New Bioactive Prenylflavonoids and Dibenzocycloheptene Derivative from Roots of *Dendrolobium lanceolatum*

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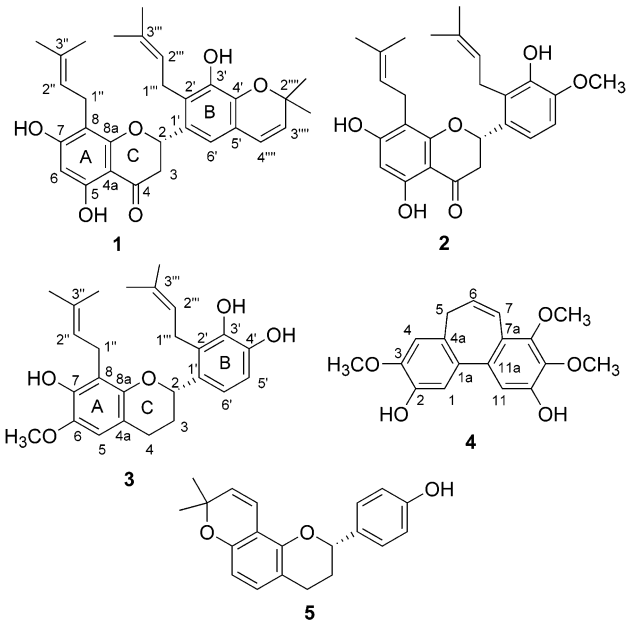
Two new flavanones (**1** and **2**), a new flavan (**3**), and a new rare dibenzocycloheptene derivative (**4**) together with a known flavan, 4′-hydroxy-2″,2″dimethyl-pyranoflavan (**5**), were isolated from the roots of *Dendrolobium lanceolatum*. Their structures were established on the basis of spectral evidence, and an X-ray analysis was performed to confirm the structure of **4**. Compounds **1**−**3** exhibited antimalarial activity with IC_{50} values of 2.6, 3.3, and 3.1 μg/mL, respectively. Compounds **1**−**5** showed moderate antimycobacterial activity with MIC values of 6.3, 12.5, 25, 25, and 50 μg/mL, respectively. In addition, **1** showed strong cytotoxicity against cancer cell lines KB, BC, and NCI-H187 with IC_{50} values of 1.2, 1.6, and 0.6 μg/mL, respectively, while **2** showed moderate cytotoxicity against the NCI-H187 cell line with an IC_{50} value of 8.1 μg/ mL.

Dendrolobium lanceolatum (Dunn) Schindl. (Leguminosae-Papilonoideae) is a shrub, 1−3 m in height, growing widely in the northeastern part of Thailand. It is known as Kraduk-Khiat or Kraduk-Ueng, and a water decoction of the roots is used traditionally as a diuretic and for urinary disease.[1] The synonyms available are *Lespedeza lanceolata* Dunn and *Desmodium lanceolatum* (Dunn) Schindl.[2] Neither a phytochemical investigation nor the biological activity of this plant has been previously reported. However, data of its synonymous *Lespedeza* and *Desmodium* species have been reported.[3−14] As part of our search for bioactive constituents from Thai plants, the hexane and CH_2Cl_2 extracts of air-dried roots of *D. lanceolatum* exhibited antiplasmodial activity against *Plasmodium falciparum* (IC_{50} 5.5 and 2.0 μg/mL, respectively), antimycobacterial activity against *Mycobacterium tuberculosis* (MIC 100 μg/mL for both), and cytotoxic activity against several tumor cell lines (IC_{50} range 6−20 μg/mL). We report herein the isolation, characterization, and bioactivities of four new compounds: two flavanones (**1** and **2**), a flavan (**3**), and a rare dibenzocycloheptene derivative (**4**), along with one known compound, 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan (**5**).[15]



Results and Discussion

Hexane and CH_2Cl_2 extracts of *D. lanceolatum* roots were separated and purified by silica gel column chromatography to afford **1**−**4**, together with the known flavan **5**. Structures of these compounds were elucidated by spectroscopic methods, including 2D NMR experiments (COSY, HSQC, HMBC, and NOESY). The structure of **4** was confirmed by X-ray analysis.

Compound **1** was obtained as a pale yellow amorphous powder and had the molecular formula $C_{30}H_{34}O_6$ as deduced from the ESI-TOF mass spectrum (observed *m*/*z* 491.2440 $(M + H)^+$). The IR spectrum of **1** showed strong absorptions at 1638 cm^{-1} (chelated C═O group) and 3406 cm^{-1} (OH). UV absorption maxima at λ_{max} 287 and 337-(sh) nm were indicative of a flavanone structure.[16] The ^1H and ^{13}C NMR (Table 1) together with HSQC experiments of **1** indicated the presence of one ketone carbonyl, 12 sp^2 quarternary, six sp^2 methine, one sp^3 quarternary, one sp^3 methine, three methylene, and six methyl carbons. The spin systems located at δ 5.46 (1H, dd, J = 13.6, 2.5 Hz, H-2), 3.05 (1H, dd, J = 17.2, 13.6 Hz, H-3α), and 2.70 (1H, dd, J = 17.2, 2.5 Hz, H-3β) together with a carbonyl resonance at δ 197.0 in the ^{13}C NMR spectrum indicated the presence of flavanone skeleton. The presence of two *cis*-coupled olefinic protons at δ 6.32 and 5.61 (both 1H, d, J = 9.8 Hz) together with two methyl group resonances at δ 1.48 (6H, s) in the ^1H NMR spectrum and a quaternary carbon at δ 77.7 in the ^{13}C NMR spectrum indicated a 2,2-dimethylpyran system. Since there were only two aromatic proton signals at δ 6.02 (1H, s, H-6) and 6.78 (1H, s, H-6′), the number of substituents on ring A and ring B were indicated. Two sets of resonances indicated the presence of 3-methyl-2-butenyl groups. A chelated hydroxyl at C-5 showed a signal at δ 12.03 (s), while the other two hydroxyl groups displayed signals at δ 6.27 (s, OH-7) and 5.60 (s,

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Table 1. ^{1}H and ^{13}C Spectral Data (δ, ppm) of Compounds **1**−**3** in $CDCl_3$[a]

	1		**2**		**3**	
position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
	5.46 dd (13.6, 2.5)	76.2	5.49 dd (13.6, 2.7)	76.2	5.03 dd (10.5, 1.9)	75.2
3α	3.05 dd (17.2, 13.6)	42.9	3.07 dd (17.2, 13.6)	42.8	1.96−2.20 m	29.6
3β	2.70 dd (17.2, 2.5)	42.9	2.72 dd (17.2, 2.7)	42.8	1.96−2.20 m	29.6
4		197.0		197.0	2.94 ddd (16.1, 11.3, 5.4) 2.71 ddd (16.1, 5.4, 3.1)	25.9
4a		103.0		103.1		111.6
5		162.3		162.3	6.45 s	108.8
6	6.02 s	96.7	6.03 s	96.8		140.7
7		163.7		163.7		142.5
8		106.1		106.2		116.1
8a		160.1		160.1		147.6
1′		129.2		129.9		132.4
2′		126.3		125.8		125.4
3′		142.4		143.6		142.1
4′		139.3		146.6		143.5
5′		118.9	6.81 d (8.4)	117.6	6.78 d (8.4)	112.9
6′	6.78 s	115.2	7.06 d (8.4)	108.4	6.98 d (8.4)	118.9
1″	3.29 d (7.2)	24.7	3.28 d (7.2)	21.8	3.34 d (6.8)	22.6
2″	5.19 br t (7.2)	121.7	5.18 br t (7.2)	121.7	5.23 br t (7.0)	122.7
3″		134.9		134.9		131.4
1‴	3.42 d (6.4)	21.8	3.46 d (6.4)	24.6	3.34 d (6.6)	25.4
2‴	5.08 br t (6.4)	122.3	5.09 br t (6.4)	122.3	5.19 br t (7.0)	122.1
3‴		132.3		132.4		134.8
2⁗		77.7				
3⁗	5.61 d (9.8)	130.3				
4⁗	6.32 d (9.8)	121.9				
OH-5	12.03 s		12.04 s			
OH-7	6.27 s		6.27 s		5.61 s	
OH-2′					5.47 s	
OH-3′	5.60 s		5.81 s			
OH-4′					5.42 br s	
CH_3-3″	1.71 s (6H)	17.8, 17.9	1.68 s, 1.71 s	17.8 17.9	1.65 br s 1.74 s	17.8 18.0
CH_3-3‴	1.67 s (6H)	25.6, 25.8	1.70 s, 1.66 s	25.6 25.8	1.67 s 1.80 s	25.7 25.8
CH_3-2⁗	1.48 s (6H)	28.2, 28.3				
OCH_3-6					3.82 s	56.5
OCH_3-4′			3.91 s	56.0		

[a] Figures in parentheses are coupling constants in Hz.

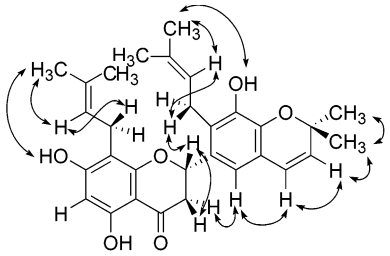

Figure 1. Selected NOESY correlations for compound **1**.

OH-3′). The HMBC spectrum clearly demonstrated the ^3J correlations of H-6 to C-4a and C-8; hydroxy proton at C-5 to C-6 and C-4a; hydroxy proton at C-7 to C-6 and C-8; H-1″ to C-7, C-8a, and C-3″; H-2 to C-4, C-2′, and C-6′; hydroxy proton at C-3′ to C-2′ and C-4′; H-6′ to C-2, C-2′, C-4′, and C-4⁗; H-1‴ to C-1′, C-3′, and C-3‴; H-3⁗ to C-5′ and CH_3-2⁗; and H-4⁗ to C-4′, C-6′, and C-2⁗. These results indicated that two 3-methyl-2-butenyl groups were connected to C-8 of ring A and C-2′ of ring B, whereas the dimethylpyran ring was fused to C-4′ and C-5′. The NOESY spectral data also supported this substitution pattern by showing the correlations of H-2 to H-3$_\beta$ and H-1‴; H-3 to H-2 and H-6′; and H-3⁗ to H-4⁗and CH_3-2⁗, where the other cross-peaks are as shown in Figure 1. Thus, the ^{1}H and ^{13}C assignments of **1** were made by a combination of COSY, HSQC, HMBC, and NOESY experiments and by comparison with the related compound, euchrestaflavanone C.[17] The specific optical rotation of **1** (−67.7°) together with the *trans* diaxial coupling constant of H-2 and H-3 ($J_{2,3ax}$ = 13.6 Hz) suggested the *S*-configuration at C-2 like those of known flavanones.[17] On the basis of the above spectroscopic evidence, the structure of **1** was elucidated as 5,7,3′-trihydroxy-4′,5′-(2⁗,2⁗-dimethylpyran)-8,2′-di(3-methyl-2-butenyl)-(2*S*)-flavanone.

Compound **2** was obtained as a pale yellow amorphous powder and had the molecular formula $C_{26}H_{30}O_6$ as deduced from the ESI-TOF mass spectrum (observed *m*/*z* 461.1944 $(M + Na)^+$). The IR spectrum of **2** showed strong absorptions at 1648 cm^{-1} (chelated C═O group) and 3380 cm^{-1} (OH). The UV absorption at λ_{max} 287 and 337(sh) nm again suggested a flavanone structure. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**. The obvious differences were an absence of the 2,2-dimethylpyran unit in ring B, which was displaced by a methoxy group (δ 3.91, s) on C-4′, and a proton on C-5′ (δ 6.81, d, J = 8.4 Hz, H-5′) that showed coupling to H-6′ (δ 7.06, d, J = 8.4 Hz). The HMBC data supported structure **2** by showing correlations of H-2 to C-4, C-2′, and C-6′; H-6 to C-4a and C-8; hydroxy proton at C-5 to C-6 and C-4a; hydroxy proton at C-7 to C-6 and C-8; hydroxy proton at C-3′ to C-2′ and C-4′; H-5′ to C-1′ and C-3′; H-6′ to C-2, C-2′, and C-4′; H-1″ to C-7, C-8a, and C-3″; and H-1‴ to C-1′, C-3′, and C-3‴. Key NOE

observations confirmed the substitution pattern. The NOESY spectrum of **2** showed correlations of H-2 to H-3$_\beta$ and H-1‴; H-3$_\beta$ to H-2 and H-6′; and H-5′ to H-6′, while the other correlations on ring A were similar to those of **1**. The complete assignment of protons and carbons in **2** (Table 1) was established by analyses of ^{1}H−^{1}H COSY, DEPT, HSQC, HMBC, and NOESY spectra. The assignment of *S*-configuration at C-2 was based on the specific optical rotation (−50.8°) and *trans* diaxial coupling (13.6 Hz) between H-2 and H-3 in ^{1}H NMR similar to those of known flavanones.[17] On the basis of these data, **2** was determined to be 5,7,3′-trihydroxy-4′-methoxy-8,2′-di(3-methyl-2-butenyl)-(2*S*)-flavanone.

Compound **3** was obtained as colorless crystals and had the molecular formula $C_{26}H_{32}O_5$ as deduced from the ESI-TOF mass spectrum (observed *m*/*z* 447.2146 (M + Na)$^+$). The IR spectrum of **3** showed absorptions at 1626, 1503 cm^{-1} (C=C) and 3375 cm^{-1} (OH). The UV spectrum displayed λ_{max} 207 and 287 nm, suggesting a simple aromatic chromophore. The ^{1}H and ^{13}C NMR spectra of **3** were similar to those of **2** except for the absence of a carbonyl signal at δ 197.0, which was replaced by the methylene protons H-4 at δ 2.94 (1H, ddd, J = 16.1, 11.3, 5.4 Hz) and 2.71 (1H, ddd, J = 16.1, 5.4, 3.1 Hz). The HMBC spectrum exhibited correlations of H-2 to C-4, C-2′, and C-6′; H-4 to C-2, C-4a, C-5, and C-8a; H-5 to C-4, C-7, and C-8a; methoxy protons to C-6; hydroxy proton at C-7 to C-6 and C-8; H-1″ to C-7, C-8, C-8a, and C-3″; H-1‴ to C-1′, C-3′, and C-3‴; hydroxy proton at C-3′ to C-2′, C-3′, and C-4′; hydroxy proton at C-4′ to C-3′, C-4′, and C-5′; H-5′ to C-3′ and C-1′; and H-6′ to C-2, C-2′, and C-4′. The NOESY spectrum showed correlations of H-2 to H-3 and H-1‴; H-3 to H-2 and H-6′; H-5 to H-4 and OCH$_3$-6; hydroxy proton at C-7 to CH$_3$-3″; hydroxy proton at C-3′ to CH$_3$-3‴; and hydroxy proton at C-4′ and H-5′ to H-6′. The HMBC and NOESY spectral evidence indicated the substitution pattern of **3**. The configuration of C-2 was suggested as *S* by the specific optical rotation value (−27.9°), and *trans* diaxial coupling (10.5 Hz) was apparent between H-2 and H-3. Thus, the structure of **3** was assigned as 7,3′,4′-trihydroxy-6-methoxy-8,2′-di(3-methyl-2-butenyl)-(2*S*)-flavan.

Compound **4** was obtained as colorless crystals and had the molecular formula $C_{18}H_{18}O_5$ as deduced from the ESI-TOF mass spectrum (observed *m*/*z* 315.1240 (M + H)$^+$). The IR spectrum of **4** showed absorptions at 3483 (OH) and 1511 (aromatic C=C). The ^{1}H NMR spectrum revealed three aromatic protons as three singlet signals at δ 7.09 (H-1), 7.02 (H-11), and 6.70 (H-4) and *cis* olefinic protons at δ 6.64 (1H, d, J = 10.4 Hz, H-7) and 6.15 (1H, m, H-6). A broad two-proton signal at δ 3.18−2.75 was assigned to the methylene (H-5) bearing an aromatic ring and an olefinic unit. The other aromatic ring substituents were two hydroxy (δ 5.80 and 5.47) and three methoxy groups (δ 3.98, 3.94, and 3.87). The ^{13}C NMR and DEPT spectra indicated 18 carbons attributable to nine sp^2 quarternary, five sp^2 methine, one sp^3 methylene, and three methyl carbons. HMBC correlations were observed from H-1 to C-3, C-4a, and C-11a; H-4 to C-2, C-3, C1a, C-4a, and C-5; H-6 to C-5 and C-7a; H-7 to C-11a, C-5, and C-8; H-11 to C-1a, C-7a, and C-9; hydroxy proton at C-2 to C-1, C-2, and C-3; and hydroxy proton at C-10 to C-9, C-10, and C-11, where the three methoxy protons correlated with their corresponding carbons, C-3, C-8, and C-9. The NOESY spectrum displayed correlations between H-1 and H-11, H-4 and OCH$_3$-3, H-6 and H-7, and H-7 and OCH$_3$-8. Thus, **4** was identified as a 3,8,9-trimethoxy-5*H*-dibenzo[*a*,*c*]-cycloheptene-2,10-diol. The structure of **4** was also confirmed by X-ray analysis (Figure 2). A few 5H-dibenzocycloheptene derivatives have been reported as synthesis products.[18,19] This is the first dibenzocycloheptene derivative from a natural source.

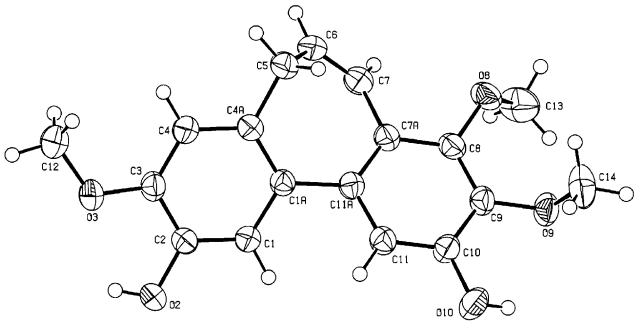

Figure 2. ORTEP diagram of the crystal structure of compound **4**.

The structure of flavan **5** was elucidated by analysis of ^{1}H, ^{13}C, ^{1}H−^{1}H-COSY, HSQC, and HMBC spectral data and confirmed by literature data comparison.[15]

The bioactivity test results of the isolated compounds **1**−**5** are shown in Table 2. Compounds **1**−**3** exhibited activity against *P. falciparum* with respective IC$_{50}$ values of 2.6, 3.1, and 3.3 μg/mL, while **1**−**5** exhibited moderate activity against *M. tuberculosis* with respective MIC values of 6.3, 12.5, 25, 25, and 50 μg/mL. Compound **1** also exhibited cytotoxicity against KB, BC, and NCI-H187 cell lines with respective IC$_{50}$ values of 1.2, 1.7, and 0.6 μg/mL, while **2** showed moderate cytotoxicity against the NCI-H187 cell line (IC$_{50}$ = 8.1 μg/mL).

Experimental Section

General Experimental Procedures. CC was carried out on silica gel 60 (230−400 mesh). NMR spectra were recorded in CDCl$_3$ on a Varian Mercury Plus 400 spectrometer, using residual CHCl$_3$ (δ 7.26) as an internal standard. IR spectra were carried out on a Tensor 27 Bruker (OPUS version 4) or Perkin-Elmer Spectrum One spectrophotometers. UV spectra were measured in MeOH on an Agilent 8453 UV−visible spectrophotometer. ESI-TOF mass spectra were obtained from a Micromass LCT mass spectrometer, and the lock mass calibration was applied for the determination of the accurate mass. Optical rotations were obtained using a JASCO DIP-1000 digital polarimeter. Melting points were determined using a Gallenkamp melting point apparatus and were uncorrected.

Plant Material. Roots of *D. lanceolatum* (Dunn) Schindl. were collected from Nakhon Phanom Province, Thailand, in April 2002 and identified by Prof. Pranom Chantaranothai, Department of Biology, Khon Kaen University. A voucher specimen (S. Kanokmedhakul 2) was deposited at the herbarium of the Department of Biology, Faculty of Science, Khon Kaen University, Thailand.

Extraction and Isolation. Air-dried roots of *D. lanceolatum* (5.5 kg) were ground and extracted successively with hexane (4 L × 3) and CH$_2$Cl$_2$ (4 L × 3) at room temperature. The filtered samples were combined, and the solvents were evaporated in vacuo to yield crude hexane (44.7 g) and CH$_2$Cl$_2$ extracts (18.0 g). The hexane extract was initially subjected to silica gel (500 g) CC and eluted with increasing concentrations of EtOAc in hexane followed by MeOH in EtOAc. Each fraction (100 mL) was monitored by TLC; fractions with similar TLC patterns were combined to yield eight major fractions (F$_1$−F$_8$). Purification of fraction F$_3$ (19.8 g) was carried out on silica gel (400 g) eluting with the gradient system above to give eight subfractions designated as F$_{3/1}$−F$_{3/8}$. Subfraction F$_{3/4}$ (3.4 g) eluted with EtOAc/hexane (40:50, 2 L) was further purified by silica gel CC to give seven subfractions designated as F$_{3/4-1}$−F$_{3/4-7}$. Subfraction F$_{3/4-3}$ was rechromatographed on a silica gel column eluted with a

Table 2. Biological Activities of Compounds **1**−**5**

compound	antimalarial (IC_{50}, μg/mL)	antimycobacterial (MIC, μg/mL)	cytotoxicity (IC_{50}, μg/mL)		
			KB[a]	BC[b]	NCl-H187[c]
1	2.6	6.3	1.2	1.7	0.6
2	3.3	12.5	inactive[d]	inactive[d]	8.1
3	3.1	25.0	inactive[d]	inactive[d]	inactive[d]
4	inactive[d]	50.0	inactive[d]	inactive[d]	inactive[d]
5	inactive[d]	25.0	inactive[d]	inactive[d]	inactive[d]
artemisinin	0.001				
isoniazid		0.04 ± 0.09			
kanamycin sulfate		2.0−5.0			
ellipticine			0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1

[a] Human epidermoid carcinoma in the mouth. [b] Human breast cancer cells. [c] Human lung cancer cells. [d] Inactive at 20 μg/mL.

gradient system of hexane/EtOAc to give a pale yellow solid, **1** (14.7 mg). Further chromatography of subfraction $F_{3/4-6}$ on silica gel eluted with a gradient system of hexane/EtOAc afforded **2** (86.2 mg) and **3** (117.1 mg). Purification of the CH_2Cl_2 extract (18 g) on silica gel (300 g) eluted with a gradient of hexane/EtOAc gave eight fractions, F'_1−F'_8. Fraction F'_2 was rechromatographed on a silica gel column eluted with hexane and a gradient of EtOAc to yield 21.9 mg of compound **5**. Fraction F'_4 was rechromatographed on a silica gel column eluted with hexane and a gradient of EtOAc to yield compound **4** (6.8 mg).

Antimalarial Assay. Antimalarial activity was evaluated against the parasite *Plasmodium falciparum* (K1, multidrug-resistant strain), using the method of Trager and Jensen.[20] Quantitative assessment of malarial activity in vitro was determined by means of the microculture radioisotope technique based on the method described by Desjardins et al.[21] The inhibitory concentration (IC_{50}) represents the concentration that causes 50% reduction in parasite growth as indicated by the in vitro uptake of [^{3}H]-hypoxanthine by *P. falciparum*. The standard compound was artemisinin (Table 2).

Antimycobacterial Assay. Antimycobacterial activity was assessed against *Mycobacterium tuberculosis* H37Ra using the Microplate Alamar Blue Assay (MABA).[22] Standard drugs, isoniazid and kanamycin sulfate, were used as the reference compounds (Table 2).

Cytotoxicity Assay. Cytotoxic assays against human epidermoid carcinoma (KB), human breast cancer (BC), and human small cell lung cancer (NCI-H187) cell lines were performed employing the colorimetric method as described by Skehan and co-workers.[23] The reference substance was ellipticine (Table 2).

Compound 1: pale yellow amorphous powder; mp 188−190 °C; $[\alpha]_D^{26.8}$ −67.7° (*c* 0.68, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 211 (5.06), 230 (5.04), 287 (4.70) 337 (4.05) nm; IR (KBr) ν_{max} 3406, 2971, 2926, 1638, 1439 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; ESI-TOF MS *m*/*z* 491.2440 [M + H]$^+$ (calcd for $C_{30}H_{34}O_6$ + H, 491.2435).

Compound 2: pale yellow amorphous powder; mp 162−164 °C; $[\alpha]_D^{27.5}$ −50.8° (*c* 0.78, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 206 (4.50), 287 (3.88), 337 (3.50) nm; IR (KBr) ν_{max} 3380, 2924, 1648, 1605, 1498, 1437, 1270, 1064, 827, 789 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; ESI-TOF MS *m*/*z* 461.1944 [M + Na]$^+$ (calcd for $C_{26}H_{30}O_6$ + Na, 461.1940).

Compound 3: colorless crystals; mp 128−129 °C; $[\alpha]_D^{25.6}$ −27.9° (*c* 1.20, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 207 (4.70), 287 (3.60) nm; IR (KBr) ν_{max} 3375, 2962, 2914, 2853, 1626, 1503, 1485, 1335, 1289, 1055 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; ESI-TOF MS *m*/*z* 447.2146 [M + Na]$^+$ (calcd for $C_{26}H_{32}O_5$ + Na, 447.2147).

Compound 4: colorless needles; mp 194−196 °C; UV (MeOH) λ_{max} (log ϵ) 206 (3.94), 247 (3.88), 294 (3.40) nm; IR (KBr) ν_{max} 3483, 3033, 2962, 2939, 1511, 1487, 1271 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.09 (1H, s, H-1), 7.02 (1H, s, H-11), 6.70 (1H, s, H-4), 6.64 (1H, d, *J* = 10.4 Hz, H-7), 6.15 (1H, m, H-6), 5.80 (1H, s, O*H*-10), 5.47 (1H, s, O*H*-2), 3.98 (3H, s, OC*H*$_3$-9), 3.94 (3H, s, OC*H*$_3$-3), 3.87 (3H, s, OC*H*$_3$-8), 3.18−2.75 (2H, br m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.7 (C, C-8), 147.8 (C, C-10), 146.6 (C, C-3), 143.9 (C, C-2), 138.5 (C, C-9), 136.5 (C, C-11a), 134.5 (C, C-4a), 131.1 (C, C-1a), 130.0 (CH, C-6), 123.4 (CH, C-7), 123.2 (C, C-7a), 116.2 (CH, C-1), 111.2 (CH, C-11), 109.3 (CH, C-4), 61.2 (CH$_3$, O*C*H$_3$-9), 60.8 (CH$_3$, O*C*H$_3$-8), 56.2 (CH$_3$, O*C*H$_3$-3), 33.2 (CH$_2$, C-5); ESI-TOF MS *m*/*z* 315.1240 [M + H]$^+$ (calcd for $C_{18}H_{18}O_5$ + H, 315.1233).

X-ray Structure Determination of Compound 4. Crystal data of **4**: $C_{18}H_{18}O_5$, MW 314.34, orthorhombic, $P2_12_12_1$, a = 9.1692(2) Å, b = 10.5530(3) Å, c = 15.8312(5) Å, V = 1531.87(7) Å^3, D_x = 1.363 g/cm^3, Z = 4. A total of 16 122 reflections, of which 2008 were unique (1823 observed, $|F_o| > 4\sigma|F_o|$), were measured at room temperature from a 0.25 × 0.20 × 0.15 mm^3 colorless crystal using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) on a Bruker-Nonius kappaCCD diffractometer. The crystal structure was solved by direct methods using SIR-97, and then all atoms except hydrogen atoms were refined anisotropically by a full-matrix least-squares method on F^2 using SHELXL-97 to give a final R-factor of 0.0374 (R_w = 0.1050 for all data) with a data-to-parameter ratio of 9.61:1.

Crystallographic data of compound **4** have been deposited at the Cambridge Crystallographic Data Centre under the reference number CCDC 220155. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

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Note Added after ASAP: There was a typo in the ESI-TOF MS data for compound **2** in the version posted on May 1, 2004. The correction appears in the version posted on May 17, 2004.

Supporting Information Available: X-ray crystallographic tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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