Antiplasmodial Isoflavanones from the Roots of *Sophora mollis*

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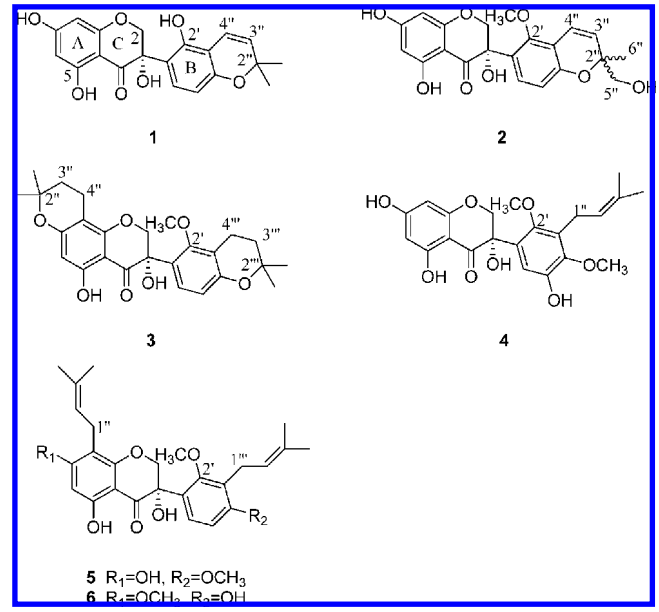
Received March 3, 2009

Six new prenylated isoflavanones named sophoronols A−F (**1**−**6**), together with eight phenolic constituents, were isolated from the roots of *Sophora mollis*. Their structures and stereochemistry were established by 1D and 2D NMR techniques, especially HMBC and NOESY as well as CD results. Componds **3** and **5** exhibited moderate anitplasmodial activity against the CQS D10 strain of *Plasmodium falciparum*, with IC_{50} values of 12.9 and 12.8 μM, respectively.

While searching the literature for biologically active substances from natural sources, a number of plants in the genus *Sophora* (Leguminosae) were reported for the presence of flavonoids that exhibited PTP1B inhibitory activity, moderate cytotoxicity, and antimicrobial activity.[1−3] Lavandulyl flavanones isolated from the roots of *Sophora flavescens* have shown promising antiplasmodial activity.[4] The literature on the genus *Sophora* revealed that the roots of *S. mollis* have received less attention. In the course of our screening for antiplasmodial chemical constituents, we found that the *n*-hexane and acetone extracts of the roots of *S. mollis* showed promising antiplasmodial activity. Further investigations of the antiplasmodial compounds led to the isolation of six new prenylated isoflavanones, named sophoronols A−F (**1**−**6**), along with four known isoflavanones, namely, sophoronol (**7**),[5,6] echinoisoflavanone (**8**),[5] tomentosanol B (**9**),[7] maackiain (**10**),[8] an isoflavone, 4′,7,8-trihydroxyisoflavone (**11**),[9] a flavone, 3′,4′,7-trihydroxyflavone (**12**),[10] one chalcone, isoliquiritigenin (**13**),[11] and a coumarin, scopoletin (**14**).[12] In this paper, we report the isolation and spectroscopic structural characterization of the new compounds as well as their antiplasmodial and cytotoxic activities.



Results and Discussion

Compound **1** was obtained as a white powder. Its molecular formula was determined as $C_{20}H_{18}O_7$ by HRESIMS (*m*/*z*393.0955, $[M + Na]^+$). Its UV spectrum showed absorption bands at λ_{max} 331, 290, and 228 nm. The ^{1}H NMR showed two one-proton doublets at δ 4.58 and 4.06 (each J = 11.7 Hz), two overlapped aromatic proton singlets [δ_H 5.68 (2H, s, H-6 and H-8)], and *o*-coupled one-proton doublets [δ_H 6.26 (1H, d, J = 8.4 Hz, H-5′) and 7.15 (1H, d, J = 8.4 Hz, H-6′)]. The ^{13}C NMR and DEPT patterns showed both oxygenated methylene and quaternary carbon resonances at δ 73.5 (C-2 and C-3) and a carbonyl resonance at δ 194.2 (C-4). All of these observations were indicative of a 3-hydroxyisoflavanone skeleton for **1**.[4] In addition, the ^{1}H NMR and ^{13}C NMR data of **1** exhibited the presence of a 2,2-dimethylpyran ring due to the presence of a *gem*-dimethyl resonance [δ_H 1.33 (6H, s, H-5″and H-6″)], an olefinic group [δ_H 5.62 (1H, d, J = 10.2 Hz, H-3″) and 6.62 (1H, d, J = 10.2 Hz, H-4″)], and an oxygenated quaternary carbon [δ_C 75.9 (C-2″)]. Accordingly, the ^{1}H and ^{13}C NMR data of **1** were similar to those of sophoronol from *S. koreensis*,[4,5] with the exception of an *O*-methyl group. The location of the 2,2-dimethylpyran unit on ring B was determined on the basis of the HMBC correlations shown in Figure 1. Moreover, compound **1** was optically active and gave a negative

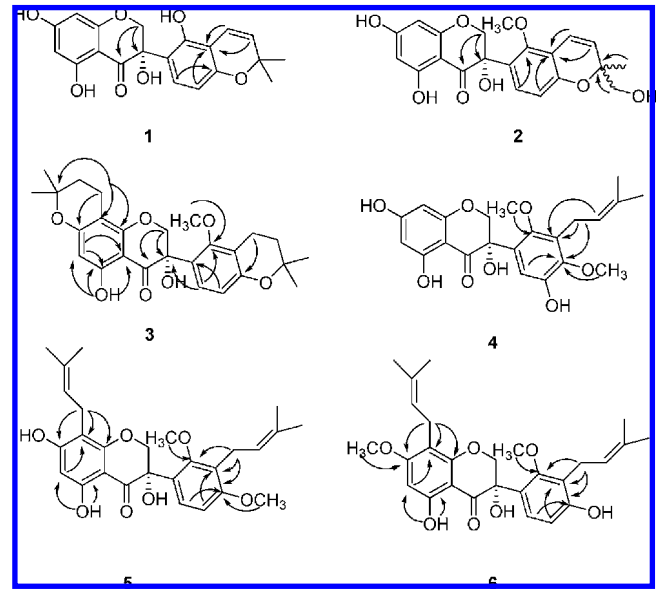


Figure 1. Key HMBC correlations of compounds **1**−**6**.

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10.1021/np900144c CCC: $40.75
Published on Web 07/02/2009

Cotton effect at 330 nm and a positive Cotton effect at 296 nm in the circular dichroism (CD) spectrum. These data are consistent with those of phyllanone, which has been assigned a 3*S* configuration.[6] Thus, the structure of sophoronol A (**1**) was determined as 3*S*-3,5,7,2′-tetrahydroxy-2″,2″-dimethylpyrano[5″,6″:3′,4′]-isoflavanone.

Compound **2** was obtained as a white powder. Its molecular formula was determined as $C_{21}H_{20}O_8$ by HRESIMS (*m/z* 423.1055, $[M + Na]^+$). Similar to **1**, the UV, CD, and ^1H and ^{13}C NMR data of **2** were characteristic of an isoflavanone skeleton. The ^1H and ^{13}C NMR data of **2** resembled those of sophoronol A except that a hydroxymethyl group was in place of one of the two methyl groups of sophoronol A (**1**), indicated by the signals at δ_H 3.62 (2H, s, H-5″), δ_C 69.3 (C-5″). The C-3 configuration of **2** was also determined as *S* on the basis of its CD data. Hence, compound **2** was named sophoronol B, and its structure was established as 3*S*-3,5,7,4‴-tetrahydroxy-2′-methoxy-2″,2″-dimethylpyrano[5″,6″:3′,4′]-isoflavanone.

Compound **3** was isolated as a white powder. Its molecular formula was determined as $C_{26}H_{30}O_7$ by HRESIMS (*m/z* 477.1891, $[M + Na]^+$). The UV, CD, and ^1H and ^{13}C NMR data of **3** resembled those of an isoflavanone. In the ^1H NMR spectrum, an aromatic proton at δ 6.00 (1H, s, H-6) belonged to ring A and two *o*-coupled protons resonating at δ 6.58 (1H, d, J = 8.4 Hz, H-5′) and 7.26 (1H, d, J = 8.4 Hz, H-6′) were assigned to the B-ring protons. In addition, an *O*-methyl [δ_H 3.71 (3H, s, 2′-OCH3)] and two 2,2-dimethyldihydropyran moieties, with signals at δ 2.56 (2H, t, J = 6.9 Hz, H-4″), 1.75 (2H, m, H-3″), 1.33, 1.32 (3H × 2, s, H-5″and H-6″), and 2.72 (2H, t, J = 6.9 Hz, H-4‴), 1.75 (2H, m, H-3‴), 1.35, 1.33 (3H × 2, s, H-5‴ and H-6‴) were also observed. In the ESI mass spectrum, the prominent fragment at *m/z* 263 ($[M - B]^+$) indicated that a hydroxy and a 2,2-dimethyldihydropyran moiety were part of ring A. Consequently, an *O*-methyl and a 2,2-dimethyldihydropyran group were fused to ring B. The fusion site of the 2,2-dimethyldihydropyran moiety to ring A was established at C-7 and C-8 by an HMBC experiment, in which H-4″ (δ_H 2.56) and H-3″ (δ_H 1.75) both correlated with C-8 (δ_C 101.0); H-3″ also coupled with C-7 (δ_C 163.2) and C-9 (δ_C 159.6). In addition, the hydrogen-bonded OH at δ 11.57 (5-OH) and H-6 (δ_H 6.00) both correlated with C-5 (δ_C 161.9). The fusion site of the 2,2-dimethyldihydropyran moiety at ring B, i.e., at C-3′ (δ_C 114.9) and C-4′ (δ_C 155.8), was also deduced by correlations of H-3‴ (δ_H 1.75) with C-3′ (δ_C 114.9) and of H-4‴ (δ_H 2.72) with C-3′, C-2′ (δ_C 156.5) and C-4′ (δC 155.8). A cross-peak between the OCH_3 at δ 3.71 and C-2′ indicated that the OCH_3 of ring B was at C-2′. Thus, compound **3**, named sophoronol C, was characterized. The C-3 configuration of **3** was also determined as *S* by its CD data.

Compound **4** was obtained as a white powder, and its molecular formula was determined as $C_{22}H_{24}O_8$ by HRESIMS (*m/z* 439.1373, $[M + Na]^+$). The UV, CD, and ^1H and ^{13}C NMR data of **4** were characteristic of an isoflavanone skeleton. The ^1H NMR spectrum showed the presence of two *O*-methyls [δ_H 3.75 (3H, s, 2′-OCH_3) and 3.70 (3H, s, 4′-OCH_3)] and a prenyl group [δ_H 3.33 (2H, d, J = 5.4 Hz, H-1″), 5.19 (1H, t, J = 5.4 Hz, H-3″), 1.68 and 1.73 (3H × 2, s, H-5″and H-4″)]. In addition, the signals around δ 6 0.0 [δ_H 6.00 (1H, s, H-6) and 5.91 (1H, s, H-8)] belonged to ring A, while the aromatic singlet [δ_H 6.98 (1H, s, H-6′)] indicated that the B-ring was substituted by five groups. From the HMBC data, the prenyl and two *O*-methyls should be located at C-3′, C-2′, and C-4′, respectively. The C-3 configuration of **4**, named sophoronol D, was also determined as *S* by its CD data.

Compounds **5** and **6** were isolated as white powders, and the molecular formulas were both determined as $C_{27}H_{32}O_7$ by HRESIMS (*m/z* 491.2043, $[M + Na]^+$). The UV, CD, and ^1H and ^{13}C NMR data of **5** and **6** indicated both having an isoflavanone skeleton. The ^1H NMR spectrum of **5** showed the presence of a single aromatic proton [δ_H 6.05 (1H, s, H-6)], two *o*-coupled aromatic protons [δ_H 6.64 (1H, d, J = 8.4 Hz, H-5′) and 7.20 (1H, d, J = 8.4 Hz, H-6′)], two *O*-methyls [δ_H 3.86 (3H, s, 2′-OCH_3) and 3.82 (3H, s, 4′-OCH_3)], and a pair of prenyl groups. In the ESI mass spectrum, the prominent fragment at *m/z* 263 ($[M - B]^+$) indicated that a prenyl and two hydroxy groups were substituted on the ring A. Consequently, the B-ring moiety carried two *O*-methyls and a prenyl group. Similar to **3**, the HMBC of **5** further established that the two prenyl groups should be located at C-8 and C-3′, respectively (Figure 1).

Closely similar to compound **5**, with the aid of ESIMS, which showed a prominent fragment at *m/z* 277 ($[M - B]^+$) and HMBC (Figure 1), the structure of **6** was also characterized. Both configurations at C-3 of compound **5** and **6** were inferred to be *S* from their CD data. Hence, compounds **5** and **6** were identified as the new isoflavanones sophoronols E and F, respectively.

Eight known phenolic constituents were also isolated and characterized by comparison with literature data as four known isoflavanones, sophoronol (**7**),[5,6] echinoisoflavanone (**8**),[5] tomentosanol B (**9**),[7] maackiain (**10**),[8] an isoflavone, 4′,7,8-trihydroxyisoflavone (**11**),[9] a flavone, 3′,4′,7-trihydroxyflavone (**12**),[10] a chalcone, isoliquiritigenin (**13**),[11] and a coumarin, scopoletin (**14**).[12]

The acetone extract of *S. mollis* roots showed promising antiplasmodial activity with an IC_{50} value of 13.5 μg/mL, while the *n*-hexane extract from the roots showed moderate activity with an IC_{50} value of 29.4 μg/mL.

These isolated compounds were further tested against the chloroquine-sensitive (CQS) strain of *Plasmodium falciparum* (D10), with an IC_{50} value of 4.0×10^{-5} μM for the reference drug chloroquine (Table 3). The results showed that sophonorol C (**3**) and E (**5**) showed moderate activity and were most active with IC_{50} values of 12.9 and 12.8 μM, respectively. These two compounds showed no *in vitro* cytotoxicity against the Chinese hamster ovarian (CHO) cell line (Table 3). 4′,7,8-Trihydroxyisoflavone (**11**) and 3′,4′,7-trihydroxyisoflavone (**12**) also showed moderate activity, with IC_{50} values of 17.8 and 19.3 μM, but an increase in cytotoxicity was observed with 3′,4′,7-trihydroxyisoflavone. Tomentosanol B (**9**), isoliquiritigenin (**13**), sophonorol F (**6**), and echinoisoflavanone (**8**) showed lower activity, with IC_{50} values 25.3, 32.0, 41.0, and 42.1 μM, respectively, and were not selective to the malaria parasite (SI ≤ 5). These data indicated that the observed antiplasmodial activity of the four compounds might be due to their cytotoxic activity. Maackiain (**10**), scopoletin (**14**), sophonorol (**7**), and sophonorols A (**1**), B (**2**), and D (**4**) hardly showed any antiplasmodial activity (>100 μM) against the CQS strain of *P. falciparum.*

All the data showed some useful information on the structure−antiplasmodial activity relationship. It seemed that the isoflavanones of which both the A and B rings were substituted by prenyl or dimethyldihydropyran groups (**3**, **5**, **9**), showed much higher antiplasmodial activity and lower cytotoxicity. While substituted by dimethylpyran groups, the compounds (**1**, **2**) lost their antiplasmodial activity. In addtion, the location of an isoprenyl group at either C-6 or C-8 (**5**, **6**, **9**) did not significantly affect the antiplasmodial activity. When comparing echinoisoflavanone (**8**) with sophoronol D (**4**), hydroxylation at C-5′ decreased its antiplasmodial activity significantly. In addition, the cytotoxicity observed by these compounds supports previous reports on the cytotoxic effect of isoflavanones.[13]

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectra were obtained on a Shimadzu UV-2450 UV−visible spectrophotometer. IR spectra were measured on a Nicolet FTIR 750 spectrophotometer. The CD spectra were recorded in MeOH on a JASCO J-810 spectrometer. ^1H NMR, ^{13}C NMR, DEPT, HSQC, and HMBC spectra were recorded at 400 MHz for ^1H and at 100 MHz for ^{13}C with Bruker AMX-300/400 instruments in deuterated solutions. HRESIMS was carried out using Micromass Q-Tof Global mass spectrometers. ESIMS were recorded

Table 1. ^{1}H NMR (δ_H, J in Hz) (400 MHz) Data of Compounds **1**−**6**

position	**1**[b]	**2**[c]	**3**[a]	**4**[a]	**5**[a]	**6**[a]
2	4.58 d (11.7)	4.06 d (12)	4.84 dd (11.7)	4.20 d (12)	4.26 d (11.7)	4.24 d (11.4)
	4.06 d (11.7)	4.66 d (12)	4.28 dd (11.7)	4.78 d (12)	4.89 d (11.7)	4.84 d (11.4)
3			3.72 s (OH)			
5	11.60 s		11.57 s	11.77 s	11.75 s	11.86 s
6	5.68 s	5.93 s	6.00 s	6.00 s	6.05 s	6.15 s
7						
8	5.68 s	5.89 s		5.91 s		
5′	6.26 d (8.4)	6.64 d (8.4)	6.58 d (8.4)	6.98 s	6.64 d (8.7)	6.58 d (8.7)
6′	7.15 d (8.4)	7.40 d (8.4)	7.26 d (8.4)		7.20 d (8.7)	7.27 d (8.7)
1″				3.33 d (5.4)	3.28 d (6.9)	3.19 d (6.9)
2″				5.19 t (5.4)	5.20 t (6.9)	5.10 t (6.9)
3″	5.62 d (10.2)	5.76 d (10.2)	1.75 (m)			
4″	6.62 d (10.2)	6.63 d (10.2)	2.56 t (6.9)	1.73 s	1.74 s	1.64 s
5″	1.33 s	3.62 s	1.33 s	1.68 s	1.68 s	1.72 s
6″	1.33 s	1.31 s	1.32 s			
1‴					3.33 d (6.0)	3.36 d (6.3)
2‴					5.20 t (6.0)	5.22 t (6.3)
3‴			1.75 (m)			
4‴			2.72 t (6.0)		1.74 s	1.79 s
5‴			1.35 s		1.77 s	1.85 s
6‴			1.33 s			
7-OCH_3						3.85 s
2′-OCH_3		3.63 s	3.71 s	3.75 s	3.86 s	3.65 s
4′-OCH_3				3.70 s	3.82 s	

[a] Measured in $CDCl_3$. [b] Measured in DMSO-d_6. [c] Measured in methanol-d_4.

Table 2. ^{13}C NMR (δ) (100 MHz) Data of Compounds **1**−**6**

position	**1**[b]	**2**[c]	**3**[a]	**4**[a]	**5**[a]	**6**[a]
2	73.5, CH_2	76.2, CH_2	74.3, CH_2	74.3, CH_2	74.3, CH_2	74.2, CH_2
3	73.5, qC	75.7, qC	73.7, qC	74.5, qC	73.8, qC	73.7, qC
4	194.2, qC	197.1, qC	196.1, qC	195.4, qC	196.6, qC	196.7, qC
5	165.2, qC	166.9, qC	161.9, qC	164.9, qC	162.6, qC	163.0, qC
6	96.2, CH	96.6, CH	97.8, CH	96.1, CH	97.1, CH	92.7, CH
7	169.8, qC	168.9, qC	163.2, qC	166.2, qC	164.0, qC	165.9, qC
8	97.3, CH	96.6, CH	101.0, CH	97.5, CH	106.4, qC	109.2, qC
9	162.8, qC	164.9, qC	159.6, qC	162.9, qC	159.6, qC	158.6, qC
10	100.0, qC	102.5, qC	101.1, qC	101.3, qC	101.6, qC	101.4, qC
	129.6, qC	125.3, qC	121.8, qC	129.2, qC	123.7, qC	123.6, qC
1′	153.9, qC	156.4, qC	156.5, qC	149.2, qC	159.5, qC	156.8, qC
2′	110.6, qC	116.0, qC	114.9, qC	127.0, qC	123.5, qC	120.7, qC
3′	150.8, qC	155.3, qC	155.8, qC	146.8, qC	160.0, qC	156.8, qC
4′	107.8, CH	113.2, CH	112.8, CH	145.2, qC	106.0, CH	111.7, CH
5′	128.0, CH	129.4, CH	125.7, CH	113.0, CH	125.6, CH	126.1, CH
6′				24.5, CH_2	21.5, CH_2	21.3, CH_2
1″	75.9, qC	80.3, qC	76.2, qC	122.6, CH	122.7, CH	122.3, CH
2″	129.6, CH	128.5, CH	31.8, CH_2	132.5, qC	135.0, qC	131.5, qC
3″	117.4, CH	120.8, CH	16.0, CH_2	18.1, CH_3	17.8, CH_3	25.7, CH_3
4″	28.0, CH_3	69.3, CH_2	26.6, CH_3	25.8, CH_3	25.6, CH_3	17.6, CH_3
5″	28.1, CH_3	22.6, CH_3	26.1, CH_3			
6″					23.7, CH_2	23.9, CH_2
1‴			74.0, qC		121.6, CH	121.4, CH
2‴			32.1, CH_2		131.8, qC	135.6, qC
3‴			18.3, CH_2		25.8, CH_3	25.7, CH_3
4‴			27.4, CH_3		17.8, CH_3	17.9, CH_3
5‴			26.8, CH_3			
6‴						55.9, CH_3
7-OCH_3		63.2, CH_3	60.6, CH_3	61.0, CH_3	55.7, CH_3	62.2, CH_3
2′-OCH_3				61.9, CH_3	62.2, CH_3	
4′-OCH_3						

[a] Measured in $CDCl_3$. [b] Measured in DMSO-d_6. [c] Measured in methanol-d_4.

on a Bruker Esquire 3000 Plus spectrometer. HPLC was performed with a Waters 2695 separation module equipped with a Waters 2996 photodiode array detector and a Kromacil C18 column (4.6 × 150 mm, 0.5 μm). All solvents used were of chemical grade and purchased from the Shanghai Chemical Plant, Shanghai, China. Sephadex LH-20 (25−100 μm) was purchased from Pharmacia. MCI gel CHP 20P (75−150 μm, a high porous polymer consisting of polystrene) was purchased from Mitsubishi Chemical Ind., Tokyo, Japan. RP-18 (20−45 μm) was purchased from FuJi Silysia Chemical Ltd. Silica gel (200−300 mesh) for column chromatography was purchased from Qingdao Marine Chemical Ltd., Qingdao, China. Silica gel plates (GF-254) for TLC were purchased from Yantai Huiyou Inc., Yantai, China.

Plant Material. Roots of *S. mollis* were collected in July 2006 from Chitral in the north of Pakistan. Taxonomic identification was done by Naveed Ahmad, Department of Botany, University of Peshawar, Pakistan. A voucher specimen (16906) was deposited in the herbarium at the Department of Botany, University of Peshawar, Peshawar, Pakistan.

Extraction and Isolation Procedure. Dried and pulverized roots (2.5 kg) were extracted sequentially with *n*-hexane and acetone in a Soxhlet extractor. Each extract was concentrated *in vacuo* to give brownish syrups, 15 and 53 g, respectively. The *n*-hexane extract (15 g) was subjected to silica gel eluted with petroleum ether−acetone (95:5 to 50:50) to obtain seven fractions I−VII. Fraction III (1.2 g) was separated on a silica gel

Table 3. *In Vitro* Antiplasmodial Activity and Cytotoxicity of Compounds **1**−**14**

compound	antiplasmodial activity IC$_{50}$ value (μM)	cytotoxicity IC$_{50}$ value (μM)	selectivity[b]
sophoronol A (**1**)	NA[a]	NA[a]	
sophoronol B (**2**)	NA[a]	NA[a]	
sophoronol C (**3**)	12.9	NA[a]	
sophoronol D (**4**)	105.6	171.7	2
sophoronol E (**5**)	12.8	168.6	13
sophoronol F (**6**)	41.0	133.6	3
sophoronol (**7**)	114.5	222.7	2
echinoisoflavanone (**8**)	42.1	218.3	5
tomentosanol B (**9**)	25.3	133.6	5
maackiain (**10**)	177.0	NA[a]	
4′,7,8-trihydroxyisoflavone (**11**)	17.8	NA[a]	
3′,4′,7-trihydroxyflavone (**12**)	19.3	49.3	3
isoliquiritigenin (**13**)	32.0	45.9	1
scopoletin (**14**)	493.6	NA[a]	
chloroquine[c]	4.0×10^{-5}		
emetine[c]		0.12	

[a] NA = no activity: the compound shows no activity at the highest concentration measured. [b] Selectivity index (SI) = IC$_{50}$ (CHO)/IC$_{50}$ (D10). [c] Positive control.

column using petroleum ether−acetone (90:10) to yield compound **3** (30 mg). Fraction V was also subjected to silica gel to yield scopoletin (80 mg) eluted with petroleum ether−acetone (95:5). Fraction VI (0.8 g) was first subjected to a silica gel column (petroleum ether−acetone (70: 30) and then rechromatographed on an RP-18 column (65% aqueous CH_3CN) to give compounds **5** (15 mg) and **6** (10 mg). The acetone extract (53 g) was applied to MCI and gradually eluted with 30, 50, 70, and 90% aqueous MeOH. The 50% aqueous MeOH fraction (12 g) was purified sequentially by CC on silica gel ($CHCl_3$−MeOH (20:1)), Sephadex LH-20 (MeOH), and RP-18 columns (60% aqueous MeOH) to yield maackiain (180 mg), isoliquiritigenin (22 mg), and compound **4** (15 mg). The 70% aqueous MeOH fraction (15 g) was first separated with CC on silica gel eluted with $CHCl_3$−MeOH (99:1 to 80:20) to obtain five fractions, I−V. Fraction I was applied to a silica gel column to give 4′,7,8-trihydroxyisoflavone (32 mg) with eluent petroleum ether−EtOAc−MeOH (15:5:1). Fraction II (0.7 g) was subjected to an RP-18 column (35% aqueous CH_3CN) to yield sophoronol (16 mg), **1** (40 mg), and echinoisoflavanone (30 mg). Fraction IV (0.2 g) was first applied to a Sephadex LH-20 column with MeOH as eluent, followed by further purification with an RP-18 column (65% aqueous MeOH) to afford **2** (9 mg), tomentosanol B (18 mg), and 3′,4′,7-trihydroxyflavone (45 mg).

Sophoronol A (1): white powder; $[\alpha]^{25}_D$ +200 (*c* 0.3, MeOH); UV (MeOH) λ_{max} (log ε) 331 (3.00), 290 (3.38), 228 (3.66) nm; CD (*c* 0.36, MeOH) $[\theta]_{330}$ −3.4, $[\theta]_{296}$ +12.3; IR (KBr) ν_{max} 3400, 1656, 1620, 1500 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 763.1 [2 M + Na]$^+$, 393.0 [M + Na]$^+$, 369.1 [M − H]$^-$; HRESIMS *m*/*z* 393.0955 [M + Na]$^+$ (calcd for $C_{20}H_{18}NaO_7$, 393.0950).

Sophoronol B (2): white powder; $[\alpha]^{25}_D$ +159 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 290 (3.14), 228 (3.30) nm; CD (*c* 0.36, MeOH) $[\theta]_{330}$ −4.1, $[\theta]_{296}$ + 14.7; IR (KBr) ν_{max} 3425, 2920, 2850, 1700, 1635, 1600, 1475 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 423.1 [M + Na]$^+$, 399.1 [M − H]$^-$; HRESIMS *m*/*z* 423.1055 [M + Na]$^+$ (calcd for $C_{21}H_{20}NaO_8$, 423.1056).

Sophoronol C (3): white powder; $[\alpha]^{25}_D$ +113 (*c* 0.3, MeOH); UV (MeOH) λ_{max} (log ε) 297 (3.43) nm; CD (*c* 0.36, MeOH) $[\theta]_{318}$ −9.4, $[\theta]_{297}$ +28.0; IR (KBr) ν_{max} 3465, 2975, 1645, 1585, 1480 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 477.3 [M + Na]$^+$, 263.1 [M − B]$^+$; HRESIMS *m*/*z* 477.1891 [M + Na]$^+$ (calcd for $C_{26}H_{30}NaO_7$, 477.1889).

Sophoronol D (4): white powder; $[\alpha]^{25}_D$ +164 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 291 (3.04) nm; CD (*c* 0.3, MeOH) $[\theta]_{330}$ −1.9, $[\theta]_{284}$ +33.1; IR (KBr) ν_{max} 3410, 2935, 1640, 1590, 1475 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 855.4 [2 M + Na]$^+$, 439.2 [M + Na]$^+$, 415.1 [M − H]$^-$; HRESIMS *m*/*z* 439.1373 [M + Na]$^+$ (calcd for $C_{22}H_{24}NaO_8$, 439.1369).

Sophoronol E (5): white powder; $[\alpha]^{25}_D$ +190 (*c* 0.2, MeOH); UV (MeOH): λ_{max} (log ε) 295 (3.15) nm; CD (*c* 0.3, MeOH) $[\theta]_{317}$ −12.6, $[\theta]_{294}$ +29.6; IR (KBr): ν_{max} 3450, 2940, 1640, 1580, 1465 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 491.3 [M + Na]$^+$, 263.0 [M − B]$^+$; HRESIMS *m*/*z* 491.2043 [M + Na]$^+$ (calcd for $C_{27}H_{32}NaO_7$, 491.2046).

Sophoronol F (6): white powder; $[\alpha]^{25}_D$ +150 (*c* 0.3, MeOH); UV (MeOH) λ_{max} (log ε) 292 (3.35) nm; CD (*c* 0.3, MeOH) $[\theta]_{317}$ −8.4, $[\theta]_{293}$ +34.3; IR (KBr) ν_{max} 3440, 2920, 1642, 1473 cm^{-1}; ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m*/*z* 491.2 [M + Na]$^+$, 277.1 [M − B]$^+$; HRESIMS *m*/*z* 491.2043 [M + Na]$^+$ (calcd for $C_{27}H_{32}NaO_7$, 491.2046).

Antiplasmodial Assay. The samples were tested in triplicate on two separate occasions against a chloroquine-sensitive (CQS) strain of *Plasmodium falciparum* (D10). Continuous *in vitro* cultures of asexual erythrocyte stages of *P. falciparum* were maintained as described by Trager and Jensen.[14] Quantitative assessment of *in vitro* antiplasmodial activity was determined using the parasite lactate dehydrogenase assay.[15] Chloroquine diphosphate (Sigma) was used as the reference drug in all antiplasmodial experiments. Samples were tested according to a well-established method.[16]

Cytotoxicity Assay. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was used to determine cellular growth and survival.[17] The test samples were tested in triplicate on one occasion against the Chinese hamster ovarian (CHO) cell line. Emetine dihydrochloride (Sigma) was used as the reference drug in all cytotoxicity experiments. Samples were tested according to a well-established method.[16]

Acknowledgment. One of the authors (J.R.) acknowledges the financial support by the Higher Education Commission, Pakistan, under its indigenous Ph.D scheme. This work was also supported by the Chinese National High-Tech R&D Program (grants 2007AA02Z147, 2006AA020602), the National Natural Science Foundation of China (grants 90713046, 30772638), and CAS Foundation (grant KSCX2-YW-R-18).

Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and HMBC spectra for compounds **1**−**6** are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Long, C.; Derek, T. N.; MinKyun, N.; Phuong, T. T.; John, S. M.; Dieudonné, N.; Joseph, T. M.; Zacharias, T. F.; Jong, S. A.; Won, K. O. *J. Nat. Prod.* **2007**, *70*, 1039–1042.
(2) Gomotsang, B.; Runner, R. T. M.; Berhanu, A. G.; Cornelius, C. W. W. *Planta Med.* **2002**, *68*, 615–620.
(3) Ding, P.; Chen, D.; Kenneth, F. B.; Alexander, K. N.; Wang, X.; Lee, K. H. *Helv. Chim. Acta* **2004**, *87*, 2574–2580.
(4) Kim, Y. C.; Kim, H.-S.; Wataya, Y.; Sohin, D. H.; Kand, T. H.; Kim, M. S.; Kim, Y. M.; Lee, G.-M.; Chang, J.-D.; Park, H. *Biol. Pharm. Bull.* **2004**, *27*, 748–750.
(5) Kim, C.-K.; Ebizuka, Y.; Sankawa, U. *Chem. Pharm. Bull.* **1989**, *37*, 2879–2881.
(6) (a) Monache, F. D.; Monache, G. D.; Marini-Bettolo, G. B.; Albuquerque, M. F. D.; Mello, F. D.; Lima, O. G. D. *Gazz. Chim. Ital.* **1977**, *107*, 189–192. (b) Manki, K.; Ichiro, Y.; Yoshiki, S. *Chem. Pharm. Bull.* **1978**, *26*, 3863–3870.
(7) Tanaka, T.; Linuma, M.; Asai, F.; Ohyama, M.; Burandt, C. L. *Phytochemistry* **1997**, *46*, 1431–1438.
(8) Linuma, M.; Tanaka, T.; Kawai, M. *Phytochemistry* **1991**, *30*, 3773–3775.
(9) Chang, T. S. *J. Agric. Food Chem.* **2007**, *55*, 2010–2015.
(10) Kure, N.; Torsell, K. B. G.; Ellemose, S. *Acta Chem. Scand.* **1995**, *49*, 524–529.
(11) Veitch, N. C.; Sutton, P. S. E.; Kite, G. C.; Ireland, H. E. *J. Nat. Prod.* **2003**, *66*, 210–216.
(12) Shafizadeh, F.; Melnikoff, A. B. *Phytochemistry* **1970**, *9*, 1311–1315.
(13) Shirataki, Y.; Wakae, M.; Yamamoto, Y.; Hashimoto, K.; Satoh, K.; Ishihara, M.; Kikuchi, H.; Nishikawa, H.; Minagawa, K.; Motohashi, N.; Sakagami, H. *Anticancer Res.* **2004**, *24*, 1481–1488.
(14) Trager, W.; Jensen, J. B. *Science* **1976**, *193*, 673–675.
(15) Makler, M. T.; Ries, J. M.; Williams, J. A.; Bancroft, J. E.; Piper, R. C.; Gibbins, B. L.; Hinrichs, D. J. *Am. J. Trop. Med. Hyg.* **1993**, *48*, 739–741.
(16) Pillay, P.; Vleggaar, R.; Maharaj, V. J.; Smith, P. J.; Lategan, C. A. *J. Ethnopharmacol.* **2007**, *112*, 71–76.
(17) Mosmann, T. *J. Immunol. Methods* **1983**, *65*, 55–63.

NP900144C