Candenatenins A−F, Phenolic Compounds from the Heartwood of *Dalbergia candenatensis*

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Chemical investigation of the CH_2Cl_2 extract of the heartwood of *Dalbergia candenatensis* afforded six new phenolic compounds, designated candenatenins A−F (**1**−**6**), as well as four known compounds, (2*R*,3*R*)-3,5-dihydroxy-7-methoxyflavanone (**7**), 4-hydroxy-3-methoxy-8,9-methylenedioxypterocarpan (**8**), nutiducol (**9**), and sophoraflavanone A (**10**). The structures of the new compounds were determined by 1D- and 2D-NMR spectroscopic studies as well as by MS analysis. The cytotoxic activities of the isolated compounds are also reported.

Dalbergia species (Leguminosae) are known for their deeply pigmented heartwood of varying colors, which are valued for use in wooden crafts, as well as traditional medicine. In Thailand, the heartwood of *D. candenatensis*, which is a deep red color, has been used as an antibacterial and a red dyestuff. Previously, the isolation of monomeric isoflavonoids and neoflavonoids from the MeOH extract of the heartwood was reported.[1,2] As part of our search for bioactive constituents from Thai medicinal plants, the CH_2Cl_2 extract of the heartwood of *D. candenatensis* exhibited cytotoxic activity against HT-29 (colon cancer), KB (human oral cancer), MCF-7 (breast adenocarcinoma), and HeLa (human cervical cancer) cell lines. We report herein the isolation and characterization of six new compounds (**1**−**6**) and their cytotoxic evaluation.

The CH_2Cl_2 extract of *D. candenatensis* heartwood was separated and purified by silica gel column chromatography to afford compounds **1**−**6**, together with four known compounds: (2*R*,3*R*)-3,5-dihydroxy-7-methoxyflavanone (**7**),[3] 4-hydroxy-3-methoxy-8,9-methylenedioxypterocarpan (**8**),[4] nitiducol (**9**),[5] and sophoraflavanone A (**10**).[6] The structures of the known compounds were identified by comparison of their observed and reported physical data.

Results and Discussion

Candenatenin A (**1**) was obtained as a colorless, viscous oil. The HREIMS of **1** showed an $[M]^+$ at *m/z* 316.3454, suggesting the molecular formula $C_{18}H_{20}O_5$ with nine degrees of unsaturation. The IR spectrum showed a stretching frequency of hydroxy (3390 cm^{-1}) and aromatic (1588 cm^{-1}) functionalities. The UV spectrum displayed absorption bands at λ_{max} 210 and 259 nm, suggesting the presence of a conjugated aromatic chromophore. The ^1H NMR spectroscopic data (Table 1) displayed the presence of *ortho*-coupled AB-type protons at δ 6.83 (H-6′) and 6.66 (H-5′) (each 1H, d, J = 8.4 Hz) and of ABC-type protons at δ 6.90 (1H, d, J = 2.7 Hz, H-2″), 6.72 (1H, d, J = 8.7 Hz, H-5″), and 6.65 (1H, dd, J = 8.7, 2.7 Hz, H-6″), suggesting the presence of 1,2,3,4-tetrasubstituted and 1,3,4-trisubstituted benzene rings, respectively. The signals of ABX_2-type protons appeared at δ 6.71 (1H, dd, J = 15.9, 1.5 Hz, H-3), 6.25 (1H, dt, J = 15.9, 6.9 Hz, H-2), and 3.47 (2H, dd, J = 6.9, 1.5 Hz, H-1), which agreed with the protons of a 1,3-diarylpropene skeleton. In addition, three *O*-methyl groups resonating at δ 3.93 (3′-OMe), 3.85 (2′-OMe), and 3.78 (4″-OMe) along with a broad D_2O exchangeable signal at δ 5.64 were present. These data indicated that the structure of candenatenin A was closely related to that of dalberatin B[7] (Table 1), except for the arrangements of OMe and OH groups in ring B. The positions of the OMe and OH groups in candenatenin A (**1**) were located at C-4″ and C-3″, respectively, whereas those of dalberatin B at C-5″ and C-2″, respectively. The observed HMBC correlations (Table 1) of H-2″ (δ 6.90) with C-4″ (δ 150.9), C-3″ (δ 149.4), C-1″ (δ 127.9), C-3 (δ 125.0), and C-6″ (δ 112.4), of H-6″ (δ 6.65) with C-4″ (δ 150.9) and C-3″ (δ 149.4), and of the OMe protons at δ 3.78 (4″-OMe) with C-4″ (δ 150.9) confirmed the assignments. Moreover, the cross-peak between the OMe protons at δ 3.78 (4″-OMe) and a methine proton at δ 6.72 (H-5″) was also observed in the NOESY experiment. The large coupling constant between H-2 and H-3 (J = 15.9 Hz) indicated that the olefinic bond had an *E*-configuration. Thus, candenatenin A was identified as **1**.

Candenatenin B (**2**), $C_{15}H_{16}O_2$ ($[M]^+$ *m/z* 228.1048), was isolated as a colorless, viscous oil. Its IR spectrum displayed a conjugated carbonyl stretching frequency (1673 cm^{-1}). The ^{13}C NMR data (Table 2) showed a total of 15 carbons with a conjugated carbonyl carbon at δ 198.9. The ^1H NMR data of **2** (Table 2) exhibited the characteristics of a cinnamyl moiety at δ 7.23−7.40 (5H, m, H-2″-H-6″), 6.56 (1H, d, J = 15.9 Hz, H-3), 6.28 (1H, dt, J = 15.9, 7.5 Hz, H-2), and 2.61 (2H, dd, J = 12.6, 7.5 Hz, 2H-1). The coupling constant of 15.9 Hz between H-2 and H-3 supported the *E*-configuration. The remaining proton signals at δ 6.79 (1H, d, J = 10.2 Hz, H-2′), 5.96 (1H, d, J = 10.2 Hz, H-3′), 2.71 (1H, m, H-5′a), 2.64 (1H, m, H-6′a), 2.49 (1H, m, H-5′b), and 2.20 (1H, m, H-6′b) were assigned to the protons of an α,β-unsaturated cyclohexenone moiety by the COSY spectrum. The presence of an OH group at C-1′ was indicated by the correlations of the methylene protons at δ 2.61 (2H, dd, J = 12.6, 7.5 Hz, 2H-1) with C-1′ (δ 70.1) and C-2′ (δ 153.1), of an olefinic proton at δ 5.96 (H-3′) with C-1′ (δ 70.1) and C-5′ (δ 34.3), and of an olefinic proton at δ 6.28 (H-2) with C-1′ (δ 70.1) and C-1″ (δ 124.8) in the HMBC spectrum. The CD spectrum of **2** showed positive and negative Cotton effects at 292 and 339 nm, respectively, which were in agreement with those of piperkadsin A,[8] thus establishing the 1′*R* configuration of **2**. Therefore, candenatenin B was deduced to be **2**.

Candenatenin C (**3**) was isolated as a colorless, viscous oil, and its molecular formula was determined to be $C_{16}H_{19}O_3$ ($[M + H]^+$ *m/z* 259.1334) by ESITOFMS. The ^1H and ^{13}C NMR spectra (Table 2) of **3** showed similarity to those of **2**, except for the appearance of the OMe protons at δ 3.84 in **3**. The ^1H NMR data displayed the presence of a 1,2-disubstituted benzene ring at δ 7.42 (1H, dd, J = 8.4, 1.5 Hz, H-6″), 7.24 (1H, td, J = 8.4, 1.5 Hz, H-4″), 6.93 (1H, td, J = 8.4, 1.5 Hz, H-5″), and 6.86 (1H, dd, J = 8.4, 1.5 Hz, H-3″), suggesting an OMe group at C-2″. The location of the OMe group was confirmed by NOESY data, in which the OMe signal displayed cross-peaks with H-3 and H-3″. The configuration at C-1′ was estimated as *R* from the CD spectrum, which showed a negative

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Chart 1

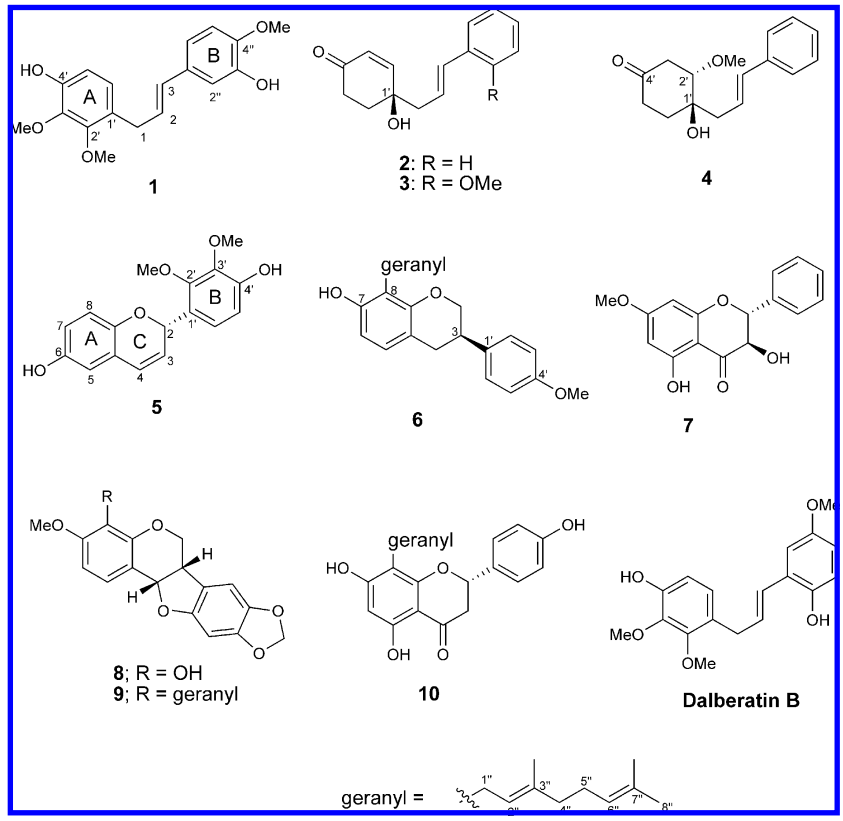

Table 1. NMR Data of **1** and Dalberatin B in $CDCl_3$ (multiplicities, *J* in Hz)[a]

	candenatenin A (**1**)			dalberatin B	
no.	δ_C	δ_H	HMBC ($^1H \rightarrow {}^{13}C$)	δ_C	δ_H
1	33.3	3.47 dd (6.9, 1.5)	2, 3, 1′, 2′, 6′	33.4	3.49 d (6.6)
2	130.5	6.25 dt (15.9, 6.9)	1, 3, 1′, 1″	132.0	6.28 dt (15.8, 6.6)
3	125.0	6.71 dd (15.9, 1.5)	1, 2, 1″, 2″, 6″	124.9	6.58 d (15.8)
1′	125.6			125.4	
2′	150.7			150.7	
3′	139.8			140.0	
4′	148.1			148.2	
5′	110.3	6.66 d (8.4)	1′, 3′, 4′, 6′	110.3	6.68 d (8.4)
6′	124.8	6.83 d (8.4)	1, 1′, 2′, 4′	124.8	6.84 d (8.4)
1″	127.9			125.2	
2″	113.2	6.90 d (2.7)	3, 1″, 3″, 4″, 6″	146.7	
3″	149.4			116.5	6.71 d (8.4)
4″	150.9			113.8	6.66 dd (8.4, 3.3)
5″	114.3	6.72 d (8.7)	3, 4″	153.7	
6″	112.4	6.65 dd (8.7, 2.7)	3″, 4″	112.1	6.86 d (3.3)
2′-OMe	60.5	3.85 s	2′	60.5	3.87 s
3′-OMe	60.7	3.93 s	3′	60.7	3.93 s
4′-OH		5.64 br s	3′, 4′, 5′		5.65 br s
2″-OH					4.78 br s
4″-OMe	56.3	3.78 s	4″		
5″-OMe				55.6	3.75 s

[a] Assignments were made using HMQC and HMBC data.

Cotton effect at 340 nm. From these data, the new candenatenin C was characterized as **3**.

Candenatenin D (**4**) was obtained as a colorless, viscous oil. The HREIMS gave a molecular ion peak at *m*/*z* 260.1415 consistent with the molecular formula $C_{16}H_{20}O_3$, indicating seven degrees of unsaturation. The ^1H NMR data of **4** (Table 2) were similar to those of **2**, except that compound **4** showed the presence of an oxymethine proton at δ 3.51 (1H, dd, $J = 3.0$, 2.1 Hz, H-2′), an OMe group at δ 3.40 (3H, s, 2′-OMe), and methylene protons at δ 2.86 (1H, dd, $J = 14.7$, 3.0 Hz, H-3′a) and 2.56 (1H, dd, $J = 14.7$, 2.1 Hz, H-3′b) instead of the α,β-unsaturated ketone moiety of **2**. The OMe group was located at C-2′ from the HMBC correlations of oxymethine proton H-2′ (δ 3.51) with the carbon at δ 56.9 (OMe) and of OMe at δ 3.40 with the carbon at δ 83.6 (C-2′). The relative configuration of **4** was determined on the basis of coupling constants. The small *J* value of H-2′ ($J = 3.0$ and 2.1 Hz) indicated that H-2′ should be equatorially oriented. In the NOESY spectrum, the oxymethine H-2′ and an OMe group showed a cross-peak with a proton at δ 2.63 (H-1), suggesting that the cinnamyl moiety should be equatorially oriented; therefore the OH and OMe groups were *trans*. Although the absolute configuration of **4** could not be directly assigned by analysis of its CD spectrum, C-1′ was presumed to have the *R*-configuration based on compounds **2** and **3**, whereas the absolute configuration of C-2′ was deduced to be *S* by NOESY results. Thus,

Table 2. ^{1}H and ^{13}C NMR Data of **2**−**4** in $CDCl_3$ (multiplicities, *J* in Hz)[a]

	candenatenin B (**2**)		candenatenin C (**3**)		candenatenin D (**4**)	
no.	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	43.7	2.61 dd (12.6, 7.5)	44.1	2.62 dd (12.6, 7.5)	42.3	2.63 m
						2.48 dd (14.1, 7.8)
2	122.9	6.28 dt (15.9,7.5)	123.4	6.20 dt (15.9,7.5)	124.0	6.26 dt (15.6, 7.8)
3	135.4	6.56 d (15.9)	130.4	6.87 d (15.9)	135.2	6.55 d (15.6)
1′	70.1		70.0		72.2	
2′	153.1	6.79 d (10.2)	153.5	6.80 d (10.2)	83.6	3.51 dd (3.0, 2.1)
3′	129.1	5.96 d (10.2)	128.8	5.96 d (10.2)	40.4	2.86 dd (14.7, 3.0)
						2.56 dd (14.7, 2.1)
4′	198.9		199.4		210.4	
5′	34.3	2.71 m; 2.49 m	34.4	2.68 m; 2.50 m	36.9	2.67 m; 2.23 m
6′	35.1	2.64 m; 2.20 m	35.0	2.45 m; 2.15 m	32.7	2.18 m; 1.82 m
1″	124.8		125.0		136.9	
2″	128.4		156.7		126.2	
3″	126.3		110.9	6.86 dd (8.4, 1.5)	128.7	
4″	127.8	7.23−7.40 m	128.9	7.24 td (8.4, 1.5)	126.7	7.24−7.42 m
5″	126.3		120.7	6.93 td (8.4, 1.5)	126.2	
6″	128.4		126.8	7.42 dd (8.4, 1.5)	128.7	
2′-OMe					56.9	3.40 s
2″-OMe			55.5	3.84 s		

[a] Assignments were made using HMQC and HMBC data.

Table 3. NMR Data of **5** in $CDCl_3$ (multiplicities, *J* in Hz)[a]

no.	δ_C	δ_H	HMBC (^{1}H→ ^{13}C)
2	71.2	6.13 dd (3.6, 1.8)	3, 4, 8a, 2′, 6′
3	125.8	5.76 dd (9.9, 3.6)	2, 4a, 1′
4	124.1	6.48 dd (9.9, 1.8)	2, 5, 4a, 8a
4a	122.3		
5	113.0	6.53 d (2.7)	4, 6, 8a
6	149.7		
7	115.6	6.55 dd (8.4, 2.7)	5, 6, 8, 8a
8	116.6	6.60 d (8.4)	4a, 6, 8a
8a	146.9		
1′	125.5		
2′	150.4		
3′	139.8		
4′	149.9		
5′	110.5	6.67 d (8.4)	1′, 3′, 4′
6′	123.8	7.06 d (8.4)	2, 2′, 3′, 4′
2′-OMe	61.3	3.94 s	2′
3′-OMe	60.8	3.94 s	3′

[a] Assignments were made using HMQC and HMBC data.

Table 4. NMR Data of **6** in $CDCl_3$ (multiplicities, *J* in Hz)[a]

no.	δ_C	δ_H	DEPT	HMBC (^{1}H→ ^{13}C)
2	71.2	4.34 m; 3.95 m	CH_2	3, 4, 1′
3	37.8	3.15 m	CH	4a, 2′/6′
4	32.5	2.94 m	CH_2	2, 3, 5, 1′
4a	104.5		C	
5	127.6	6.78 d (8.1)	CH	4, 6, 7, 8a
6	108.4	6.41 d (8.1)	C	4a, 5, 7, 8
7	153.9		C	
8	114.1		C	
8a	152.0		C	
1′	133.6		C	
2′/6′	128.3	7.16 d (8.7)	CH	3, 1′, 4′, 6′
3′/5′	114.2	6.89 d (8.7)	CH	1′, 2′, 4′, 5′, 6′
4′	159.0		C	
1″	22.3	3.41 br d (6.9)	CH_2	7, 8, 8a, 2″, 3″
2″	121.9	5.26 br t (6.9)	CH	8, 3″-Me, 4″
3″	138.1		C	
3″-Me	16.2	1.80 s	CH_3	2″, 3″, 4″
4″	39.7	2.06 m	CH_2	3″, 5″, 6″
5″	26.5	2.06 m	CH_2	3″, 4″, 6″
6″	123.9	5.06 br t (6.0)	CH	4″, 7″, 7″-Me, 8″
7″	132.0		C	
7″-Me	17.2	1.56 s	CH_3	6″, 7″, 8″
8″	25.7	1.68 s	CH_3	6″, 7″, 7″-Me
4′-OMe	55.3	3.81 s	CH_3	4′

[a] Assignments were made using HMQC and HMBC data.

candenatenin D was deduced to be **4**. Since the isolation process was carried out in MeOH, candenatenin D (**4**) could be an artifact via 1,4-Michael addition of MeOH to **2**.

Candenatenin E (**5**) was obtained as a colorless, viscous oil with a molecular formula of $C_{17}H_{17}O_5$ as deduced from the HRESITOFMS data ($[M + H]^+$ *m/z* 301.1076). The IR spectrum showed absorption bands at 3397 (OH) and 1595 (C═C) cm^{-1}. The UV absorption bands at λ_{max} 209 and 271 nm suggested the presence of a conjugated aromatic chromophore. The ^{1}H NMR data (Table 3) displayed the characteristics of flav-3-ene[9] at δ 6.48 (1H, dd, *J* = 9.9, 1.8 Hz, H-4), 6.13 (1H, dd, *J* = 3.6, 1.8 Hz, H-2), and 5.76 (1H, dd, *J* = 9.9, 3.6 Hz, H-3). In the aromatic region, the ^{1}H NMR data showed the presence of *ortho*-coupled AB-type protons at δ 7.06 (1H, d, *J* = 8.4 Hz, H-6′) and 6.67 (1H, d, *J* = 8.4 Hz, H-5′) and ABC-type protons at δ 6.60 (1H, d, *J* = 8.4 Hz, H-8), 6.55 (1H, dd, *J* = 8.4, 2.7 Hz, H-7), and 6.53 (1H, d, *J* = 2.7 Hz, H-5). Two OMe signals were also observed at δ 3.94 (6H, s) and were attached to C-3′ and C-2′, while two OH groups were attached to C-4′ and C-6 on the basis of HMBC correlations (Table 3). The CD spectrum showed a negative Cotton effect at 281 nm, consistent with the 2*S*-configuration.[10] From the above spectroscopic evidence, candenatenin E was determined to be **5**.

Candenatenin F (**6**), $C_{26}H_{32}O_3$ ($[M]^+$ *m/z* 392.5345), was isolated as a colorless, viscous oil. The UV spectrum showed the characteristic absorption bands of isoflavans[11] at λ_{max} 220 and 283 nm. This result was supported by a set of aliphatic proton signals at δ 4.34 (1H, m, H-2a), 3.95 (1H, m, H-2b), 3.15 (1H, m, H-3), and 2.94 (2H, m, H-4) in the ^{1}H NMR spectrum. In addition, two sets of aromatic protons were also observed. The first set was *para*-disubstituted aromatic protons at δ 7.16 (2H, d, *J* = 8.7 Hz, H-2′, H-6′) and 6.89 (2H, d, *J* = 8.7 Hz, H-3′, H-5′) and the other *ortho*-coupled protons at δ 6.78 (1H, d, *J* = 8.1 Hz, H-5) and 6.41 (1H, d, *J* = 8.1 Hz, H-6). Furthermore, the ^{1}H NMR spectra displayed an OMe group at δ 3.81 and a geranyl moiety at δ 5.26 (1H, br t, *J* = 6.9 Hz, H-2″), 5.06 (1H, br t, *J* = 6.0 Hz, H-6″), 3.41 (2H, br d, *J* = 6.9 Hz, H-1″), 2.06 (4H, m, H-4″, H-5″), 1.80 (3H, s, 3″-Me), 1.68 (3H, s, H-8″), and 1.56 (3H, s, 7″-Me). The HMBC correlations (Table 4) of H-1″ (δ 3.41) with C-8 (δ 114.1), of OMe protons (δ 3.81) with C-4′ (δ 159.0), and of H-2′ and H-6′ (δ 7.16) with C-4′ (δ 159.0) supported the attachment of the geranyl and OMe groups at C-8 and C-4′, respectively. The observed positive Cotton effect at 297 nm in the CD spectrum of **6** led to the assignment of a 3*R*-configuration.[11] Thus, candenatenin F was determined to be the isoflavan **6**.

Compounds **1**−**10** were investigated for cytotoxic activity against HT-29 (colon cancer), KB (human oral cancer), MCF-7 (breast

adenocarcinoma), and HeLa (human cervical cancer) cell lines. The results are summarized in Table S1 (Supporting Information). Candenatenins B (**2**) and C (**3**) exhibited the highest cytotoxic inhibitory activity against HT-29 cell lines with IC_{50} values of 17.8−19.7 μM but were weakly active against KB, MCF-7, and HeLa cell lines (IC_{50} 48.8−83.7 μM). Candenatenins A (**1**) and D (**4**) and (2*R*,3*R*)-3,5-dihydroxy-7-methoxyflavanone (**7**) were found to be weakly active against HT-29, KB, MCF-7, and HeLa cell lines. The remaining compounds were found to be inactive against all tested cancer cell lines. It is interesting to note that the structural difference between compounds **2** and **4** is only in ring A (at C-2′ and C-3′). Compound **2** (IC_{50} 19.7 μM) possesses an α,β-unsaturated ketone (a double bond at C-2′ and C-3′), while **4** (IC_{50} 48.1 μM) has an OMe group. It seems that the α,β-unsaturated carbonyl moiety in **2** plays an important role in the cytotoxicity against the HT-29 cell line. The anticancer drug used as a standard in our cytotoxic assay is camptothecin, with an IC_{50} in the range 1.22−2.44 μM.

Experimental Section

General Experimental Procedures. The optical rotation values were determined with a JASCO P-1020 polarimeter. CD spectra were measured using a JASCO J-810 spectropolarimeter. UV spectra were obtained with a SPECORD S 100 (Analytikjena). The IR spectra were measured with a Perkin-Elmer FTS FT-IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded using 300 MHz Bruker FTNMR Ultra Shield spectrometers. Chemical shifts are reported in parts per million (δ) in $CDCl_3$ with TMS as an internal reference. The ESITOFMS and EIMS data were obtained from a Micromass LCT and a MAT 95 XL mass spectrometer, respectively. Quick column chromatography (QCC) and column chromatography (CC) were carried out on silica gel 60 F_{254} (Merck) and silica gel 100 (Merck), respectively. Precoated plates of silica gel 60 F_{254} and reversed-phase (RP-18 F_{254S}) were used for analytical purposes.

Plant Material. The heartwood of *D. candenatensis* was collected in April 2005 in the Sikhao district, Trang Province, Southern Thailand. The plant material was identified by Prof. Puangpen Sirirugsa, and a voucher specimen (No. SC10) was deposited in the Herbarium of the Department of Biology, Faculty of Science, Prince of Songkla University, Songkhla, Thailand.

Extraction and Isolation. Chopped, dried heartwood of *D. candenatensis* (5.0 kg) was extracted with CH_2Cl_2 (2 × 7 L, 5 days) at room temperature. The mixture was filtered and concentrated under reduced pressure to provide a brownish CH_2Cl_2 extract (50.3 g), which was further purified by QCC with hexanes and increasing polarity with EtOAc and MeOH, respectively, to give 10 fractions (D1−D10). Fraction D2 (22.4 g) was further purified by QCC with hexanes and increasing polarity with EtOAc and MeOH, respectively, to give eight subfractions (D2a−D2h). Subfraction D2b (6.1 g) was subjected to CC with CH_2Cl_2−hexanes (4:1, v/v) followed by preparative TLC with CH_2Cl_2−hexanes (5:1, v/v) to give **4** (20.3 mg) and **10** (2.7 mg). Fraction D3 (7.9 g) was subjected to QCC with hexanes and increasing polarity with EtOAc and MeOH, respectively, to afford three subfractions (D3a−D3c). Compound **6** (3.6 mg) was isolated from subfraction D3b (2.5 g) by CC with EtOAc−CH_2Cl_2 (1:49, v/v) followed by preparative TLC with CH_2Cl_2−hexanes (7:3, v/v). Subfraction D3c (1.0 g) was separated by CC with EtOAc−hexanes (1:4, v/v) followed by reversed-phase preparative TLC with MeOH−H_2O (7:3, v/v) to give **2** (3.4 mg) and **3** (14.8 mg). Fraction D5 (2.1 g) was purified by CC with EtOAc−CH_2Cl_2 (1:4, v/v) to give five subfractions (D5a−D5e). Compounds **8** (3.9 mg) and **9** (4.1 mg) were separated from subfraction D5b (451.8 mg) by CC with EtOAc−CH_2Cl_2 (1:19, v/v), while subfraction D5c (92.8 mg) was purified by reversed-phase preparative TLC with MeOH−H_2O (1:1, v/v) to provide **1** (3.4 mg) and **7** (3.0 mg). Fraction D7 (8.0 g) was subjected to QCC with hexanes and increasing polarity with EtOAc and MeOH, respectively, to give four subfactions (D7a−D7d). Subfraction D7c (620.4 mg) was further isolated by reversed-phase CC with MeOH−H_2O (3:2, v/v) followed by preparative TLC with EtOAc−CH_2Cl_2 (1:49, v/v) to give **5** (6.0 mg).

Candenatenin A (1): colorless, viscous oil; UV (MeOH) nm (log ε) 210 (3.71), 259 (3.25); IR (neat) cm^{-1} 3390, 1588, 1496; ^{1}H and ^{13}C NMR, Table 1; HREIMS [M]$^+$ *m/z* 316.3454 (calcd for $C_{18}H_{20}O_5$ 316.3438).

(1′*R*)-Candenatenin B (2): colorless, viscous oil; $[\alpha]_D^{27}$ −64.7 (*c* 0.09, MeOH); UV (MeOH) nm (log ε) 207 (3.43), 247 (3.28); CD (CH_2Cl_2, *c* 0.20) $\Delta\varepsilon_{260}$ −10.5, $\Delta\varepsilon_{292}$ +0.4, $\Delta\varepsilon_{339}$ −6.2; IR (neat) cm^{-1} 3411, 1673, 1382; ^{1}H and ^{13}C NMR, Table 2; ESITOFMS [M]$^+$ *m/z* 228.1048 (calcd for $C_{15}H_{16}O_2$ 228.1046).

(1′*R*)-Candenatenin C (3): colorless, viscous oil; $[\alpha]_D^{27}$ −38.2 (*c* 0.20, MeOH); UV (MeOH) nm (log ε) 209 (2.95), 249 (2.66); CD (CH_2Cl_2, *c* 0.20) $\Delta\varepsilon_{321}$ −13.7, $\Delta\varepsilon_{340}$ −40.2, $\Delta\varepsilon_{352}$ −36.4; IR (neat) cm^{-1} 3411, 1670, 1244; ^{1}H and ^{13}C NMR, Table 2; ESITOFMS [M + H]$^+$ *m/z* 259.1334 (calcd for $C_{16}H_{19}O_3$ 259.1329).

(1′*R*,2′*S*)-Candenatenin D (4): colorless, viscous oil; $[\alpha]_D^{27}$ −24.9 (*c* 0.25, MeOH); UV (MeOH) nm (log ε) 204 (4.02), 221 (4.28), 257 (3.93); CD (CH_2Cl_2, *c* 0.025) $\Delta\varepsilon_{245}$ −10.1, $\Delta\varepsilon_{291}$ +7.2; IR (neat) cm^{-1} 3421, 1710, 1250; ^{1}H and ^{13}C NMR, Table 2; HREIMS [M]$^+$ *m/z* 260.1415 (calcd for $C_{16}H_{20}O_3$ 260.1412).

(2*S*)-Candenatenin E (5): colorless, viscous oil; $[\alpha]_D^{27}$ −23.6 (*c* 0.24, MeOH); UV (MeOH) nm (log ε) 209 (3.37), 271 (2.88); CD (CH_2Cl_2, *c* 0.25) $\Delta\varepsilon_{245}$ +0.4, $\Delta\varepsilon_{281}$ −3.4; IR (neat) cm^{-1} 3397, 1595, 1198; ^{1}H and ^{13}C NMR, Table 3; ESITOFMS [M + H]$^+$ *m/z* 301.1076 (calcd for $C_{17}H_{17}O_5$ 301.1071).

(3*R*)-Candenatenin F (6): colorless, viscous oil; $[\alpha]_D^{27}$ −4.8 (*c* 0.18, MeOH); UV (MeOH) nm (log ε) 220 (3.84), 283 (3.32); CD (CH_2Cl_2, *c* 0.14) $\Delta\varepsilon_{266}$ −1.3, $\Delta\varepsilon_{289}$ −3.2, $\Delta\varepsilon_{297}$ +1.1, $\Delta\varepsilon_{329}$ +10.8; IR (neat) cm^{-1} 3432, 1613, 1258; ^{1}H and ^{13}C NMR, Table 4; HREIMS [M]$^+$ *m/z* 392.5345 (calcd for $C_{26}H_{32}O_3$ 392.5305).

Cytotoxicity Assay. The cytotoxicity assay was performed by the sulphorhodamine B (SRB) method described by Skehan et al.[12] In this study, four cancer cell lines obtained from the National Cancer Institute, Bangkok, Thailand, were used. MCF-7 (breast adenocarcinoma), KB (human oral cancer), HeLa (human cervical cancer), and HT-29 (colon cancer). Camptothecin, which was used as a standard, showed cytotoxic activity in the range 1.22−2.44 μM.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **1**−**6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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