Constituents of the Leaves of *Macaranga tanarius*

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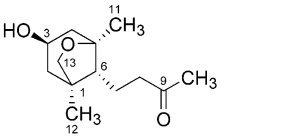
From the leaves of *Macaranga tanarius*, three new constituents, tanarifuranonol (**1**), tanariflavanone C (**2**), and tanariflavanone D (**3**), together with seven known compounds, were isolated and identified. Substances obtained in this investigation were evaluated against a panel of bioassays.

Macaranga tanarius (L.) Muell. Arg. (syn. *M. tomentosa* Bl.) (Euphorbiaceae) is known in Thailand as "Mek". A decoction of the root of this plant is drunk as an antipyretic and also as an antitussive.[1] The dried root is used as an emetic agent, whereas the fresh leaves are used to cover wounds as an anti-inflammatory.[1] In our ongoing search for biologically active compounds from Thai medicinal plants, we have investigated the constituents of *M. tanarius*. Recent investigations have been performed on *Macaranga conifera*,[2] *M. denticulata*,[3] *M. indica*,[4] *M. peltata*,[5] *M. pleiostemona*,[6] *M. schweinfurthii*,[7] and *M. triloba*,[8] as well as *M. tanarius* itself.[9−12] In the present study, the *n*-hexane and chloroform extracts of the leaves of this plant exhibited antioxidant activity in a 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical TLC autographic assay, from which three new constituents (**1**−**3**) together with seven known compounds were isolated. The known compounds, nymphaeol A (**4**),[13] nymphaeol B (**5**),[13] nymphaeol C (**6**),[13,14] tanariflavanone B,[14] blumenol A (vomifoliol),[14,15] blumenol B (7,8-dihydrovomifoliol),[14,15] and annuionone E,[16] were identified by spectroscopic methods on comparison with previously reported data. These isolates and some chemically transformed products were evaluated for their biological activities against a panel of cytotoxic and antioxidant assays as well as inhibitory activity against a cycloxygenase-2 test system.



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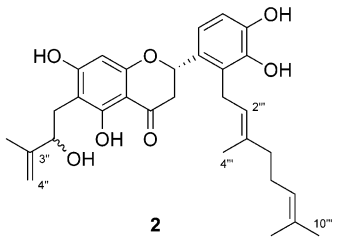

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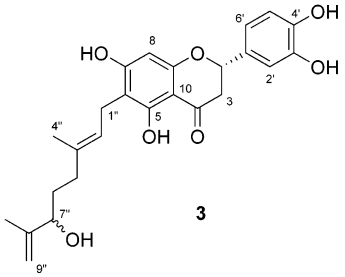

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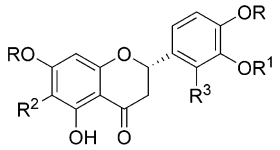

4 R = R^1 = R^3 = H, R^2 = geranyl
4b R = R^1 = Me, R^3 = H, R^2 = geranyl
5 R = R^1 = R^2 = H, R^3 = geranyl
5a R = Me, R^1 = R^2 = H, R^3 = geranyl
5b R = R^1 = Me, R^2 = H, R^3 = geranyl
6 R = R^1 = H, R^2 = prenyl, R^3 = geranyl
6a R = Me, R^1 = H, R^2 = prenyl, R^3 = geranyl
6b R = R^1 = Me, R^2 = prenyl, R^3 = geranyl

Compound **1** was obtained as a colorless oil (3.2 mg). The HRFABMS (negative mode) showed a $[M - H]^-$ ion at *m/z* 225.1484, corresponding to $C_{13}H_{21}O_3$. The IR spectrum showed the presence of hydroxyl (ν_{max} 3406 cm^{-1}), carbonyl (ν_{max} 1713 cm^{-1}), and ether (ν_{max} 1127, 1039 cm^{-1}) groups. The ^{13}C NMR spectrum indicated 13 carbons, including three methyls, five methylenes, two methines, and three quaternary carbons, among which one was a keto carbonyl (δ_C 207.8). In the ^1H NMR spectrum, three methyl singlet signals at δ_H 1.23 and 0.98 were observed, including a less shielded *CH*$_3$CO signal at δ_H 2.15, in addition to the presence of a carbinolic proton signal at δ_H 4.06. The $^1H-^1H$ COSY spectrum indicated correlations between H-8 (δ_H 2.54)/H_2-7 (δ_H 1.75 and 1.58); H_2-7/H-6 (δ_H 1.28) and between H-3 (δ_H 4.06)/H_2-2 (δ_H 1.67 and 1.41), and H_2-4 (δ_H 1.88 and 1.41). Attachments of C-4 to C-5 and C-2 to C-1 were revealed from the $^1H-^{13}C$ correlations between H-2/C-1 (δ_C 43.0), C-3 (δ_C 66.2), C-4 (δ_C 41.5), C-6 (δ_C 53.6), and C-12 (δ_C 21.6) and between H-4/C-2 (δ_C 39.8), C-3, C-5 (δ_C 83.4), C-6, and C-11 (δ_C 25.4), respectively. A connectivity between C-7 and C-6 was evident from the long range $^1H-^{13}C$ correlations particularly between H-6 (δ_H 1.28)/C-2, C-4, C-5, C-7 (δ_C 18.5), C-8 (δ_C 43.0), C-11, and C-12.

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Table 1. ^{1}H and ^{13}C NMR Spectroscopic Data and HMBC Correlations of Compound **1** (in $CDCl_3$)[a]

position	δ_H	δ_C	HMBC (^{1}H→^{13}C)
1		43.0 s	
2	1.67 m, 1.41 m	39.8 t	C-1, C-3, C-4, C-6, C-12
3	4.06 dddd (17.1, 13.5, 10.4, 6.7)	66.2 d	
4	1.88 dd (13.2, 6.7) 1.41 m	41.5 t	C-2, C-3, C-5, C-6, C-11
5		83.4 s	
6	1.28 t (6.3)	53.6 d	C-2, C-4, C-5, C-7, C-8, C-11, C-12
7	1.75 m, 1.58 m	18.5 t	C-1, C-5, C-6, C-8, C-9
8	2.54 t (7.8)	43.0 t	C-6, C-7, C-9
9		207.8 s	
10	2.15 s	30.0 q	C-8, C-9
11	1.23 s	25.4 q	C-3, C-4, C-5, C-6
12	0.98 s	21.6 q	C-1, C-2, C-3, C-6, C-13
13	3.60 d (7.7) 3.42 dd (7.7, 2.3)	77.2 t	C-1, C-2, C-4, C-5, C-6, C-12

[a] Coupling constants are listed in parentheses in Hz. Multiplicities were assigned from DEPT experiments.

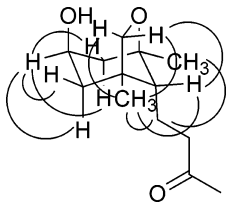

Figure 1. NOE correlations of **1**.

Placement of a keto group at C-9 (δ_C 207.8) was suggested from the ^{1}H−^{13}C correlations between H_2-7 and H_3-10 (δ_H 2.15)/C-9. The key ^3J ^{1}H−^{13}C correlation between H_2-13 (δ_H 3.60 and 3.42)/C-5 in conjunction with the absence of long range ^{1}H−^{13}C NMR correlation between H_3-12 (δ_H 0.98)/C-5 indicated an ether linkage between C(5)−O−C(13). Full assignments of the ^{1}H and ^{13}C NMR chemical shifts were established from the HMQC and HMBC correlations (Table 1). The relative configuration of **1** was revealed from the NOESY spectrum (Figure 1), which indicated the NOE interactions of H-3 with α-H and β-H of both H_2-2 and H_2-4, with the absence of the NOE effect between H-3 and H_2-13, suggesting that the OH-3 group and the ether linkage are both in β-axial arrangements. Compound **1** was therefore assigned as shown and has been given the trivial name tanarifuranonol.

Compound **2** was isolated as a yellow amorphous solid. The HRFABMS (positive mode) exhibited a $[M + H]^+$ ion at *m/z* 509.2542 and corresponded to the molecular formula $C_{30}H_{36}O_7$. The IR spectrum exhibited a hydroxyl group absorption band at ν_{max} 3430 cm^{-1} and a carbonyl group absorption band at ν_{max} 1635 cm^{-1}. The ^{13}C NMR spectrum of compound **2** showed 30 carbon signals, comprising four methyls, six methylenes including one vinylic carbon, seven methines, and 13 quaternary carbons, including one carbonyl (δ_C 196.3). The ^{1}H NMR spectrum of compound **2** in $CDCl_3$ (Table 2) exhibited the presence of nonequivalent methylene protons at δ_H 2.72 (1H, dd, J = 17.2 and 2.4 Hz) and 3.10 (1H, dd, J = 17.2 and 13.2 Hz) and a double doublet signal at δ_H 5.48 (1H, dd, J = 13.1 and 2.6 Hz, H-2) commonly found in a flavanone nucleus.[17] The low-field signal at δ_H 12.46 (1H, s) indicated a C-5-hydroxy proton intramolecularly hydrogen-bonded to the C-4 carbonyl oxygen atom. Aromatic proton signals at δ_H 6.95 (1H, d, J = 8.4 Hz) and 6.82 (1H, d, J = 8.4 Hz) indicated two *ortho*-coupled protons of a tetrasubstituted aromatic ring. Also, geranyl group signals were implied from the ^{1}H−^{1}H COSY spectrum. A signal at δ_H 3.46 (H-1‴) correlated with H-2‴ (δ_H 5.19) and also showed long-range ^{1}H−^{1}H correlations with a methyl group signal (H_3-4‴, δ_H 1.76) and the methylene proton signal at δ_H 2.08 (H_2-5‴). The H_2-5‴ signal also correlated with H_3-4‴ and H_2-6‴ (δ_H 2.06). In turn, the olefinic proton at δ_H 5.03 (H-7‴) showed a cross-peak not only with H-6‴ but also with the two methyl group signals at δ_H 1.66 (H_3-9‴) and 1.57 (H_3-10‴). In the ^{1}H−^{1}H COSY spectrum, ^{1}H−^{1}H correlations were observed of the oxymethine proton at δ_H 4.34 (H-2″) with the nonequivalent methylene proton signals at δ_H 3.10 and 2.76 (H_2-1″) and the vinylic proton signals at δ_H 4.98 and 4.88 (H_2-4″), as well as a methyl proton signal at δ_H 1.84 (H_3-5″), and indicated the presence of a 2-hydroxy-3-methylbut-3-enyl group. Long-range ^{1}H−^{13}C correlations, particularly between H-2/C-2′ and H-1‴/C-1′, C-3′, and C-2‴ supported the attachment of a geranyl group to ring B at C-2′. The ^3J ^{1}H−^{13}C correlations between H-1″/C-5, C-6, and C-7 suggested the bonding of the 2-hydroxy-3-methylbut-3-enyl group to ring A at C-6. The application of ^{1}H−^{1}H COSY, HMQC, and HMBC NMR experiments led to full assignments of the ^{1}H and ^{13}C NMR chemical shifts, as shown in Table 2. The absolute stereochemistry at C-2 in **2** was established as *S* based on the observation of a positive Cotton effect at 333 nm and a negative Cotton effect at 297 nm in its circular dichroism spectrum.[18] Accordingly, the structure of **2** was assigned as shown, and this compound has been given the trivial name tanariflavanone C.

Compound **3** was obtained as a yellow amorphous solid. Its molecular formula, $C_{25}H_{28}O_7$, was obtained from the HRFABMS (positive mode), which exhibited a $[M + H]^+$ ion at *m/z* 441.1921. The FT-IR spectrum showed absorption bands at ν_{max} 3382 and 1641 cm^{-1}, indicating the presence of hydroxyl and carbonyl groups, respectively. The ^{13}C NMR spectrum of compound **3** showed 25 carbon signals, comprising two methyls, five methylenes, seven methines, and 11 quaternary carbons including one carbonyl (δ_C 196.0). The ^{1}H NMR spectrum of compound **3** exhibited C-3 methylene protons at δ_H 2.66 (1H, dd, J = 17.2 and 2.8 Hz) and 2.97 (1H, dd, J = 12.8 and 17.1 Hz) as well as a double doublet at δ_H 5.16 (1H, dd, J = 12.8 and 2.8 Hz, H-2), commonly observed in a flavanone nucleus, as found in **2**. The presence of a 6-hydroxy-3,7-dimethylocta-2,7-dienyl group was evident from the continuous ^{1}H−^{1}H COSY correlations between H-1″(δ_H 3.20)/H-2″ (δ_H 5.20), H_3-4″ (δ_H 1.72), and H-5″ (δ_H 1.96); H-5″/H-2″, H_3-4″, and H_2-6″ (δ_H 1.58); and H-7″ (δ_H 3.94)/H_2-6″, H-9″ (δ_H 4.81 and 4.74), and H_3-10″ (δ_H1.63). The presence of a pair of AB proton doublets at δ_H 6.79 (d, 8.1) and 6.73 (d, 8.1) as well as a broad singlet signal at δ_H 6.86 indicated a trisubstituted aromatic ring. The long-range ^{1}H−^{13}C correlations in the HMBC spectrum particularly between H-1″/C-5, C-6, C-7, C-2″, and C-3″ indicated the attachment of the 6-hydroxy-3,7-dimethylocta-2,7-dienyl group at C-6 of ring A. Full assignment of all the ^{1}H and ^{13}C NMR chemical shifts (Table 2) were obtained by using ^{1}H−^{1}H COSY, HMQC, and HMBC NMR correlations. The absolute stereochemistry at C-2 in **3** was confirmed as *S* by a negative Cotton effect in the π→π^* transition region (∼300 nm) of the CD spectrum.[18] Therefore, the structure of **3** is as shown, and this compound has been assigned the trivial name tanariflavanone D.

The dimethoxy (**5a**, **6a**) and trimethoxy (**4b**, **5b**, **6b**) derivatives of compounds **4**−**6** were obtained after reacting compounds **4**, **5**, and **6** with diazomethane and purifying the products obtained using column chromatography. The

Table 2. ^{1}H and ^{13}C NMR Spectroscopic Data of Compounds **2** and **3** (in $CDCl_3$)[a]

	2			**3**	
position	δ_H	δ_C	position	δ_H	δ_C
2	5.48 dd (13.1, 2.6)	76.4 d	2	5.16 dd (12.8, 2.8)	78.9 d
3	3.10 dd (17.2, 13.2)	42.6 t	3	2.97 dd (17.1, 12.8)	43.1 t
	2.72 dd (17.2, 2.4)			2.65 dd (17.2, 2.8)	
4		196.3 s	4		196.0 s
5	OH-5, 12.46 s	161.9 s	5	OH-5, 12.18 s	164.1 s
6		106.0 s	6		108.2 s
7		161.7 s	7		160.9 s
8	6.07 s	96.7 d	8	5.91 s	95.0 d
9		165.6 s	9		161.0 s
10		102.6 s	10		102.5 s
1′		128.5 s	1′		130.7 s
2′		126.3 s	2′	6.86 br s	113.3 d
3′	5.48	142.5 s	3′		144.5 s
4′		144.9 s	4′		144.9 s
5′	6.82 d (8.4)	113.0 d	5′	6.79 d (8.1)	115.2 d
6′	6.95 d (8.4)	119.0 d	6′	6.73 d (8.1)	118.6 d
1″	3.10 m 2.76 m	28.0 t	1″	3.20 d (6.8)	20.9 t
2″	4.34 d (7.8)	77.6 d	2″	5.20 t (6.8)	122.9 d
3″		146.7 s	3″		135.6 s
4″	4.98, 4.88	110.5 t	4″	1.72 s	15.8 q
5″	1.84 s	18.6 q	5″	1.96 t (6.7)	35.8 t
1‴	3.46 br d (6.8)	25.5 t	6″	1.58 dd (6.7, 6.3)	32.8 t
2‴	5.19 t (6.4)	121.3 d	7″	3.94 t (6.2)	75.7 d
3‴		139.2 s	8″		147.2 s
4‴	1.76 s	16.3 q	9″	4.81 br s	110.8 t
				4.74 br s	
5‴	2.08 m	39.6 t	10″	1.63 s	17.5 q
6‴	2.06 m	26.3 t			
7‴	5.03 obs t (6.8)	123.7 d			
8‴		132.3 s			
9‴	1.66 s	25.7 q			
10‴	1.57 s	17.7 q			

[a] Coupling contants are listed in parentheses in Hz. Multiplicities were assigned from DEPT experiments.

spectroscopic data of these derivatives were closely related to the parent compounds with the presence of additional OMe signals in the ^{1}H and ^{13}C NMR spectra. All ^{1}H and ^{13}C chemical shifts of these compounds were fully assigned using the ^{1}H−^{1}H COSY, HMQC, and HMBC NMR correlations (Tables S1−S3, Supporting Information).

All of the isolated compounds including the methylated products **4b**, **5a**, **5b**, **6a**, and **6b**, with the exception of compound **1** and annuionone E, were tested for anti-inflammatory activity in a cyclooxygenase-2 (COX-2) inhibition assay, as well as cytotoxic activity using human oral carcinoma (KB), human breast cancer (BC), and human small cell lung cancer (NCI-H187) cell lines. Only compound **5** showed inhibitory effect in the COX-2 cell assay system with an IC_{50} value of 3.7 μg/mL. Compounds **2**, **4b**, **5**, **5a**, **5b**, **6**, **6a**, **6b**, tanariflavanone B, blumenol A, and blumenol B were inactive with all cytotoxic assays, whereas weak cytotoxic activities of **3** [BC (IC_{50} 6.5 μg/mL)] and **4** [KB (IC_{50} 4.6 μg/mL), BC (IC_{50} 2.7 μg/mL), and NCI-H187 (IC_{50} 1.5 μg/mL)] were observed. With the Vero cell line, compounds **3** and **4** showed IC_{50} values of 19.5 and 3.8 μg/mL, respectively. Compounds **2**−**6**, **6a**, and **6b** were tested for antioxidant activity with the DPPH stable radical test. Compounds **3**−**5** and **6** exhibited comparable radical-scavenging properties with IC_{50} values of 20 ± 1, 14 ± 1, 13 ± 2, and 15 ± 2 μM, respectively, and were stronger than compound **2** and 2,6-di(*tert*-butyl)-4-methylphenol (BHT), which showed IC_{50} values of 33 ± 1 and 30 ± 1 μM, respectively. Replacement of oxidizable phenolic hydroxyl groups with OMe groups as in compounds **6a** and **6b** resulted in a strong decrease of antioxidant activity, since **6a** and **6b** showed IC_{50} values of 413 ± 2 and 599 ± 2 μM, respectively.

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a JASCO DIP 1020 polarimeter. CD spectra were recorded on a JASCO J-810 spectrometer. The IR spectra were obtained on a Perkin-Elmer 1760x FT-IR spectrophotometer. ^{1}H and ^{13}C spectra were obtained with a Bruker AVANCE 400 MHz spectrometer with the solvent signal as internal reference. EIMS and HRFABMS were recorded on a Finnigan MAT 90 instrument.

Plant Material. The leaves of *Macaranga tanarius* were collected from the Krachong waterfall area, Trang Province, Thailand, in April 2001. Dr. K. Chayamarit of the Forest Herbarium, Royal Forest Department, Bangkok, kindly identified the plant material. A voucher specimen (SSMT/2001) is kept at the Department of Chemistry, Faculty of Science, Ramkhamhaeng University.

Extraction and Isolation. The *n*-hexane extract of the leaves (143.2 g) was subjected to silica gel column chromatography with a gradient of *n*-hexane−EtOAc (95:5) to $CHCl_3$−MeOH (30:70) to obtain 11 fractions. Fraction 10 was column chromatographed [silica gel, *n*-hexane−$CHCl_3$ (70:30) to $CHCl_3$−MeOH (50:50)] to give 10 subfractions (10.1−10.10). Subfraction 10.9 was further separated by reversed-phase column chromatography (C_{18} silica gel, H_2O−MeOH, 20:80 to 0:100) to give six subfractions (10.9.1−10.9. 6). Subfraction 10.9.1 was purified using reversed-phase silica gel (H_2O−MeOH, 20:80 to 0:100) to give subfractions 10.9.1.1−10.9.1.6. Subfraction 10.9.1.3 was chromatographed [silica gel, *n*-hexane−$CHCl_3$ (90:10) to $CHCl_3$−MeOH (20:80)] to give nine subfractions. Subfraction 10.9.1.3.7 contained annuionone E (17.6 mg), and subfraction 10.9.1.3.8 contained blumenol B (10.2 mg). Subfraction 10.5 was purified using silica gel column chromatography [*n*-hexane−$CHCl_3$ (10:90) to $CHCl_3$−MeOH (50:50)] and yielded six subfractions (10.5.1−10.5.6). Subfracation 10.5.4 contained compound **6** (372.7 mg). Further purification of subfraction 10.5.5 [2×, silica gel, *n*-hexane−$CHCl_3$ (10:90) to

$CHCl_3$–MeOH (50:50), then *n*-hexane–$CHCl_3$ (20:80) to $CHCl_3$–MeOH (80:20)] gave tanariflavanone B (2.7 mg).

The chloroform extract (122.3 g) of *M. tanarius* was fractionated using silica gel column chromatography with a gradient of *n*-hexane–$CHCl_3$ (10:90) to $CHCl_3$–MeOH (20:80) and yielded 13 fractions. Fraction 10 after reversed-phase column chromatography (C_{18} silica gel, H_2O–MeOH, 30:70 to 0:100) gave an additional amount of compound **6** (500 mg). Fraction 12 was purified using silica gel column chromatography [$CHCl_3$–MeOH (99.5:0.5) to (50:50)] and afforded six subfractions (12.1–12.6). Subfraction 12.2 was column chromatographed using C_{18} silica gel (H_2O–MeOH, 30:70 to 0:100) to give seven subfractions (12.2.1–12.2.7). Subfraction 12.2.2 was purified (silica gel, *n*-hexane–EtOAc, 95:5 to 70:30) to give four further subfractions (12.2.2.1–12.2.2.4). Subfraction 12.2.2.1 contained compound **5** (53.7 mg), and subfraction 12.2.2.4 after column chromatography (silica gel, $CHCl_3$–MeOH, 99:1) gave compound **3** (5.3 mg). Subfraction 12.5 was rechromatographed (C_{18} silica gel, H_2O–MeOH, 30:70 to 0:100), then silica gel column chromatography ($CHCl_3$–MeOH, 99:1 to 80:20) gave 10 subfractions. Subfraction 12.5.5 contained compound **4** (17.4 mg). Fraction 11 was column chromatographed [silica gel, *n*-hexane–CH_2Cl_2 (20:80) to CH_2Cl_2–MeOH (70:30)] to yield 14 subfractions (11.1–11.14). Subfraction 11.8 was further purified using silica gel column chromatography [*n*-hexane–CH_2Cl_2 (10:90) to CH_2Cl_2–MeOH (70:30)] to obtain 12 subfractions (11.8.1–11.8.12). Subfraction 11.8.9 after column chromatography (silica gel, CH_2Cl_2–MeOH, 100:0 to 70:30) gave an additional quantity of compound **6** (10.1 mg). Subfraction 11.8.12 was carefully purified using C_{18} column chromatography (H_2O–MeOH, 50:50 to 0:100) to give 15 subfractions. Subfraction 11.8.12.11 contained compound **2** (5.6 mg). Fraction 13 was fractionated using silica gel column chromatography (CH_2Cl_2–MeOH, 100:0 to 70:30) to yield 15 subfractions. Subfraction 13.15 was further purified (silica gel, $CHCl_3$), and a fraction of medium polarity (subfraction 13.15.10) was fractionated using C_{18} column chromatography (H_2O–MeOH, 40:60 to 0:100). The most polar fraction after further column chromatography (2×, silica gel, CH_2Cl_2–MeOH, 98:2, then CH_2Cl_2–MeOH, 99:1) yielded compound **1** (4.5 mg) and blumenol A (21.1 mg).

Tanarifuranonol (1): oil; $[\alpha]_D$ 13.3° (*c* 0.08, $CHCl_3$); IR (KBr) ν_{max} 3406, 2931, 2870, 1768, 1713, 1455, 1434, 1378, 1265, 1168, 1127, 1039, 1013, 824, 723, 642, 538 cm^{-1} ; ^1H and ^{13}C NMR data, see Table 1; HRFABMS (negative mode) $[M - H]^-$ 225.1484 (calcd for $C_{13}H_{21}O_3$, 225.1491).

Tanariflavanone C (2*S*)-5,7,3′,4′-tetrahydroxy-6-(2-hydroxy-3-methylbut-3-enyl)-2′-(geranyl)flavanone (2): amorphous solid; $[\alpha]_D$ −3.1° (*c* 0.27, MeOH); CD (*c* 9.6×10^{-4} M, EtOH, 23 °C, $\Delta\epsilon$) 254 (1.31), 297 (−1.92), 333 (0.24) nm; IR (KBr) ν_{max} 3430, 2922, 1635 (br), 1455, 1340, 1294, 1158, 1095, 1005, 902, 817, 758, 550 cm^{-1}; ^1H and ^{13}C NMR data, see Table 2; HMBC correlations H-2/C-1′, C-2′, C-6′; H-3/C-2, C-4, C-9; H-8/C-6, C-7, C-9, C-10; H-5′/C-1′, C-3′, C-4′; H-6′/C-2′, C-4′; H-1″/C-5, C-6, C-7, C-2″, C-3″; H-2″/C-6, C-1″, C-4″, C-5″; H-4″/C-2″, C-3″, C-5″; H-5″/C-2″, C-3″, C-4″; H-1‴/C-1′, C-3′, C-2‴, C-3‴; H-2‴/C-1‴, C-4‴, C-5‴; H-4‴/C-2‴, C-3‴, C-5‴; H-5‴/C-2‴, C-4‴, C-6‴, C-7‴; H-6‴/C-3‴, C-5‴; H-9‴/C-7‴, C-8‴, C-10‴; H-10‴/C-7‴, C-8‴, C-9‴; 5-OH/C-5, C-6, C-10; HRFABMS (positive mode) $[M + H]^+$ 509.2542 (calcd for $C_{30}H_{37}O_7$, 509.2539).

Tanariflavanone D (2*S*)-5,7,3′,4′-tetrahydroxy-6-(6-hydroxy-3,7-dimethylocta-2′,7′-dienyl)flavanone (3): pale yellow amorphous solid; $[\alpha]_D$ −12.7° (*c* 0.24, MeOH); CD (*c* 1.0×10^{-3} M, EtOH, 23 °C, $\Delta\epsilon$) 254 (0.52), 302 (−1.05), 333 (0.82) nm; IR (KBr) ν_{max} 2919, 1738, 1635, 1455, 1338, 1296, 1159, 1085, 1019, 815, 777, 453 cm^{-1}; ^1H and ^{13}C NMR data (measured in $CDCl_3$), see Table 2; HMBC correlations H-2/C-3, C-1′, C-2′, C-6′; H-3/C-2, C-4, C-10, C-1′; H-8/C-4, C-6, C-10; H-2′/C-2, C-3′, C-4′, C-6′; H-5′/C-1′, C-3′; H-6′/C-2, C-2′, C-4′; H-1″/C-5, C-6, C-7, C-2″, C-3″; H-2″/C-6, C-1″, C-4″, C-5″; H-4″/C-2″, C-5″; H-5″/C-2″, C-4″, C-6″, C-7″; H-6″/C-5″, C-7″; H-7″/C-5″, C-6″, C-8″, C-9″, C-10″; H-9″/C-7″, C-8″, C-10″; H-10″/C-7″, C-8″, C-9″; HRFABMS (positive mode) $[M + H]^+$ 441.1921 (calcd for $C_{25}H_{29}O_7$, 441.1914).

Bioassays. An anti-inflammation (COX-2) assay was performed by analyzing for PGE_2 production in the presence of test samples, as described previously by Kirtikara and coworkers.[19] The cytotoxicity assays were performed using the colorimetric method as described by Skehan and co-workers.[20,21] Antioxidant assay for radical-scavenging properties of test compounds was undertaken using a DPPH stable radical.[22]

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds **1**–**3**, the tabulated ^1H and ^{13}C NMR spectroscopic data of compounds **4b**, **5a, 5b, 6a**, and **6b** (Tables S1–S3). This material is available free of charge via the Internet at http://pubs.acs.org.

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