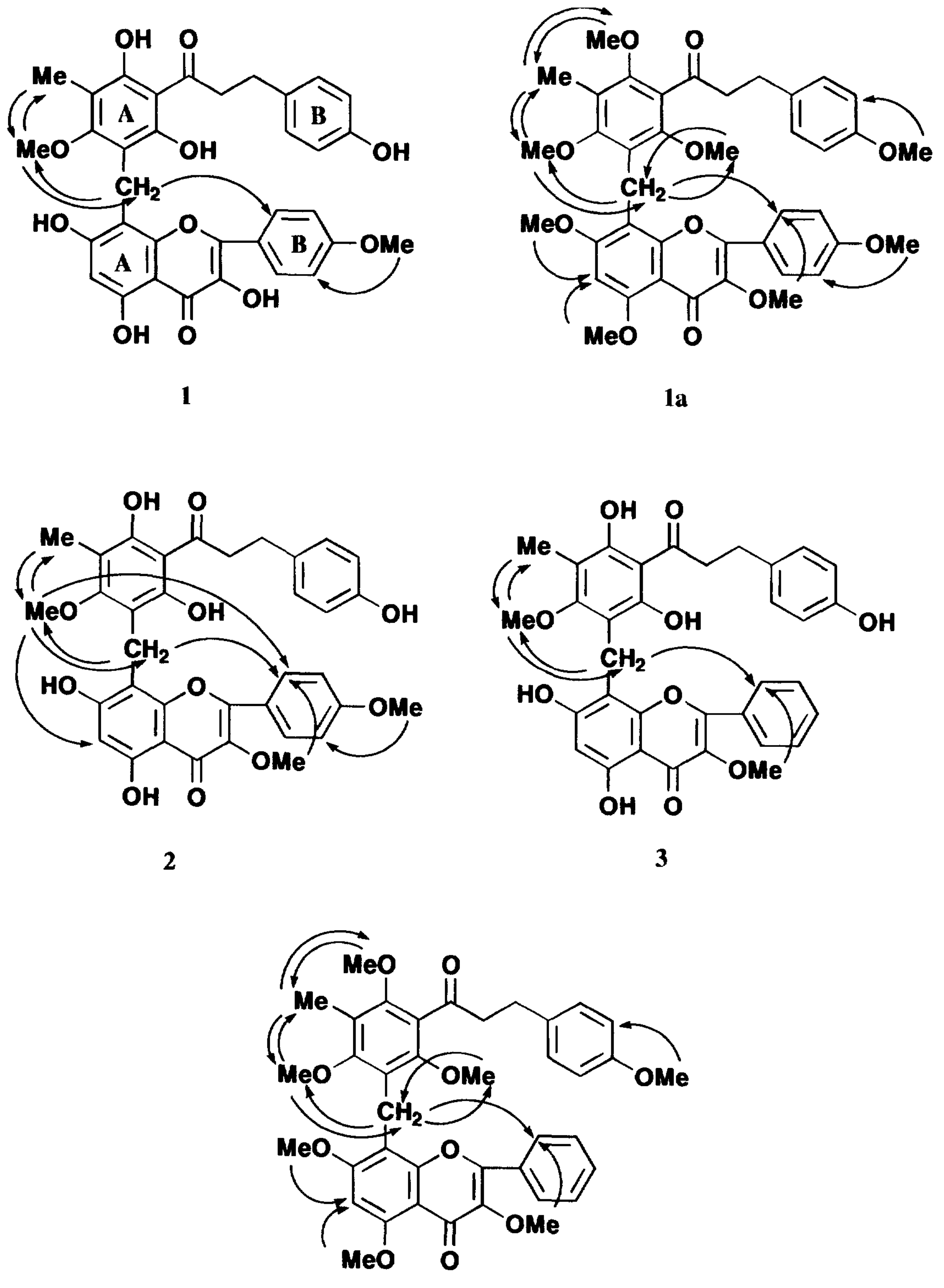


Fig. 1. Predominant fragment ions of **1**, **2** and **1a** in EIMS.

ene at δ 4.21 and a methyl group at δ 2.03 attaching to an aromatic ring in addition to another methoxyl at δ 3.51 and a chelated hydroxyl group at δ 12.23. Permethlyation of **1** gave an octamethyl ether (**1a**: *m/z* 698 in EIMS), indicating that **1** had six hydroxyl groups. One of the two *para*-substituted benzene rings, a CH_2CH_2 sequence and a carbonyl group (δ_c 207.6) were allotted to a dihydrochalcone residue in **1**, which was supported by fragment ions at *m/z* 121, 120 and 107 in the EIMS (Fig. 1). The methylene group was assignable to Ar-C$\underline{H}_2$-Ar compared with **5** and **6**. Consequently, the flavonol moiety is linked with the dihydrochalcone through the methylene group. By means of the NOEs observed in **1** and **1a**, the methoxyl (δ 3.51), the methyl and the methylene groups were located at C-4″, C-5″ and C-3‴ as shown in Fig. 2. The A-ring in the dihydrochalcone moiety was wholly substituted by analysis of the EIMS of **1a** (*m/z* 577 and 563 in Fig. 1). The relationship of NOEs in **1** and **1a** (Fig. 2) indicated that the A-ring in the dihydrochalcone was a 2‴,6‴-dihydroxy-4‴-methoxy-5‴-methyl substitution and that the methylene group was located at C-3‴. The above substitution was substantiated by COLOC spectrum (Fig. 3). Furthermore, the ^{1}H NMR spectra and the EIMS fragments of **1** and **1a** (*m/z* 135, 134 and 121) showed that the B-ring in the dihydrochalcone had a hydroxyl group at C-4″. In the ^{13}C NMR spectrum, two quaternary carbons at δ 146.9 and 136.9, which superimposed those of **5** were assignable to C-2 and C-3 in the flavonol, indicating that the flavonol was a kaempferol 4′-methyl ether. The position of the methylene group in the kaempferol was determined to be at C-8 by the following reasons. A singlet aromatic proton (δH 6.33) and its root carbon (δC 98.9) were superimposable on those of **4**. The NOEs were observed between the methylene and the protons at C-2′ and C-6′ on the kaempferol both in **1** and **1a**, and also between the proton (δ 6.67) and two methoxyl groups [δ 3.92 (C-7) and 3.94 (C-5)] in **1a**. In the COLOC spectrum, the long range correlations were observed between the chelated hydroxyl group (δ 12.23) and three carbons [δ 98.9 (*d*, C-6), 104.6 (*s*, C-10) and 160.3 (*s*, C-5), and between the methylene protons and three quaternary carbons [δ 106.9 (C-8), 155.1 (C-9) and 162.0 (C-7)], suggesting that the methylene group was located at C-8 on the kaempferol. Consequently, **1** must be the 4″-hydroxyl derivative of **4**.

Compound **2**, obtained as a yellow amorphous solid, showed a positive reaction to the $FeCl_3$ test. In the negative ion FABMS, the $[M-H]^-$ was exhibited at *m/z* 627 which is different from **1** by 14 amu (one methyl). The ^{1}H NMR spectrum was superimposable to that of **1** except for the methoxyl and a chelated hydroxyl signal. The EIMS and the ^{1}H NMR spectrum including NOE experiments (Fig. 2) showed that **2** has the same dihydrochalcone moiety as **1** and that the moiety was linked at C-8 of a flavonol. Permethylation of **2** resulted in **1a**, that is, one of six hydroxyl groups in **1** was methylated in **2**. A fragment ion appeared at *m/z* 314 (**2**′) in the EIMS (Fig. 1) showed that the flavonol unit was a kaempferol dimethyl ether. Among the three methoxyl signals at δ 55.4, 60.2 and 60.3 in ^{13}C NMR spectrum, the former two were located at C-4′ in the kaempferol and a C-4‴ in the dihydrochalcone. The NOE experiment of **2** and the chemical shifts of the methoxyl carbon (δ 60.3) indicated that the other methoxyl group was substituted at C-3. Then the kaempferol was methylated at C-3 and C-4′. Consequently, the structure of this biflavonoid was depicted as **2**.

Compound **3**, a yellow amorphous powder, showed a positive reaction to $FeCl_3$. The UV and ^{1}H NMR spectrum showed that **3** is also a cognate of **1** and **2**. In the negative ion FABMS, the $[M-H]^-$ was exhibited at *m/z* 597 which is different from **2** by 16 amu (one



3a

Fig. 2. NOEs in the NOE difference spectrum of **1**, **2**, **3** and permethyl ethers (**1a** and **3a**).

hydroxyl). The EIMS and ^{1}H NMR spectrum including NOE experiments of **3** and **3a** (a permethyl ether of **3**) showed that **3** had the same dihydrochalcone moiety as **1** and **2**. In the ^{1}H NMR spectrum, the signals based on a flavonol moiety were observed at δ 3.88 (3H, *s*, OMe), 6.14 (1H, *s*), 7.62 (3H, *m*), 8.35 (2H, *d* like *m*) and a chelated hydroxyl group (δ 12.76), showing that the B-ring of the flavonol was unsubstituted. A fragment ion corresponding to the flavonol appeared at *m/z* 284 in the EIMS. In addition to the

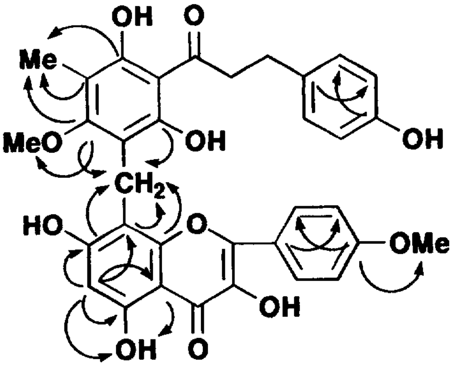


Fig. 3. CH long range correlations in COLOC spectrum of **1**.

NOE experiments of **3a** and **3b** (Fig. 2), the flavonol moiety was characterized as a galangin 3-methyl ether the same as **6**. The NOEs of **3** and **3a** were observed between the methylene signal at δ 4.06 and H-2′,6′ in the galangin 3-methyl ether, indicating that the galangin was linked with the dihydrochalcone through C-8. This biflavonoid has the structure of **3**, which is the same as the derivative with another hydroxyl group introduced at C-4″ in **5**.

Compound **4** showed a positive reaction to $FeCl_3$. The EIMS showed the M^+ at m/z 330, which indicated that **4** is a flavone derivative with three hydroxyl and two methoxyl groups. The ^1H NMR spectrum supported the presence of two methoxyl (δ 3.87 and 3.92) and three hydroxyl groups [δ 7.92, 9.14 and 12.22 (chelated one)] as well as a set of two-proton doublet [δ 7.12 and 8.17 ($J = 9$ Hz)], a singlet aromatic proton (δ 6.32). By the NOE experiments, two methoxyl groups were determined to be located at C-3 and C-4′ (Fig. 4). By usual methylation, **4** gave a pentamethyl ether (**4a**). The NOE experiments (Fig. 4) showed the A-ring substitution to be a 5,7,8-trioxygenation. The structure of **4** was then characterized as 5,7,8-trihydroxy-3,4′-dimethoxyflavone (herbacetin 3,4′-dimethyl ether).

In the present study, five unusual biflavonoids were isolated and they are divided into two types in accordance with the absence/presence of a methyl group at C-3 (3-OH or 3-OMe). It is true that the substitution could be distinguished by UV spectrum in addition to shift reagents, chemical shift of the methoxyl carbon at C-3 in ^{13}C NMR spectrum and NOE experiments in ^1H NMR spectrum, but we found simple significance in the chemical shift of a hydroxyl group at C-5 OH in a flavonol moiety in the course of our study of flavonoid chemistry in *Pentagramma*. In the case of a 3-OH type (**1** and **5**), the chemical shifts appear at *ca* 12.2 ppm (**1**: 12.23; **5**: 12.28), while the 3-OMe type (**2**, **3** and **6**) appeared at *ca* 12.7 ppm (**2**: 12.74; **3**: 12.76; **6**: 12.72) in acetone-d_6. This rule could be applicable to simple flavonol derivatives such as kaempferol 4′-methyl ether (12.17), **4** (12.22), kaempferol 3,4′-dimethyl ether (12.78), and galangin 3-methyl ether (12.57). The chemical shift of a hydroxyl group at C-5 will alter to a lower field when a substituent is introduced at C-5 [3–5]. The above rule was further adapted to a flavonol unsubstituted at C-6.

In the ^1H NMR spectra of the biflavonoids (**1**–**3**, **5** and **6**), methoxy signals at C-4‴ in a dihydrochalcone moiety were observed in a higher field (δ 3.13–3.51) (see Table 3). In the ^1H NMR spectra of the permethyl ethers (**1a**, **3a**, **5a** and **6a**), similar behaviour of methoxyl signals at C-4‴, C-2‴ and C-6‴ in a dihydrochalcone moiety were observed compared with those of a flavonol moiety. In the case of a monomeric dihydrochalcone having a similar A-ring substitution such as 4,2′,6′-trihydroxy-3′,5′-dimethyl-4′-methoxydihydrochalcone, an unusual chemical shift was not observed (C-4′ OMe: δ 3.70). The above phenomena may be caused by a steric effect between flavonol and dihydrochalcone moieties in the biflavones.

EXPERIMENTAL

Plant material and extraction was described in a previous paper [1].

Isolation. The acetone extract (10 g) was chromatographed on a Si gel (200 g) eluted with a n-hexane-acetone mixture. The n-hexane–acetone (3:1) fraction was further subjected to Si CC eluted with cyclohexane–acetone (3:1) to give kaempferol (8 mg) and **4** (15 mg) as pure form. The n-hexane–acetone (1:1) fraction was further chromatographed on Si eluted with n-hexane–acetone (4:1) and the eluent was purified by prep. TLC developed with $CHCl_3$–MeOH (8:1) and cyclohexane–EtOH (5:1) to give **3** (10 mg). The following n-hexane–acetone (1:1) fraction was dissolved in a n-hexane–acetone mixture after concentration to give a yellow powder, which was filtered. The crude power was repeatedly recrystallized from MeOH to give **1** (65 mg). The filtrate was subjected to Si CC (100 g) eluted with $CHCl_3$–EtOH (20:1) and to Sephadex LH-20 CC eluted with MeOH. The eluent was finally purified by prep. TLC [n-hexane–acetone (2:1)] to give **2** (12 mg). The fraction also gave p-methoxybenzoic acid (3 mg). Kaempferol and p-

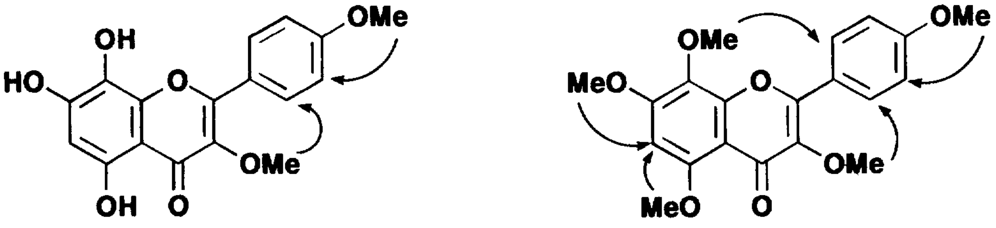


Fig. 4. NOEs in the difference NOEs in **4** and its permethyl ether (**4a**).

Table 1. ^1H NMR spectral data of **1**, **2** and **3**

No.	**1**	**2**	**3**
C-6	6.33 (*s*)	6.03 (*s*)	6.14 (*s*)
C-11	4.21 (*s*)	4.05 (*s*)	4.06 (*s*)
C-2′,6′	8.31 (*d*, 9)	8.33 (*d*, 9)	8.35 (*d* like *m*)
C-3′,5′	7.11 (*d*, 9)	7.14 (*d*, 9)	7.62 (*m*)
C-4′			7.62 (*m*)
C-2″,6″	7.06 (*d*, 8)	7.13 (*d*, 8)	7.08 (*d*, 8)
C-3″,5″	6.74 (*d*, 8)	6.73 (*d*, 8)	6.60 (*d*, 8)
C-7″	2.87 (*t*, 8)	2.89 (*t*, 8)	2.87 (*d*, 8)
C-8″	3.41 (*t*, 8)	3.54 (*t*, 8)	3.52 (*t*, 8)
Me	2.03 (*s*)	1.93 (*s*)	2.14 (*s*)
OMe	3.51 (*s*, 4‴) 3.91 (*s*, 4′)	3.31 (*s*, 4‴) 3.84 (*s*, 3) 3.92 (*s*, 4′)	3.31 (*s*, 4‴) 3.88 (*s*, 3)
C-5-OH	12.23 (*s*)	12.74 (*s*)	12.76 (*s*)

All protons were assigned by HH COSY spectrum and NOE experiments. Measured in acetone-d_6.

Table 2. ^{13}C NMR spectral data of **1**, **2** and **3**

No.	**1**	**2**	**3**
C-2	146.9	155.0	155.1
C-3	136.9	138.7	139.6
C-4	176.9	178.7	178.9
C-5	160.3	165.0	165.4
C-6	98.9	101.3	101.2
C-7	162.0	171.3	171.3
C-8	106.9	108.2	108.0
C-9	155.1	154.8	154.9
C-10	104.6	103.4	103.7
C-11	17.4	18.8	18.6
C-1′	124.5	124.8	131.1
C-2′,6′	130.2	131.0	129.4
C-3′,5′	114.8	114.7	130.2
C-4′	162.0	161.0	132.5
C-1″	133.2	134.0	133.8
C-2″,6″	130.1	130.2	130.2
C-3″,5″	115.9	115.9	114.7
C-7″	30.6	31.0	30.9
C-8″	47.7	47.7	47.7
C-9″	207.6	207.7	207.7
C-1‴	108.9	110.2	110.0
C-2‴	159.3	162.3	161.0
C-3‴	112.7	114.7	114.4
C-4‴	164.4	163.0	164.9
C-5‴	110.5	105.4	106.3
C-6‴	160.8	163.0	163.0
Me	9.1	8.7	8.7
C-3-OMe		60.3	60.4
C-4′-OMe	55.7	55.4	
C-4‴-OMe	61.0	60.2	60.3

Measured in acetone-d_6. Compound **1** was assigned by the aid of CH COSY and COLOC spectrum.

methoxybenzoic acid was identified by comparison with authentic samples.

Compound **1**, 8-[2,4-*dihydroxy*-6-*methoxy*-5-*methyl*-3-{1-*oxo*-3-(4-*hydroxyphenylpropyl*)}*phenyl*]*methylene*-3,5,7-*trihydroxy*-2-(4-*methoxyphenyl*)-4*H*-1-*benzopyran*-4-*one*. A yellow powder, $FeCl_3$ (+), negative ions FABMS: *m*/*z* 613 $[M-H]^-$, IR (KBr, cm^{-1}): 3300 (OH), 1650 (C=O), 1620 (C=C), UV (nm, MeOH): 276, 332sh, 347; +NaOMe: 287, 342, 427 sh; $+AlCl_3$; 276, 351, 427; $+AlCl_3/HCl$: 276, 351, 427; +NacOAc: 280, 325sh, 390sh; $+NacOAc/H_3BO_3$: 276, 320, 375sh, EIMS *m*/*z* (rel. int.): 302 (43), 300 (5), 285 (7), 284 (9), 283 (10), 181 (100), 154 (40), 152 (4), 121 (3), 120 (12), 107 (24), 91 (6), 77 (11). The ^1H NMR and ^{13}C NMR spectral data are in Tables 1 and 2.

Methylation of **1**. Compound **1** (5 mg) was treated with MeI/K_2CO_3 in dry acetone under reflux. The reaction mixture was poured into water and extracted with EtOAc. The EtOAc phase was concentrated *in vacuo* and purified by preparative TLC [*n*-hexane-acetone (5:1)] to give **1a** (3.8 mg) as a pale yellow amorphous solid. **1a**: EIMS *m*/*z* (rel. int.): 698 (M^+, 100), 697 (63). 683 (25), 667 (13), 651 (3), 637 (2), 577 (28), 563 (15), 536 (18), 535 (16), 517 (10), 505 (5), 489 (3), 433 (2), 419 (3), 391 (5), 368 (50), 341 (50), 311 (10), 297 (8), 282 (12), 267 (4), 236 (4), 207 (8), 193 (18), 181 (20), 154 (12), 135 (21), 121 (48), 91 (12), 77 (8), ^1H NMR (400 MHz, acetone-d_6) δ: 2.11 (3H, *s*, C5‴-Me), 2.82 (2H, *t*, $J =$ 8 Hz, CH_2, H-7‴), 2.92 (2H, *t*, $J = 8$ Hz, H-8‴), 4.23 (2H, *s*, CH_2, H-11), 6.67 (1H, *s*, Ar-H, H-6), 6.79 (2H, *d*, $J = 8$ Hz, H-3″, 5″), 7.00 (2H, *d*, $J = 8$ Hz, H-2″, 6″), 7.00 (2H, *d*, $J =$ 9 Hz, H-3′, 5′), 7.82 (2H, *d*, $J = 9$ Hz, H-2′, 6′). The methoxyl signals are listed in Table 3.

Compound **2**, 8-[2,4-*dihydroxy*-6-*methoxy*-5-*methyl*-3-{1-*oxo*-3-(4-*hydroxyphenylpropyl*)}*phenyl*]*methylene*-5,7-*trihydroxy*-3-*methoxy*-2-(4-*methoxyphenyl*)-4*H*-1-*benzopyran*-4-*one*. A yellow amorphous, $FeCl_3$ (+), negative ion FABMS: *m*/*z* 627 $[M-H]^-$, UV (MeOH, nm): 279, 364; +NaOMe: 282, 383sh; $+AlCl_3$: 280, 303sh, 346, 397; $+AlCl_3/HCl$: 282, 305sh, 344, 407; +NacOAc: 281, 364; $+NacOAc/H_3BO_3$: 280, 361, EIMS *m*/*z* (rel. int.): 314 (19), 313 (9), 302 (37), 285 (8), 284 (11), 283 (11), 271 (8), 253 (3), 241 (2), 228 (2), 196 (7), 194 (4), 181 (100), 166 (4), 154 (38), 121 (4), 120 (13), 107 (25). Methylation of **2** (4 mg) in a similar manner described above gave **1a** (3.2 mg). The ^1H and ^{13}C NMR spectral data are shown in Tables 1 and 2.

Compound **3**, 8-[2,4-*dihydroxy*-6-*methoxy*-5-*methyl*-3-{1-*oxo*-3-(4-*hydroxyphenylpropyl*)}*phenyl*]*methylene*-5,7-*trihydroxy*-3-*methoxy*-2-*phenyl*-4*H*-1-*benzopyran*-4-*one*. A yellow powder, $FeCl_3$ (+), negative ion FABMS: *m*/*z* 597 $[M-H]^-$, UV (MeOH, nm): 279, 351; +NaOMe: 282, 349, 355; $+AlCl_3$: 278, 336, 410; +NacOAc: 282, 355; $+NacOAc/H_3BO_3$: 280, 355, EIMS *m*/*z* (rel. int.): 314 (10), 302 (46), 285 (12), 284 (34), 283 (25), 194 (10), 182 (12), 181 (100), 166 (12), 154 (12), 121 (4), 120 (13), 107 (33), 107 (23), 77 (14). The ^1H and ^{13}C NMR spectral data are shown in Tables 1 and 2. Methylation of **3** (4 mg) in the same manner described above to give **3a** (3 mg) which was purified by prep. TLC [*n*-hexane–acetone (3:1)]. **3a**:

Table 3. Methoxyl signals of biflavonoids in the ^{1}H NMR spectrum

	1	**2**	**3**	**5**	**6**	**1a**	**3a**	**5a**	**6a**
C-3		3.86	3.88		3.78	3.78	3.78	3.77	3.78
C-5						3.92	3.94	3.92	3.94
C-7						3.94	3.95	3.93	3.95
C-4′	3.91	3.92		3.91		3.83		3.85	
C-4″						3.74	3.74		
C-2‴						3.37	3.36	3.37	3.36
C-4‴	3.51	3.31	3.31	3.50	3.47	3.49	3.41	3.47	3.47
C-6‴						3.60	3.60	3.59	3.59

Measured in acetone-d_6. All methoxyl signals were assigned by NOE experiments.

A solid, EIMS *m/z* (rel. int.): 668 (M^+, 100), 667 (54), 654 (13), 653 (26), 637 (14), 547 (33), 533 (26), 505 (12), 357 (8), 325 (35), 311 (52), 267 (13), 193 (18), 134 (10), 121 (64), ^{1}H NMR (400 MHz, acetone-d_6) δ: 2.10 (3H, *s*, C⁗-Me), 2.77–2.88 (4H, *m*, CH_2CH_2, H-7″, 8″), 4.22 (2H, *s*, CH_2, H-11), 6.68 (1H, *s*, Ar-H), 6.79 (2H, *d*, $J = 9$ Hz, H-3″, 5″), 7.09 (2H, *d*, $J = 9$ Hz, H-2″, 6″), 7.44 (3H, *m*, H-3′, 4′, 5′), 7.83 (2H, *d*, like *m*, H-2′, 6′). The methoxyl signals are listed in Table 3.

Compound **4**, *(5,7,8-trihydroxy-3,4′-dimethoxyflavone: herbacetin 3,4′-dimethyl ether*. A yellow powder, $FeCl_3$ (+), EIMS *m/z* (rel. int.): 314 (100), 313 (80), 271 (56), 153 (79), 135 (20), UV (MeOH, nm): 279, 304, 365, +NaOMe: 267, 351; +$AlCl_3$: 225, 302, 3226, 355sh, 431; +$AlCl_3$/HCl: 287, 316, 330sh, 352, 426; +$AlCl_3$/HCl: 287, 316, 330sh, 352, 426; +NacOAc: 294, 384; +NacOAc/H_3BO_3: 291, 308sh, 368, ^{1}H NMR (400 MHz, acetone-d_6) δ: 3.87 (3H, *s*, C-3-OMe), 3.92 (3H, *s*, C-4′-OMe), 6.32 (1H, *s*, H-6), 7.12 (2H, *d*, $J = 9$ Hz, H-3′, 5′), 8.17 (2H, *d*, $J = 9$ Hz, H-2′, 6′), 7.92, 9.14 (1H each, *s*, C-7,8-OH), 12.22 (C-5-OH), ^{13}C NMR (100 MHz, acetone-d_6) δ: 153.6, 155.2, 156.3 (C-3, 5 and 7, interchangeable with each other), 139.2 (C-2), 179.7 (C-4), 99.1 (C-6), 125.4 (C-8), 145.8 (C-9), 105.6 (C-19), 123.8 (C-1′), 131.0 (C-2′, 6′), 114.8 (C-3′, 5′), 55.8 (C-4′-OMe), 60.2 (C-3-OMe). In a similar manner to that described above, **4** (5 mg) was methylated to give **4a** (3.5 mg) as a solid after purification by prep. TLC using $CHCl_3$–MeOH (10:1). **4a**: EIMS *m/z* (rel. int.): 372 (M^+, 100), 371 (88), 357 (50), 353 (37), 341 (35), 279 (30), 167 (31), 149 (38), 135 (46), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.89 (3H, *s*, C-3-OMe), 3.90 (3H, *s*, C-4′-OMe), 3.93 (3H, *s*, C-8-OMe), 3.99 (3H, *s*, C-5-OMe), 4.00 (3H, *s*, C-7-OME), 6.41 (1H, *s*, H-6), 7.12 (2H, *d*, $J = 8$ Hz, H-3′, 5′), 8.16 (2H, *d*, $J = 8$ Hz, H-2′, 6′).

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