Phenolic Constituents of the Roots of *Sophora flavescens*

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From the roots of *Sophora flavescens* collected in Taiwan, four new prenylflavonoids, sophoraflavanone K (**1**), sophoraflavanone L (**2**), 8-lavandulylkaempferol (**3**), and cyclokuraridin (**4**), a new arylbenzofuran, 2-(2,4-dihydroxy-5-prenylphenyl)-5,6-methylenedioxybenzofuran (**5**), and a new prenyldibenzoyl derivative, sophoradione (**6**), were isolated. The structures of **1**−**6** were determined by spectroscopic data analysis. Compounds **2**−**6** were evaluated for cytotoxic activity against the KB epidermoid carcinoma cell line.

The root of *Sophora flavescens* Ait. (Leguminosae) is a Chinese herb found to exhibit antibacterial, anti-inflammatory, antipyretic, antiarrhythmic, antiasthmatic, antiulcerative, and antineoplastic effects and is used to treat jaundice, leukorrhea, carbuncles, pyogenic infections of the skin, scabies, enteritis, and dysentery.[1] In previous studies, quinolizidine alkaloids, flavonoids, benzofuran, and triterpenoids have been isolated from the roots of *S. flavescens*.[2−16] In the course of screening for cytotoxic constituents from herbs growing in Taiwan, we found that a crude extract of the roots of *S. flavescens* exhibited cytotoxic activity against KB tumor cells. In this paper, we report the isolation and structure elucidation of six new compounds (**1**−**6**) and their cytotoxic activities against a KB tumor cell line.

The dried, chipped roots of *S. flavescens* were extracted with MeOH. The MeOH extract was suspended in water to give water-soluble and water-insoluble portions. The water-insoluble portion was chromatographed repeatedly using Sephadex LH-20, silica gel, preparative TLC, and HPLC to afford six new compounds, sophoraflavanone K (**1**), sophoraflavanone L (**2**), 8-lavandulylkaempferol (**3**), cyclokuraridin (**4**), 2-(2,4-dihydroxy-5-prenylphenyl)-5,6-methylenedioxybenzofuran (**5**), and sophoradione (**6**).

The HREIMS of compound **1** indicated a molecular ion peak at *m*/*z* 454.1991, which corresponded to the molecular formula $C_{26}H_{30}O_7$. Hydroxyl (3395 cm^{-1}) and carbonyl (1635 cm^{-1}) absorptions were observed in the IR spectrum. The ^{1}H NMR spectrum of **1** showed resonances for a methoxy group at δ_H 3.67 and a chelated hydroxyl group at δ_H 12.40 and typical flavanone[17] signals at δ_H 2.55 (1H, dd, J = 2.5, 17.0 Hz, H-3α), 3.08 (1H, dd, J = 13.0, 17.0 Hz, H-3β), and 5.57 (1H, dd, J = 2.5, 13.0 Hz, H-2). It also exhibited signals for a lavandulyl group[4,17] at δ 1.44 (3H, s, H$_3$-6″), 1.50 (3H, s, H$_3$-7″), 1.58 (3H, d, J = 1.0 Hz, H$_3$-10″), 2.01 (2H, m, H$_2$-3″), 2.49 (1H, m, H-2″), 2.53 (2H, m, H$_2$-1″), 4.43 (1H, br s, H-9″b), 4.47 (1H, d, J = 1.0 Hz, H-9″a), and 4.93 (1H, t, J = 2.5 Hz, H-4″). Like other lavandulyl flavonoids isolated from *S. flavescens*, the absolute configuration at C-2″ of the lavandulyl group in compound **1** has not been determined.[18] The HMBC correlations of OH-5 (δ_H 12.40)/C-6, C-10 and H-1″/C-7, C-9 clearly revealed that the lavandulyl group is linked to C-8. Furthermore, two singlet signals at δ_H 6.35 (1H) and 6.98 (1H) suggested that the B-ring of **1** is 1,2,4,5-tetrasubstituted. In the NOE experiment, irradiation of the methoxy group at δ_H 3.67 caused enhancement of H-6′ (δ_H 6.98), correlating with C-2 in the HMBC spectrum. Thus, the linkage of the methoxy group to C-5′ was confirmed. On the basis of the above evidence, the new compound sophoraflavanone K (**1**) was determined to be 5,7,2′,4′-tetrahydroxy-8-lavandulyl-5′-methoxyflavanone.

The EIMS of **2** showed a molecular ion at *m*/*z* 424, corresponding to a molecular formula of $C_{25}H_{28}O_6$. The IR spectrum exhibited hydroxyl (3432 cm^{-1}) and carbonyl (1629 cm^{-1}) absorptions. The NMR signals at δ_H 2.77 (1H, dd, J = 2.8, 17.2 Hz), 3.11 (1H, dd, J = 12.8, 17.2 Hz), and 5.67 (1H, dd, J = 2.8, 12.8 Hz) indicated that **2** is also a flavanone. In the ^{1}H NMR spectrum of **2**, an aromatic proton at δ_H 6.13 (s), an ABX system of aromatic protons at δ_H 6.47 (1H, d, J = 2.4 Hz), 6.43 (1H, dd, J = 2.4, 8.4 Hz), and 7.33 (1H, d, J = 8.4 Hz), and a chelated hydroxyl group at δ_H 12.26 were apparent. Also revealed were a 3,3-dimethylallyl group at δ_H 1.58 (3H, s, H$_3$-4″), 1.61 (3H, s, H$_3$-5″), 3.22 (2H, d, J = 7.2 Hz, H-1‴), and 5.15 (1H, t, J = 7.2 Hz, H-2″) and a 3,3-dimethylallyloxy moiety at δ_H 1.76 (3H, s, H-4‴), 1.78 (3H, s, H-5‴), 4.63 (2H, d, J = 6.8 Hz, H-1‴), and 5.49 (1H, t, J = 6.8 Hz, H-2‴). The 3,3-dimethylallyl group was assigned to C-8, which was supported by HMBC cross-peaks: OH-5/C-5, C-6, and C-10 and H-1″/C-3″, C-7, C-8, and C-9. HMBC connectivities from H-1‴ to C-3‴ and C-7 indicated that the 3,3-dimethylallyloxy moiety was attached to C-7. Thus, compound **2** was characterized as 5,2′,4′-trihydroxy-7-(γ,γ-dimethylallyloxy)-8-(γ,γ-dimethylallyl)flavanone and has been named sophoraflavanone L.

The molecular formula of **3** was shown to be $C_{25}H_{26}O_6$ by HREIMS analysis. The IR spectrum exhibited the presence of hydroxyl (3316 cm^{-1}) and carbonyl (1629 cm^{-1}) groups. UV absorptions at λ_{max} 373, 307, and 272 nm indicated its flavonol character. The ^{1}H NMR spectrum of **3** showed an aromatic proton singlet at δ_H 6.20 (H-6) and a typical A_2B_2 system at δ_H 6.90 (2H, d, J = 9.0 Hz, H-3′,5′) and 8.08 (2H, d, J = 9.0 Hz, H-2′,6′). Like compound **1**, compound **3** also displayed the signals of a lavandulyl group at δ_H 1.38 (3H, s), 1.46 (3H, s), 1.59 (3H, s), 2.05 (2H, m), 2.52 (1H, m), 2.84 (2H, m), 4.44 (1H, br s), 4.50 (1H, br s), and 4.91 (1H, m). From the HMBC spectrum, correlations between OH-5 (δ_H 11.98) and C-5, C-6, and C-10 as well as between H$_2$-1″ (δ_H 2.84) and C-7, C-8, and C-9 were evident, which was used to assign the linkage of the lavandulyl group to C-8. Therefore, compound **3** was identified as 8-lavandulylkaempferol.

The molecular formula of **4** was shown to be $C_{26}H_{30}O_6$ on the basis of ESIMS and from the ^{1}H and ^{13}C NMR spectra. Comparison of its ^{1}H and ^{13}C NMR data (δ_H 8.02 and 8.15; δ_C 193.7) with kuraridin[10] and other chalcones indicated that **4** is a chalcone. The ^{1}H NMR spectrum of **4** showed a methoxy group (δ_H 3.91), an ABX system of aromatic protons [δ_H 6.44 (dd, J = 2, 8.8 Hz), 6.49 (d, J = 2.0 Hz), and 7.52 (d, J = 8.8 Hz)], an aromatic proton [δ_H 5.91 (s)], and a chelating hydroxyl group (δ_H 15.08). It also revealed a 2,2-dimethyldihydropyran moiety [δ_H 1.23 (3H, s), 1.42

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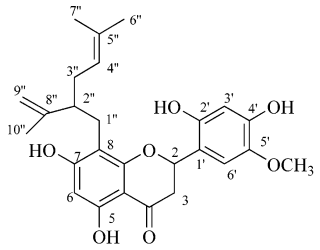
Chart 1



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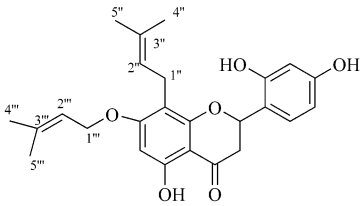

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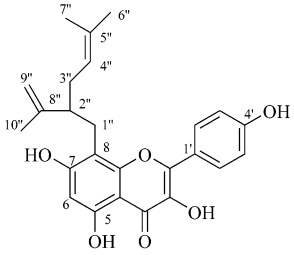

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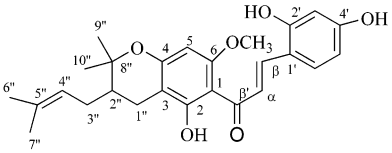

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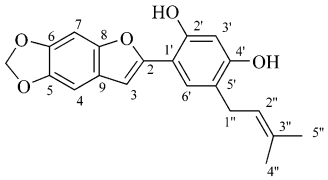
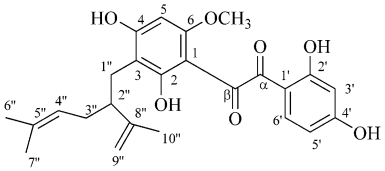


5



6

(3H, s), 1.73 (1H, m), 2.14 (1H, dd, J = 10.0, 16.8 Hz), and 2.72 (1H, dd, J = 5.2, 16.8 Hz)] and a 3,3-dimethylallyl group [δ_H 1.53 (3H, s), 1.66 (3H, s), 1.87 (1H, m), 2.27 (1H, m), and 5.20 (1H, t, J = 6.8 Hz)]. The locations of the pyran ring and 3,3-dimethylallyl group in **4** were established by HMBC analysis, in which cross-peaks were observed between OH-5 (δ_H 15.08) and C-1 and C-3, between H-1″ (δ_H 2.14 and 2.72) and C-2, C-4, C-3″, and C-8″, and between H-2″ (δ_H 1.73) and C-3 and C-4″. Thus, the pyran ring was determined to be fused to C-3 and C-4 of the benzene ring and the 3,3-dimethylallyl moiety was attached to C-2″. The position of the methoxy group was assigned at C-6 by a NOE measurement, in which irradiation of methoxy protons at δ_H 3.91 caused the enhancement of H-5 (δ_H 5.91). Accordingly, the structure of cyclokuraridin (**4**) was determined as 2,2′,4′-trihydroxy-6-methoxy-6″,6″-dimethyl-5″-prenyldihydropyrano[2″,3″:4,3]chalcone.

Compound **5** was obtained as a brown solid, and its molecular formula was established as $C_{20}H_{18}O_5$ by HREIMS. The IR spectrum of **5** showed the presence of hydroxyl (3353 cm^{-1}), aromatic ring (1619, 1608, 1498 cm^{-1}), and methylenedioxy (1035, 936 cm^{-1}) groups, and the UV spectrum with absorption maxima at λ_{max} 322 and 347 nm was consistent with a 2-phenylbenzofuran skeleton.[19] The ^{1}H NMR spectrum of **5** showed four aromatic singlet signals at δ_H 7.00, 7.09, 7.14, and 7.60, an olefinic proton at δ_H 6.60, one methylenedioxy group at δ_H 6.01, and a 3,3-dimethylallyl group at δ_H 1.75 (3H, s), 1.77 (3H, s), 3.34 (2H, d, J = 7.5 Hz), and 5.38 (1H, m). In the HMBC spectrum, cross-peaks between H-3 and C-1′, C-4, and C-8, between H-6′ and C-2, C-2′, C-4′, and C-1″, and between H-1″ and C-4′, C-6′, and C-3″ indicated the linkage of the 3,3-dimethylallyl group to C-5′. From the above results, compound **5** was determined as 2-(2,4-dihydroxy-5-prenylphenyl)-5,6-methylenedioxybenzofuran.

Compound **6** was obtained as a yellow-green oil, and its molecular formula was established as $C_{25}H_{28}O_7$ by HREIMS. The IR spectrum of **6** revealed the presence of hydroxyl (3322 cm^{-1}) and carbonyl (1619 cm^{-1}) groups. The ^{13}C NMR and DEPT spectra showed that there were three methyls, three methylenes, one methoxy, six methines, 10 quaternary carbons, and two carbonyl carbons present in the molecule. In the ^{1}H NMR spectrum, signals for a methoxy group at δ_H 3.51 (3H, s), a lavandulyl group at δ_H 1.56 (3H, s), 1.63 (3H, d, J = 1.2 Hz), 1.72 (3H, s), 2.14 (2H, m), 2.60 (1H, m), 2.70 (2H, m), 4.58 (1H, br s), 4.62 (1H, br s), and 5.07 (1H, m), and a chelated hydroxyl group at δ_H 12.82 (1H, s) were observed. Also revealed was an ABX system of protons at δ_H 6.42 (1H, d, J = 1.6 Hz), 6.43 (1H, dd, J = 1.6, 7.2 Hz), and 7.28 (1H, d, J = 7.2 Hz). The HMBC spectrum further showed the correlations of OH-2/C-1 and C-3, H-6′ (δ_H 7.28)/C-α (δ_C 195.4), C-2′, and C-4′, and H-1″ (δ_H 2.70)/C-2, C-3, and C-4, which suggested the linkage of the lavandulyl group at C-3. The position of the methoxy group was assigned at C-6 by the NOE measurement, in which enhancement was observed for H-5 (δ_H 6.06) after irradiation of methoxy protons at δ_H 3.51. Thus, the new compound sophoradione (**6**) was assigned as 2,4,2′,4′-tetrahydroxy-3-lavandulyl-6-methoxybenzil.

Isolates **2**−**6** were tested for cytotoxic activity against the KB tumor cell line. It was found that compounds **2**−**6** showed IC_{50} values of 7.1, 24.3, 15.1, 8.0, and 29.4 μg/mL, respectively.

Experimental Section

General Experimental Procedures. Melting points were determined on a Yanaco MP-I3 micro-melting point apparatus without correction. Optical rotations were taken with a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a Nicolet Avatar 320 FT-IR spectrometer. UV spectra were measured on a Hitachi U-3200 spectrophotometer. NMR spectra were recorded at 500 MHz for ^{1}H and 125 MHz for ^{13}C on a Varian Unity INOVA-500 spectrometer or at 400 MHz for ^{1}H and 100 MHz for ^{13}C on a Bruker AVANCE-400 spectrometer. EIMS and HREIMS were obtained using Finnigan MAT GCQ and JEOL

JMS-700 spectrometers, respectively. LCMS spectra were taken on a Finnigan LCQ. HPLC was performed on a Hewlett-Packard series 1100 pump system equipped with a Hewlett-Packard UV/vis detector.

Plant Material. The roots of *Sophora flavescens* were collected in July 2003, from Hualien Hsien, Taiwan, and authenticated by Mr. J. C. Ou, Research Fellow, National Research Institute of Chinese Medicine. The voucher specimen (NRICM-03-011) was deposited at the Herbarium of the National Research Institute of Chinese Medicine, Taipei, Taiwan.

Extraction and Isolation. The dried, chipped roots of *S. flavescens* (8 kg) were extracted with MeOH (80 L × 3). The combined extracts were evaporated in vacuo to give a black residue, which was suspended in water (10 L) and centrifuged (9000 rpm, 30 min) to give water-soluble and water-insoluble portions. The water-insoluble portion was chromatographed on a silica gel (70−230 mesh) column eluted with gradient solvent systems of *n*-hexane−EtOAc (10:1 → 1:5), EtOAc, and EtOAc−MeOH (10:1 → 1:5) to yield 10 fractions. Fraction 4 (*n*-hexane−EtOAc = 2:1 eluate) was further chromatographed on Sephadex LH-20 (MeOH) and silica gel (70−230 mesh, $CHCl_3$−MeOH = 1:0, 25:1, 20:1, 10:1) columns to yield four fractions, 4-1−4-4. Fraction 4-3 was purified with a Sephadex LH-20 (MeOH) column to afford **3** (114 mg). Fraction 5 (*n*-hexane−EtOAc = 1:1 eluate) was chromatographed on Sephadex LH-20 (MeOH) to yield six fractions, 5-1−5-6. Fraction 5-2 was further separated with silica gel (230−400 mesh, CH_2Cl_2−acetone = 20:1) and Sephadex LH-20 (MeOH) columns and then with preparative TLC (CH_2Cl_2−acetone = 10:1) to give **1** (5.5 mg) and **6** (17.5 mg). Fraction 5-5 was further purified with silica gel (230−400 mesh, *n*-hexane−acetone = 3:1) and preparative TLC (CH_2Cl_2−acetone = 10:1) to afford **5** (7.5 mg). Fraction 7 (EtOAc eluate) was subjected to Sephadex LH-20 (MeOH) and silica gel (230−400 mesh, $CHCl_3$−MeOH = 20:1 → 10:1) columns to give **2** (21 mg) and **4** (8 mg).

Sophoraflavanone K (1): brown solid; $[\alpha]^{25}_D$ +50 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 294 (4.42), 231 (sh), 203 (4.85) nm; IR (KBr) ν_{max} 3395, 1635, 1519, 1451, 1377, 1345, 1309, 1198, 1156, 1107 cm^{-1}; ^1H NMR (Me_2CO-d_6, 500 MHz) δ 12.40 (1H, s, OH-5), 6.98 (1H, s, H-6′), 6.35 (1H, s, H-3′), 5.89 (1H, s, H-6), 5.57 (1H, dd, J = 2.5, 13.0 Hz, H-2), 4.93 (1H, t, J = 2.5 Hz, H-4″), 4.47 (1H, d, J = 1.0 Hz, H-9″a), 4.43 (1H, br s, H-9″b), 3.67 (3H, s, OCH_3-5′), 3.08 (1H, dd, J = 13.0, 17.0 Hz, H-3β), 2.55 (1H, dd, J = 2.5, 17.0 Hz, H-3α), 2.53 (2H, m, H_2-1″), 2.49 (1H, m, H-2″), 2.01 (2H, m, H_2-3″), 1.58 (3H, d, J = 1.0 Hz, H_3-10″), 1.50 (3H, s, H_3-7″), 1.44 (3H, s, H_3-6″); ^{13}C NMR (Me_2CO-d_6, 125 MHz) δ 197.2 (C, C-4), 166.5 (C, C-7), 162.3 (C, C-9), 161.8 (C, C-5), 148.4 (C, C-4′, C-8″), 148.0 (C, C-2′), 141.4 (C, C-5′), 130.9 (C, C-5″), 123.8 (CH, C-4″), 115.7 (C, C-1′), 111.6 (CH, C-6′), 110.7 (CH_2, C-9″), 107.8 (C, C-10), 103.6 (CH, C-3′), 102.2 (C, C-8), 94.6 (CH, C-6), 74.5 (CH, C-2), 56.6 (CH_3, OCH_3-5′), 46.9 (CH, C-2″), 42.2 (CH_2, C-3), 31.5 (CH_2, C-3″), 26.7 (CH_2, C-1″), 25.2 (CH_3, C-7″), 18.2 (CH_3, C-10″), 17.3 (CH_3, C-6″); EIMS *m*/*z* 454 $[M]^+$ (7), 436 (20), 331 (14), 313 (100), 272 (11), 165 (9); HREIMS *m*/*z* 454.1991 (calcd 454.1992 for $C_{26}H_{30}O_7$).

Sophoraflavanone L (2): colorless prisms; mp 125−127 °C (MeOH); $[\alpha]^{25}_D$ ±0 (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 341 (3.80), 292 (4.53), 220 (sh) nm; IR (KBr) ν_{max} 3432, 1629, 1598, 1461, 1361, 1303, 1230, 1177, 1088 cm^{-1}; ^1H NMR (Me_2CO-d_6, 400 MHz) δ 12.26 (1H, s, OH-5), 7.33 (1H, d, J = 8.4 Hz, H-6′), 6.47 (1H, d, J = 2.4 Hz, H-3′), 6.43 (1H, dd, J = 2.4, 8.4 Hz, H-5′), 6.13 (1H, s, H-6), 5.67 (1H, dd, J = 2.8, 12.8 Hz, H-2), 5.49 (1H, t, J = 6.8 Hz, H-2‴), 5.15 (1H, t, J = 7.2 Hz, H-2″), 4.63 (2H, d, J = 6.8 Hz, H-1‴), 3.20 (2H, d, J = 7.2 Hz, H-1″), 3.11 (1H, dd, J = 12.8, 17.2 Hz, H-3β), 2.77 (1H, dd, J = 2.8, 17.2 Hz, H-3α), 1.78 (3H, s, H-5‴), 1.76 (3H, s, H-4‴), 1.61 (3H, s, H-5″), 1.58 (3H, s, H-4″); ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ 198.4 (C, C-4), 165.6 (C, C-7), 163.5 (C, C-5), 160.4 (C, C-9), 159.4 (C, C-4′), 156.2 (C, C-2′), 138.9 (C, C-3‴), 131.1 (C, C-3″), 128.7 (CH, C-6′), 123.6 (CH, C-2″), 120.2 (CH, C-2‴), 117.7 (C, C-1′), 109.3 (C, C-8), 107.8 (CH, C-3′), 103.4 (CH, C-5′), 103.4 (C, C-10), 93.8 (CH,C-6), 75.2 (CH, C-2), 66.2 (CH_2, C-1‴), 42.7 (CH_2, C-3), 25.9 (CH_3, C-5″), 25.8 (CH_3, C-4‴), 22.3 (CH_2, C-1″), 18.2 (CH_3, C-5‴), 17.8 (CH_3, C-4″); EIMS (30 eV) *m*/*z* 424 $[M]^+$ (42), 338 (100), 295 (91), 283 (81), 219 (99), 177 (50), 165 (46); HREIMS *m*/*z* 424.1884 (calcd 424.1886 for $C_{25}H_{28}O_6$).

8-Lavandulylkaempferol (3): yellow prisms; mp 175−177 °C; $[\alpha]^{25}_D$ +38 (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 373 (4.22), 307 (4.14), 272 (4.35) nm; IR (KBr) ν_{max} 3316, 1629, 1592, 1529, 1372, 1309, 1272, 1141 cm^{-1}; ^1H NMR (Me_2CO-d_6, 500 MHz) δ 11.98 (1H, s, OH-5), 8.08 (2H, d, J = 9.0 Hz, H-2′, 6′), 6.90 (2H, d, J = 9.0 Hz, H-3′, 5′), 6.20 (1H, s, H-6), 4.91 (1H, m, H-4″), 4.50 (1H, br s, H-9a″), 4.44 (1H, br s, H-9b″), 2.84 (2H, m, H_2-1″), 2.52 (1H, m, H-2″), 2.05 (2H, m, H_2-3″), 1.59 (3H, s, H_3-10″), 1.46 (3H, s, H_3-7″), 1.38 (3H, s, H_3-6″); ^{13}C NMR (Me_2CO-d_6, 125 MHz) δ 176.9 (C, C-4), 162.7 (C, C-7), 160.2 (C, C-4′), 160.0 (C, C-5), 155.4 (C, C-9), 148.8 (C, C-8″), 146.8 (C, C-2), 136.5 (C, C-3), 132.0 (C, C-5″), 130.4 (CH, C-2′, C-6′), 124.1 (CH, C-4″), 123.6 (C, C-1′), 116.4 (CH, C-3′, C-5′), 111.7 (CH_2, C-9″), 106.6 (C, C-8), 104.1 (C, C-10), 98.7 (CH, C-6), 48.0 (CH, C-2″), 32.0 (CH_2, C-3″), 28.0 (CH_2, C-1″), 25.9 (CH_3, C-7″), 19.0 (CH_3, C-10″), 17.9 (CH_3, C-6″); EIMS *m*/*z* 422 $[M]^+$ (17), 299 (100); HREIMS *m*/*z* 422.1732 (calcd 422.1730 for $C_{25}H_{26}O_6$).

Cyclokuraridin (4): red crystals; mp 103−105 °C; $[\alpha]^{25}_D$ −170 (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 390 (4.50), 310 (sh), 254 (3.89) nm; IR (KBr) ν_{max} 3385, 1608, 1456, 1414, 1351, 1309, 1225, 1109 cm^{-1}; ^1H NMR (Me_2CO-d_6, 400 MHz) δ 15.08 (1H, s, OH-2), 8.15 (1H, d, J = 15.6 Hz, H-β), 8.02 (1H, d, J = 15.6 Hz, H-α), 7.52 (1H, d, J = 8.8 Hz, H-6′), 6.49 (1H, d, J = 2.0 Hz, H-3′), 6.44 (1H, dd, J = 2.0, 8.8 Hz, H-5′), 5.91 (1H, s, H-5), 5.20 (1H, t, J = 6.8 Hz, H-4″), 3.91 (3H, s, OCH_3-6), 2.72 (1H, dd, J = 5.2, 16.8 Hz, H-1″a), 2.27 (1H, m, H-3″a), 2.14 (1H, dd, J = 10.0, 16.8 Hz, H-1″b), 1.87 (1H, m, H-3″b), 1.73 (1H, m, H-2″), 1.66 (3H, s, H-7″), 1.53 (3H, s, H-6″), 1.42 (3H, s, H-9″), 1.23 (3H, s, H-10″); ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ 193.7 (C, C-β′), 166.3 (C, C-2), 161.8 (C, C-6, C-4′), 161.0 (C, C-4), 159.6 (C, C-2′), 139.4 (CH, C-β), 133.4 (C, C-5″), 131.2 (CH, C-6′), 124.7 (CH, C-α), 123.5 (CH, C-4″), 115.8 (C, C-1′), 109.1 (CH, C-5′), 106.2 (C, C-1), 103.7 (CH, C-3′), 102.8 (C, C-3), 92.3 (CH, C-5), 79.9 (C, C-8″), 56.1 (CH_3, OCH_3-6), 41.9 (CH, C-2″), 30.6 (CH_2, C-3″), 27.8 (CH_3, C-9″), 25.9 (CH_3, C-7″), 22.4 (CH_2, C-1″), 21.3 (CH_3, C-10″), 17.9 (CH_3, C-6″); ESIMS *m*/*z* 461 $([M + Na]^+)$.

2-(2,4-Dihydroxy-5-prenylphenyl)-5,6-methylenedioxybenzofuran (5): brown solid; UV (MeOH) λ_{max} (log ϵ) 347 (4.48), 322 (4.46), 281 (4.10) nm; IR (KBr) ν_{max} 3353, 1619, 1608, 1498, 1461, 1372, 1314, 1230, 1172, 1141, 1120, 1035, 936 cm^{-1}; ^1H NMR (Me_2CO-d_6, 500 MHz) δ 7.60 (1H, s, H-6′), 7.14 (1H, s, H-3), 7.09 (1H, s, H-4), 7.00 (1H, s, H-7), 6.60 (1H, s, H-3′), 6.01 (2H, s, OCH_2O), 5.38 (1H, m, H-2″), 3.34 (2H, d, J = 7.5 Hz, H-1″), 1.77 (3H, s, H_3-4″), 1.75 (3H, s, H_3-5″); ^{13}C NMR (Me_2CO-d_6, 125 MHz) δ 156.4 (C, C-4′), 154.2 (C, C-2), 154.1 (C, C-2′), 149.4 (C, C-8), 146.3 (C, C-6), 145.3 (C, C-5), 131.9 (C, C-3″), 127.7 (CH, C-6′), 124.3 (CH, C-2″), 124.2 (C, C-9), 120.7 (C, C-5′), 110.6 (C, C-1′), 104.5 (CH, C-3), 103.8 (CH, C-3′), 102.0 (CH_2, OCH_2O), 99.8 (CH, C-7), 93.7 (CH,C-4), 28.5 (CH_2, C-1″), 25.9 (CH_3, C-4″), 17.8 (CH_3, C-5″); EIMS *m*/*z* 338 $[M]^+$ (100), 283 (71), 255 (9), 226 (8); HREIMS *m*/*z* 338.1154 (calcd 338.1154 for $C_{20}H_{18}O_5$).

Sophoradione (6): yellow-green oil; $[\alpha]^{22}_D$ +6 (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 311 (4.60), 276 (sh), 236 (sh) nm; IR (liquid film) ν_{max} 3322, 1619, 1508, 1445, 1372, 1309, 1240, 1135, 1098 cm^{-1}; ^1H NMR (Me_2CO-d_6, 400 MHz) δ 12.82 (1H, s, OH-2), 7.28 (1H, d, J = 7.2 Hz, H-6′), 6.43 (1H, dd, J = 1.6, 7.2 Hz, H-5′), 6.42 (1H, d, J = 1.6 Hz, H-3′), 6.06 (1H, s, H-6), 5.07 (1H, m, H-4″), 4.62 (1H, br s, H-9″a), 4.58 (1H, br s, H-9″b), 3.51 (3H, s, OCH_3-6), 2.70 (2H, m, H_2-1″), 2.60 (1H, m, H-2″), 2.14 (2H, m, H_2-3″), 1.72 (3H, s, H_3-10″), 1.63 (3H, d, J = 1.2 Hz, H_3-7″), 1.56 (3H, s, H_3-6″); ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ 195.4 (C, C-α), 194.5 (C, C-β), 167.0 (C, C-4), 166.4 (C, C-2), 166.2 (C, C-2′), 166.1 (C, C-4′), 162.1 (C, C-6), 149.0 (C, C-8″), 134.4 (CH, C-6′), 131.6 (C, C-5″), 124.4 (CH, C-4″), 111.4 (CH_2, C-9″), 110.8 (C, C-1′), 109.5 (CH, C-5′), 108.9 (C, C-3), 103.8 (CH, C-3′), 103.2 (C, C-1), 92.0 (CH, C-5), 56.1 (CH_3, OCH_3-6), 47.5 (CH, C-2″), 32.1 (CH_2, C-3″), 27.3 (CH_2, C-1″), 25.9 (CH_3, C-7″), 18.8 (CH_3, C-10″), 17.9 (CH_3, C-6″); EIMS *m*/*z* 440 $[M]^+$ (13), 303 (98), 261 (30), 179 (95), 153 (100), 137 (18); HREIMS *m*/*z* $[M]^+$ 440.1834 (calcd 440.1835 for $C_{25}H_{28}O_7$).

Cytotoxicity Assays. An epidermoid carcinoma cell line (KB; CCRC 60017) was purchased from the Food Industry Research and Development Institute (FIRDI, Taiwan). The cytotoxic activities of the isolated compounds on the KB cell line were examined by a previously described method.[20] Camptothecin was employed as the compound for positive control, which exhibited an IC_{50} value of 2.24 μg/mL under the above conditions.

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