JOURNAL OF NATURAL PRODUCTS

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Wilsonols A–L, Megastigmane Sesquiterpenoids from the Leaves of *Cinnamomum wilsonii*

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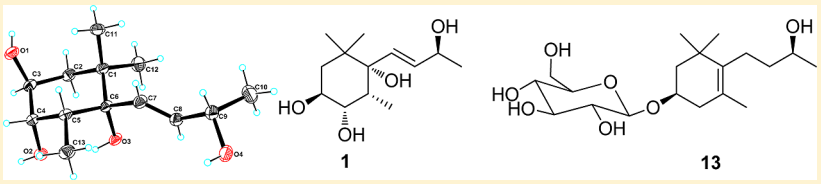
Supporting Information



ABSTRACT: Twelve new megastigmane sesquiterpenoids, wilsonols A–L (**1**–**12**), were isolated from the leaves of *Cinnamomum wilsonii*, along with seven known analogues (**13**–**19**). The structures of compounds **1**–**12** were established by spectroscopic analyses. The absolute configurations of **1**–**5** were determined by single-crystal X-ray diffraction analysis with Cu Kα irradiation, and the absolute configurations of **6**–**12** were determined by the modified Mosher's method. Compounds **1**–**9** and **13**–**19** were evaluated for in vitro cytotoxicity against five human cancer cell lines, HL-60, SMMC-7721, A-549, MCF-7, and SW-480, and compared against the Beas-2B immortalized (noncancerous) human bronchial epithelial cell line. Compound **13** exhibited IC_{50} values ranging from 2.5 to 12 μM and selectivity indices of >10 against SMMC-7721, A-549, and MCF-7 cell lines. Selected compounds were evaluated for in vitro immunomodulatory activity.

Plants of the family Lauraceae comprise about 45 genera and 2500 species that are distributed in tropical and subtropical regions, mostly in southeastern Asia and America. These species are economically important as sources of medicine, timber, edible fruits, spices, and perfumes.[1] *Cinnamomum* is one of the largest genera of Lauraceae, with about 250 species. Bioactive diterpenoids,[2] sesquiterpenoids,[3] monoterpenoids,[4] butanolides,[3,5] dibenzocycloheptanoids,[6] flavonoids,[7] phenolic compounds,[8] and alkaloids[9] have been reported from the *Cinnamomum* species. In the course of investigating the chemical constituents of traditional Chinese medicinal and edible plants, our attention was drawn to *Cinnamomum wilsonii* Gamble (Lauraceae), an evergreen tree of medium height that is endemic to China and distributed in Guangdong, Guangxi, Hubei, Hunan, Jiangxi, Shaanxi, and Sichuan Provinces. Its leaves, branches, and bark contain high levels of volatile oil and are an excellent source of soap and food flavoring. Its edible leaves, known as "Yu-Xiang-Ye", have been used as a spice to cook fish, mutton, beef, poultry, duck, and chicken for flavoring and to remove fishy odors. The dried bark has been used medicinally to treat traumatic injuries and abdominal pain.[1] However, there are no previous reports of phytochemical studies on *C. wilsonii*. In the current study, 12 new megastigmane sesquiterpenoids (**1**–**12**) and seven known analogues (**13**–**19**), including two (**14** and **18**) not previously reported as natural products, were isolated from the leaves of *C. wilsonii*. Herein, we report the isolation and structure determination of compounds **1**–**19**, as well as the cytotoxicity and immunomodulatory activities of selected compounds.

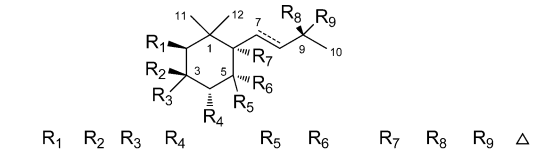
RESULTS AND DISCUSSION

A 95% EtOH extract of the leaves of *C. wilsonii* was suspended in H_2O and partitioned successively with petroleum ether, EtOAc, and *n*-BuOH. Repeated column chromatography of the EtOAc and *n*-BuOH portions on silica gel, RP (reversed-phase) C_{18}, and Sephadex LH-20 columns, followed by semi-preparative RP C_{18} HPLC, yielded 12 new (**1**–**12**) and seven known (**13**–**19**) megastigmane sesquiterpenoids.

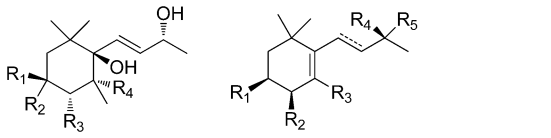
Wilsonol A (**1**) was obtained as colorless needle crystals (mp 101–102 °C, $[\alpha]^{25}_{D}$ −38). Its molecular formula was established as $C_{13}H_{24}O_4$ based on its quasi-molecular ion peak at *m*/*z* 267.1553 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_4Na$, 267.1572) in the HRESIMS spectrum, implying two degrees of unsaturation. The ^1H NMR spectrum (Table 1) of **1** exhibited signals for four methyl groups [δ_H 0.83 (s, H_3-12), 1.03 (d, H_3-

Received: April 3, 2013
Published: July 3, 2013

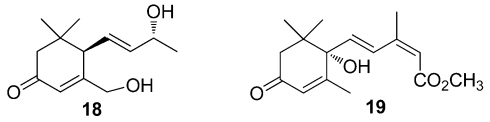
dx.doi.org/10.1021/np4002493 | *J. Nat. Prod.* 2013, 76, 1303–1312



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	Δ
1	H	OH	H	OH	H	CH_3	OH	OH	H	Δ^7
2	H	OH	H	OH	H	CH_3	OH	H	OH	Δ^7
3	H	OH	H	OH	H	CH_3	OH	=O		Δ^7
4	H	H	OH	H	H	CH_2OH	H	H	OH	Δ^7
5a	H	OH	H	OH	H	CH_3	H	H	OH	
5b	H	OH	H	OH	H	CH_3	H	OH	H	
6	H	H	OH	H	H	CH_3	OH	H	OH	
7	OH	H	H	OH	OH	CH_3	H	H	OH	Δ^7
15	H	OH	H	OH	H	CH_3	H	OH	H	Δ^7
16	H	OH	H	O-β -D-glc	H	CH_3	OH	=O		Δ^7



	R_1	R_2	R_3	R_4	R_1	R_2	R_3	R_4	R_5	Δ
8	OH	H	OH	OH	**9** OH	H	CH_2OH	OH	H	
17	H	OH	H	H	**10** OH	H	CH_2OH	H	OH	
					11 OH	H	CH_2OH	OH	H	Δ^7
					12 OH	H	CH_2OH	H	OH	Δ^7
					13 O-β -D-glc	H	CH_3	OH	H	
					14 OH	OH	CH_3	H	OH	



18 **19**

13), 1.13 (s, H_3-11), and 1.24 (d, H_3-10)], a pair of methylene protons [δ_H 1.36 (br d, J = 15.0 Hz, H-2β) and 2.00 (dd, J = 15.0, 3.2 Hz, H-2α)], a methine proton [δ_H 2.23 (dq, J = 7.2, 2.5 Hz, H-5β)], three oxygenated methines [δ_H 3.64 (dd, J = 2.8, 2.5 Hz, H-4β), 3.91 (ddd, J = 3.2, 2.8, 2.5 Hz, H-3α), and 4.29 (dq, J = 6.4, 5.9 Hz, H-9)], and two olefinic protons [δ_H 5.55 (d, J = 15.7 Hz, H-7) and 5.68 (dd, J = 15.7, 5.9 Hz, H-8)]. The ^{13}C NMR and DEPT spectra (Table 3) showed 13 carbon signals ascribable to four methyls (δ_C 13.4, C-13; 24.3, C-10; 26.7, C-12; 27.6, C-11), a methylene (δ_C 38.4, C-2), four methines (δ_C 32.7, C-5; 69.4, C-9; 72.4, C-3; 77.1, C-4) including three oxygenated ones (C-3, C-4, and C-9), two sp^2 methines (δ_C 132.7, C-7; 135.2, C-8), and two quaternary carbons (δ_C 39.3, C-1; 81.6, C-6). The double bond accounted for one degree of unsaturation, implying the presence of a ring in **1** to explain the second degree of unsaturation. Interpretation of the $^1H-^1H$ COSY and HSQC spectra of **1** revealed the presence of two partial structures, "C-2−C-3−C-4−C-5−C-13" and "C-7═C-8−C-9−C-10" (Figure 1). These two partial structures were connected through an oxygenated quaternary carbon (C-6) on the basis of HMBC correlations of H-4, H-5, H_3-13, H-7, and H-8 to C-6. HMBC correlations from H_3-11 and H_3-12 to C-1, C-2, and C-6 indicated that C-11, C-12, C-2, and C-6 were all connected with C-1, and C-2 was connected to C-6 through C-1. HMBC correlations of H_2-2 to C-1 and C-6 confirmed this connection. The relative configuration of **1** was deduced from analysis of coupling constants and the NOESY spectrum (Figure 1), which were both consistent with a chair conformation for the cyclohexane ring. The strong NOESY correlation between H-5 and H_3-11 indicated that H-5 and H_3-11 were axial bonds and assigned as β-oriented. The 3-hydroxy-1-butenyl side chain at C-6 was determined to be β-oriented based on the strong NOESY correlations of H-7 to H-5β and H_3-11β. The NOESY correlation of H-4 and H-5β and their small coupling constant J = 2.5 Hz suggested that H-4 was β-oriented. The α-orientation of H-3 was deduced from the NOESY correlations of H-3 to H-2α and H-2β, as well as the smaller coupling constants (J = 3.2, 2.8, 2.5 Hz) between H-3 and H-2α, H-2β,

Table 1. ^1H NMR [δ, mult, (J in Hz)] Data for Compounds 1−6 (400 MHz)

position	1[a]	2[a]	3[b]	4[a]	5a[a]	5b[a]	6[a]
2α	2.00 dd (15.0, 3.2)	2.00 dd (15.0, 3.2)	1.85 dd (14.5, 2.8)	1.12 dd (12.0, 12.0)	1.39 dd (14.8, 3.2)	1.39 dd (14.8, 3.2)	1.66 overlap
2β	1.36 br d (15.0)	1.36 br d (15.0)	1.23 dd (14.5, 2.8)	1.70 ddd (12.0, 3.8, 2.1)	1.67 dd (14.8, 3.2)	1.67 dd (14.8, 3.2)	1.31 ddd (12.0, 4.5, 2.3)
3α	3.91 ddd (3.2, 2.8, 2.5)	3.91 ddd (3.2, 2.8, 2.5)	3.77 ddd (5.2, 2.8, 2.8)		3.79 ddd (3.2, 3.2, 3.2)	3.83 ddd (3.2, 3.2, 3.2)	
3β				3.74 dddd (12.0, 12.0, 4.5, 3.8)			3.74 dddd (11.6, 11.6, 4.5, 4.5)
4α				1.02 ddd (12.0, 12.0, 12.0)			1.40 ddd (12.3, 12.2, 11.6)
4β	3.64 dd (2.8, 2.5)	3.64 dd (2.8, 2.5)	3.54 dd (5.2, 2.2)	2.18 ddd (12.0, 4.5, 2.1)	3.50 dd (3.2, 2.4)	3.57 dd (3.2, 2.4)	1.59 overlap
5β	2.23 dq (7.2, 2.5)	2.23 dq (7.2, 2.5)	2.27 dq (7.1, 2.2)	1.59 m	1.90 m	1.90 m	1.88 m
6α				1.53 dd (11.0, 9.1)	1.17 m	1.17 m	
7a	5.55 d (15.7)	5.55 d (15.7)	6.74 d (15.8)	5.33 dd (15.4, 9.1)	1.57m	1.57m	1.67 overlap
7b					1.07 m	1.07 m	1.54 overlap
8a	5.68 dd (15.7, 5.9)	5.68 dd (15.7, 5.9)	6.12 d (15.8)	5.49 dd (15.4, 6.0)	1.55 m	1.55 m	1.65 overlap
8b					1.43 m	1.43 m	1.53 overlap
9	4.29 dq (6.4, 5.9)	4.29 dq (6.4, 5.9)	4.22 dq (6.5, 6.0)	3.68 m	3.70 m	3.63 m	
10	1.24 d (6.4)	1.24 d (6.4)	2.21 s	1.22 d (6.5)	1.15 d (6.2)	1.18 d (6.2)	1.16 d (6.2)
11	1.13 s	1.14 s	1.11 s	0.88 s	0.98 s	0.99 s	0.99 s
12	0.83 s	0.86 s	0.73 s	0.91 s	0.90 s	0.91 s	0.98 s
13a	1.03 d (7.2)	1.00 d (7.2)	0.86 d (7.1)	3.57 dd (10.8, 2.9)	1.04 d (7.1)	1.05 d (7.1)	0.95 d (6.6)
13b				3.23 dd (10.8, 6.9)			

[a]Recorded in CD_3OD. [b]Recorded in DMSO-d_6.

dx.doi.org/10.1021/np4002493 | J. Nat. Prod. 2013, 76, 1303−1312

Table 2. ^{1}H NMR [δ, mult (J in Hz)] Data for Compounds 7−12 in CD_3OD (400 MHz)

position	7	8	9	10	11	12
2α	3.65 dd (12.5, 4.0)	1.44 dd (12.5, 4.6)	1.41 dd (12.0, 12.0)	1.41 dd (12.0, 12.0)	1.41 dd (12.0, 12.0)	1.41 dd (12.0, 12.0)
2β		1.77 dd (12.5, 12.5)	1.70 ddd (12.0, 3.6, 2.0)	1.70 ddd (12.0, 3.6, 2.0)	1.75 ddd (12.0, 3.6, 2.1)	1.75 ddd (12.0, 3.6, 2.1)
3α	2.15 ddd (12.5, 12.5, 2.8)	3.82 ddd (12.5, 9.5, 4.6)	3.87 dddd (12.0, 10.0, 5.5, 3.6)	3.87 dddd (12.0, 10.0, 5.5, 3.6)	3.91 dddd (12.0, 9.9, 5.4, 3.6)	3.91 dddd (12.0, 9.9, 5.4, 3.6)
3β	1.69 ddd (12.5, 4.0, 2.9)					
4α			1.95 dd (16.2, 10.0)	1.95 dd (16.2, 10.0)	2.04 ddd (16.6, 9.9, 2.1)	2.04 ddd (16.7, 9.9, 2.1)
4β	3.58 dd (2.9, 2.8)	3.42. d (9.5)	2.49 ddd (16.2, 5.5, 2.0)	2.49 ddd (16.2,5.5, 2.0)	2.57 dd (16.6, 5.4)	2.57 dd (16.7, 5.4)
6β	1.86 d (10.4)					
7a	5.78 ddd (15.4, 10.4, 0.9)	6.08 dd (15.9, 1.2)	2.17 ddd (13.2, 13.2, 5.0)	2.30 ddd (13.2, 13.2, 5.0)	6.05 d (15.8)	6.04 d (15.8)
7b			2.10 ddd (13.2, 13.2, 5.0)	1.97 ddd (13.2, 13.2, 5.0)		
8a	5.47 dd (15.4, 6.6)	5.76 dd (15.9, 6.2)	1.53 dddd (13.2, 13.2, 6.0, 5.0)	1.50 dddd (13.2, 13.2, 6.0, 5.0)	5.53 dd (15.8, 6.0)	5.53 dd (15.8, 6.1)
8b			1.44 dddd (13.2, 13.2, 6.0, 5.0)	1.49 dddd (13.2, 13.2, 6.0, 5.0)		
9	4.28 dq (6.6, 6.4)	4.33 ddq (6.4, 6.2, 1.2)	3.71 m	3.71 m	4.30 dq (6.4, 6.0)	4.30 dq (6.4, 6.1)
10	1.26 d (6.4)	1.27 d (6.4)	1.17 d (6.3)	1.17 d (6.3)	1.27 d (6.4)	1.27 d (6.4)
11	0.97 s	0.83 s	1.09 s	1.09 s	1.06 s	1.07 s
12	0.91 s	1.19 s	1.08 s	1.08 s	1.06 s	1.05 s
13a	1.05 s	1.20 s	4.11 d (11.8)	4.11 d (11.8)	4.12 d (11.6)	4.11 d (11.6)
13b			3.99 d (11.8)	3.99 d (11.8)	4.09 d (11.6)	4.08 d (11.6)

Table 3. ^{13}C NMR Data (δ) for Compounds 1−12 (100 MHz)

position	1[a]	2[a]	3[b]	4[a]	5a[a]	5b[a]	6[a]	7[a]	8[a]	9[a]	10[a]	11[a]	12[a]
1	39.3	39.3	38.3	35.9	35.3	35.2	41.7	40.1	40.3	39.2	39.2	38.0	38.0
2	38.4	38.4	37.0	51.3	43.0	43.0	47.5	73.7	44.3	49.5	49.5	49.0	49.0
3	72.4	72.4	69.6	67.5	72.6	72.6	67.6	34.9	70.1	65.9	65.9	65.8	65.8
4	77.1	77.1	74.8	39.9	76.6	75.4	40.9	76.5	79.0	38.3	38.3	38.4	38.4
5	32.7	32.7	30.4	40.0	34.7	34.8	36.2	74.4	79.5	129.6	129.6	130.7	130.7
6	81.6	81.6	79.5	52.9	46.5	46.3	76.5	54.0	80.8	141.9	141.9	141.9	141.9
7	132.7	132.7	151.2	130.4	26.5	26.4	33.2	127.8	131.5	25.1	25.1	126.2	126.1
8	135.2	135.2	129.9	138.9	42.6	42.3	36.0	139.9	135.9	42.4	42.4	140.6	140.7
9	69.4	69.4	197.9	69.3	69.4	69.1	70.0	69.8	69.7	69.2	69.1	69.4	69.5
10	24.3	24.3	27.2	24.1	23.5	23.5	23.8	24.1	24.4	23.4	23.4	24.0	24.0
11	27.6	27.6	26.9	21.8	23.7	23.7	26.4	15.6	27.8	29.1	29.1	28.9	28.9
12	26.7	26.7	26.4	31.8	32.1	32.1	25.2	28.7	27.3	30.1	30.1	30.4	30.4
13	13.4	13.4	13.1	66.5	17.3	17.3	16.8	27.8	26.3	63.0	63.0	64.2	64.2

[a]Recorded in CD_3OD. [b]Recorded in DMSO-d_6.

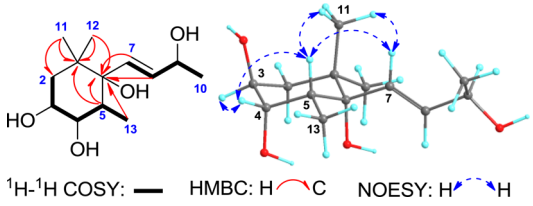


Figure 1. Key ^{1}H−^{1}H COSY, HMBC, and NOESY of 1.

and H-4. The larger coupling constant (J = 15.7 Hz) between H-7 and H-8 indicates that the geometry of the $\Delta^{7(8)}$ double bond is *E*. In order to determine its absolute configuration, a suitable crystal of **1** was obtained and subjected to single-crystal X-ray diffraction analysis using the anomalous scattering of Cu Kα radiation. The final refinement of the given coordinate (Figure 2) resulted in a Flack parameter of −0.04(11), which allowed unambiguous assignment of the absolute configuration of **1** as 3*S*,4*S*,5*R*,6*R*,9*S*.

Wilsonol B (**2**) was obtained as colorless block crystals and had the same molecular formula, $C_{13}H_{24}O_4$, as that of

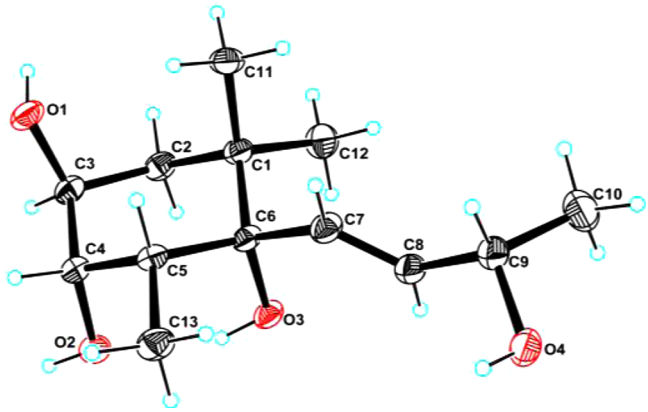


Figure 2. X-ray ORTEP drawing of compound 1.

compound **1**, according to the HRESIMS data (m/z 267.1560 [M + Na]$^+$). The ^{1}H and ^{13}C NMR spectra (Tables 1 and 3) of **2** were nearly identical to those of **1**, while the main

dx.doi.org/10.1021/np4002493 | J. Nat. Prod. 2013, 76, 1303−1312

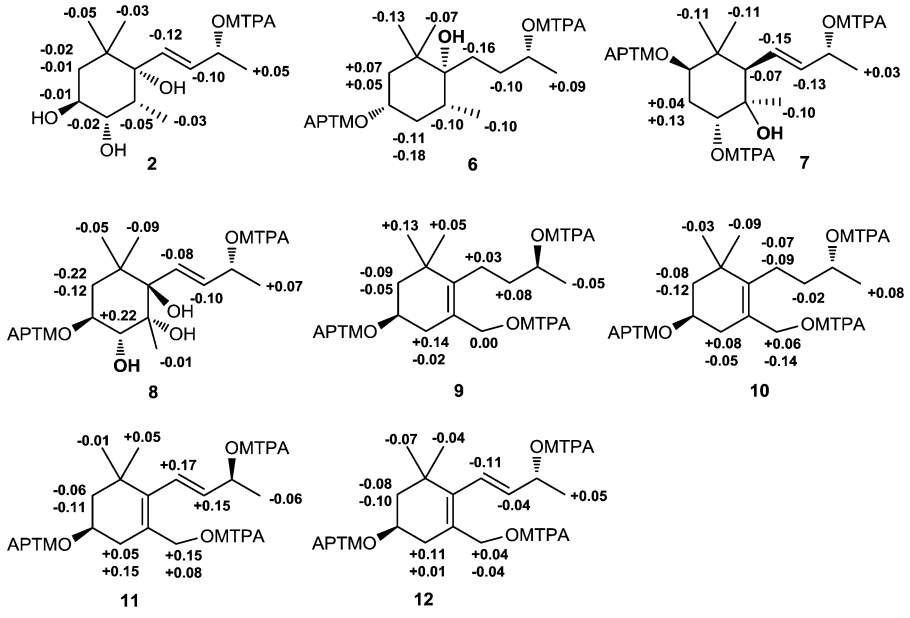


Figure 3. $\Delta\delta_{H(S-R)}$ values (in ppm) for the MTPA esters of **2** and **6**–**12**.

differences were a slight upfield shift of CH_3-13 (0.03 ppm) and a downfield shift of CH_3-11 and CH_3-12 (0.01 and 0.03 ppm, respectively) in **2** compared with those in **1**. Extensive 2D NMR analyses, including $^1H-^1H$ COSY, HSQC, HMBC, and NOESY, showed that **2** had the same gross structure as that of **1**, and both compounds had similar optical rotations. Compound **2** should be the C-9 epimer of **1**. In order to determine the absolute configuration of C-9 in **2**, (*S*)- and (*R*)-MTPA esters (**2a** and **2b**) were prepared.[11] Significant $\Delta\delta$ values ($\Delta\delta = \delta_{S\text{-MTPA-ester}} - \delta_{R\text{-MTPA-ester}}$) were observed for proton signals adjacent to C-9, as shown in Figure 3. According to the rule of the modified Mosher's method,[10] the absolute configuration of C-9 in **2** was determined to be *R*, contrasting with the *S* configuration of C-9 in **1**. The absolute configuration of **2** was confirmed as 3*S*,4*S*,5*R*,6*R*,9*R* by single-crystal X-ray diffraction analysis with Cu Kα irradiation (Figure 4).

The molecular formula of wilsonol C (**3**) was $C_{13}H_{22}O_4$ by HRESIMS, indicating three degrees of unsaturation. The UV absorption maximum at 231 nm suggested the presence of an α,β-unsaturated ketone, and the IR spectrum displayed absorption bands for hydroxyl groups (3467 cm^{-1}), a double bond (1641 cm^{-1}), and a conjugated carbonyl (1670 cm^{-1}).

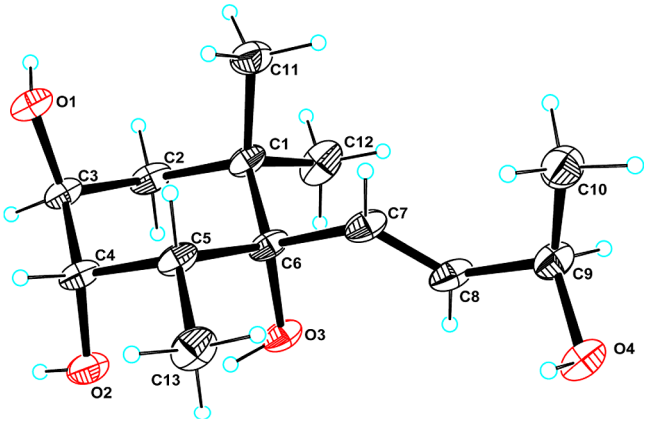


Figure 4. X-ray ORTEP drawing of compound **2**.

The ^1H and ^{13}C NMR spectra of **3** (Tables 1 and 3) were very similar to those of **1**, except that a ketone carbonyl (δ_C 197.9, C-9) in **3** replaced the oxygenated methine (δ_H 4.29, H-9; δ_C 69.4, C-9) of **1**. HMBC correlations between CH_3-10 and both C-8 and C-9 and from H-8 to both C-9 and C-10 in the HMBC spectrum of **3** established connection of the ketone carbonyl C-9 to C-8 and C-10. Detailed 1D and 2D NMR analysis established the planar structure and the relative configuration of **3**. The absolute configuration of **3** was determined to be 3*S*,4*S*,5*R*,6*R* by single-crystal X-ray diffraction analysis with Cu Kα irradiation (Figure 5).

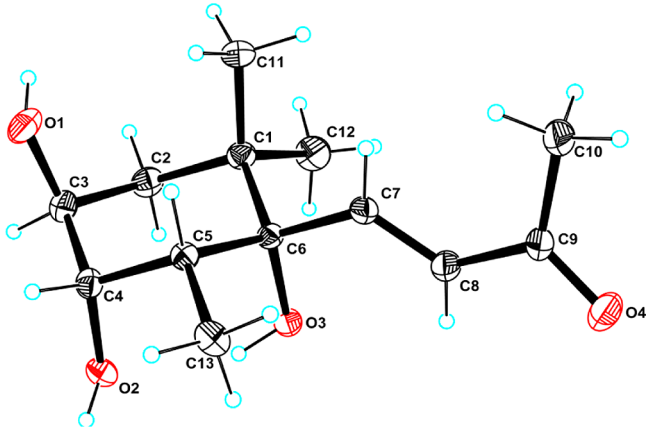


Figure 5. X-ray ORTEP drawing of compound **3**.

Wilsonol D (**4**) had the molecular formula $C_{13}H_{24}O_3$ by HRESIMS, indicating two degrees of unsaturation. Inspection of 1D and 2D NMR data (Tables 1 and 3) indicated that **4** was a megastigmane derivative. Interpretation of the $^1H-^1H$ COSY and HSQC data of **4** constructed the partial structure of "C-2–C-3–C-4–C-5(C-13)–C-6–C-7–C-8–C-9–C-10". HMBC correlations from H_3-11 and H_3-12 to C-1, C-2, and C-6 indicated that C-11, C-12, C-2, and C-6 were all connected to C-1, which completed a megastigmane skeleton. Therefore, **4** was designated as 3,9,13-trihydroxymegastigman-7-ene. The

dx.doi.org/10.1021/np4002493 | *J. Nat. Prod.* 2013, 76, 1303–1312

larger coupling constants J = 12.0 Hz between H-3 and both H-2 and H-4 and the strong NOESY correlations between H_3-11/H-3, H_3-11/H-5, and H-3/H-5 suggested that H-3, H-5, and CH_3-11 occupied the axial bonds of the chair conformation of the cyclohexane unit, which were assigned β-orientations. The α-orientation of H-6 was deduced from the larger coupling constants J = 11.0 Hz of H-6 with H-5 and the NOESY correlations between H-7 and H-5, H_3-11, H_3-12, and H_3-13 and between H-6 and H-2α and H-4α. The larger coupling constant (J = 15.4 Hz) between H-7 and H-8 indicated the *E*-geometry of the double bond. Finally, single-crystal X-ray diffraction analysis with Cu Kα irradiation (Figure 6) determined the absolute configuration of **4** as 3*S*,5*R*,6*S*,9*R*.

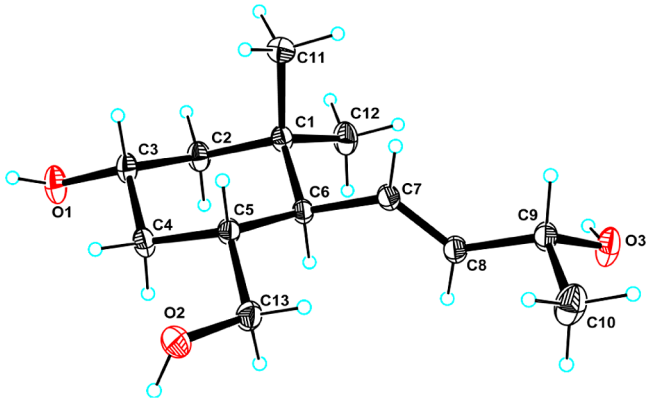


Figure 6. X-ray ORTEP drawing of compound **4**.

Wilsonol E (**5**) had the molecular formula $C_{13}H_{26}O_3$. The NMR spectra (Tables 1 and 3) indicated that compound **5** was isolated as a mixture (ca. 3:2) of two epimers (**5a** and **5b**) at C-9. The planar structure of **5** was deduced to be 3,4,9-trihydroxymegastigmane from analysis of 2D NMR data. Similar to those of **1**, the relative configuration of **5** was deduced to be H-3α, H-4β, H-5β, and H-6α from the NOESY correlations H-5/H_3-11, H-7/H_3-11, H-5/H-7, H-4/H-5, and H-3/H_2-2, as well as the smaller coupling constants J = 3.2 Hz for H-3 with both H_2-2 and H-4. Single-crystal X-ray diffraction analysis of **5** using Cu Kα irradiation confirmed the relative configuration. In the crystal structure (Figure 7), the ratio of the two epimers **5a** and **5b** was determined as 60:40. The Flack coefficient obtained [0.2(3)] for the given coordinates

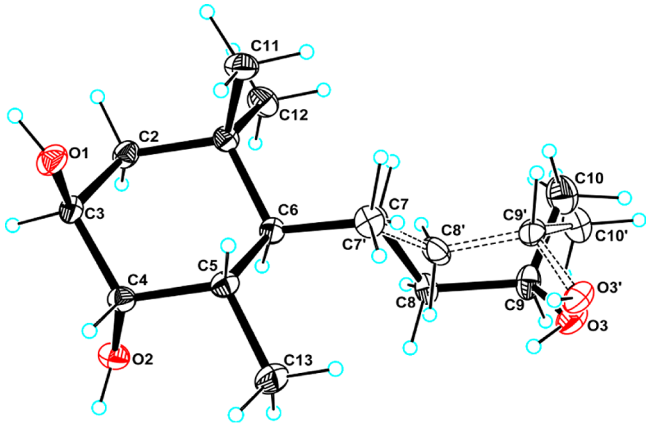


Figure 7. X-ray ORTEP drawing of compound **5**.

indicated that the absolute configurations of **5a** and **5b** were 3*S*,4*S*,5*S*,6*S*,9*S* and 3*S*,4*S*,5*S*,6*S*,9*R*, respectively.

The HRESIMS spectrum of wilsonol F (**6**) revealed the molecular formula $C_{13}H_{26}O_3$, requiring one degree of unsaturation. 1D NMR (Tables 1 and 3) and 2D NMR data of **6** established the planar structure to be 3,6,9-trihydroxymegastigmane. The cross-peaks of H-3/H_3-11 and H-3/H-5 in the NOESY spectrum of **6** indicated the *syn*-relationship of these groups, which were all assigned β-orientations. The NOESY correlation of H-7 to H_3-11 suggested the side chain was β-oriented. The absolute configurations of C-3 and C-9 in **6** were elucidated to be 3*S* and 9*R* by applying the modified Mosher's method (Figure 3). Therefore, the absolute configurations of C-5 and C-6 in **6** were determined as *R*.

Wilsonol G (**7**) was isolated as an amorphous powder, and its molecular formula was determined to be $C_{13}H_{24}O_4$. The planar structure of **7** was assigned as 2,4,5,9-tetrahydroxymegastigman-7-ene on the basis of the 1D (Tables 2 and 3) and 2D NMR analysis. The relative configuration of **7**, except for C-9, was characterized by the coupling constants and the NOESY experiment. The larger coupling constant J = 12.5 Hz of H-2 (δ 3.65, dd) with one of the H-3a protons (δ 2.15, ddd) indicated H-2 was axial and α-oriented. The smaller constants of H-4 (δ 3.58, dd, J = 2.9, 2.8 Hz) with H_2-3 protons suggested H-4 should be equatorial and therefore β-oriented. The NOESY correlations of H-6 and H-2α suggested that H-6 was also axial, which established its α-orientation. The α-orientation of CH_3-13 was deduced from the cross-peak of H_3-13 and H-6α in the NOESY spectrum. Finally, the absolute configurations of C-2 and C-9 in **7** were assigned 2*R* and 9*R* by the modified Mosher's method (Figure 3). In consideration of the relative configuration, the absolute configurations of C-4, C-5, and C-6 in **7** were assigned 4*R*, 5*R*, and 6*R*, respectively. The larger coupling constant (J = 15.4 Hz) between H-7 and H-8 indicated the *E* geometry of the double bond.

Wilsonol H (**8**) had the molecular formula $C_{13}H_{24}O_5$, as deduced from HRESIMS data. The ^{1}H and ^{13}C NMR spectra (Tables 2 and 3) of **8** closely resembled those of **2**. The major difference was the appearance of an oxygen-bearing quaternary carbon (δ_C 79.5, C-5) in **8** that replaced the methine (δ_H 2.23, dq, J = 7.2, 2.5 Hz, H-5; δ_C 32.7, C-5) in **2**. This was supported by HMBC correlations from H-3, H-4, H-7, and H_3-13 to the oxygenated quaternary carbon C-5. These data indicated that **8** was a 5-OH derivative of **2**. The planar structure of **8** was confirmed by comprehensive analysis of ^{1}H−^{1}H COSY, HSQC, and HMBC spectra (Figure 8). The geometry of the side chain double bond was assigned as *E*, based on the large coupling constant J = 15.9 Hz between H-7 and H-8. The relative configuration of **8** was determined from the analysis of NOESY correlations (Figure 8) and coupling constants. The coupling constant between H-4 and H-3 (J = 9.5 Hz) suggested a *trans*-

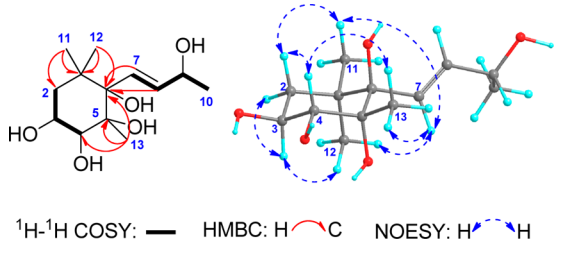


Figure 8. Key ^{1}H−^{1}H COSY, HMBC, and NOESY correlations of **8**.

dx.doi.org/10.1021/np4002493 | *J. Nat. Prod.* 2013, 76, 1303−1312

relationship of H-4 and H-3 and axial orientation. The strong NOESY correlation of H-4β and H_3-13 established the β-orientation of H_3-13. The α-orientation of the side chain was deduced from the strong NOESY correlations between H-7 and H_3-11, H_3-12, and H_3-13 and lack of NOESY correlations between H-7 and H-2β and H-4β. The absolute configurations of C-3 and C-9 in **8** were determined to be *S* and *R*, respectively, by the modified Mosher's method (Figure 3). With the relative configuration assigned, the absolute configuration of **8** is therefore 3*S*,4*R*,5*R*,6*R*,9*R*.

Wilsonol I (**9**) displayed an $[M + Na]^+$ ion peak at *m*/*z* 251.1603, suggesting a molecular formula of $C_{13}H_{24}O_3$, the same as that of **4**. The NMR data of **9** (Tables 2 and 3) indicated that **9** had structural fragments similar to those of **4**, except for the presence of a double bond in the six-membered ring of **9** (Δ^5) and the absence of the side chain double bond in **4** (Δ^7). HMBC correlations from H-3 and H_3-13 to C-5 and from H_3-11 and H_3-12 to C-6 in **9** supported this deduction. The absolute configuration of **9** was determined to be 3*S* and 9*S* by the modified Mosher's method (Figure 3). Therefore, **9** was established as (3*S*,9*S*)-3,9,13-trihydroxymegstigman-5-ene.

The HRESIMS of wilsonol J (**10**) gave a pseudomolecular ion peak at *m*/*z* 251.1607 $[M + Na]^+$, indicating, like that of **9**, a molecular formula of $C_{13}H_{24}O_3$ (calcd for $C_{13}H_{24}O_3Na$, 251.1623). The NMR data of **10** were similar to those of **9**, and HSQC, $^1H-^1H$ COSY, and HMBC spectra revealed that **10** had the same planar structure and was a stereoisomer of **9**. The chemical shift values of H_2-2, H-3, H_2-4, C-2, C-3, and C-4 in **10** were nearly identical to those of **9**, suggesting the 3*S* configuration in **10**. Thus, **10** must differ from **9** in the configuration at C-9. This was proven by NMR analysis of prepared (*S*)- and (*R*)-MTPA esters of **10** (**10a** and **10b**), which established the absolute configuration of **10** as 3*S*,9*R* (Figure 3).

Wilsonols K (**11**) and L (**12**) were isolated as white, amorphous powders. Their HRESIMS [*m*/*z* 249.1453, 249.1456 ($[M + Na]^+$), respectively] indicated the molecular formula $C_{13}H_{22}O_3$ for both **11** and **12**. The ^1H and ^{13}C NMR data revealed that **11** and **12** were structurally similar to **9** and **10** except for an additional C-7/C-8 double bond in **11** and **12**, in keeping with one additional degree of unsaturation compared with **9** and **10**. Analysis of the $^1H-^1H$ COSY, HSQC, and HMBC spectra confirmed the planar structures of **11** and **12** as the 7,8-dehydro analogues of **9** and **10**, respectively. Similarly, the absolute configurations of **11** and **12** were assigned as 3*S*,9*S* and 3*S*,9*R*, respectively, following application of the modified Mosher's method (Figure 3).

Compounds **13**–**19** were identified as (3*R*,9*S*)-megastigman-5-ene-3,9-diol 3-*O*-β-D-glucopyranoside (**13**),[11] (3*S*,4*R*,9*R*)-3,4,9-trihydroxymegastigman-5-ene (**14**),[12] (3*S*,4*S*,5*S*,6*S*,9*S*)-3,4-dihydroxy-5,6-dihydro-β-ionol (**15**),[13] lasianthionoside A (**16**),[14] (3*S*,5*S*,6*S*,9*R*)-3,6-dihydroxy-5,6-dihydro-β-ionol (**17**),[15] apocynol A (**18**),[16] and (+)-(6*S*,7*E*,9*Z*)-abscisic ester (**19**),[17] respectively, on the basis of the spectroscopic data analysis and comparison with data reported in the literature. Compounds **14** and **18** were previously reported as hydrolysis products of (3*S*,4*R*,9*R*)-3,4,6-trihydroxymegastigman-5-ene 3-*O*-β-D-glucopyranoside[12] and apocynoside I,[16] respectively, but have not been reported previously as naturally occurring.

The absolute configuration of lasianthionoside A (**16**) has been reported previously only by comparisons of optical rotation and ^{13}C NMR data with lasianthionoside C,[14] without further evidence. In order to determine its absolute configuration, compound **16** was recrystallized in MeOH containing a small amount of $CHCl_3$, and the crystal was subjected to single-crystal X-ray diffraction analysis with Cu Kα radiation. The Flack parameter, associated with the absolute configuration, was calculated to be 0.01(15), which confirmed the previously reported absolute configuration of compound **16** (Figure 9).

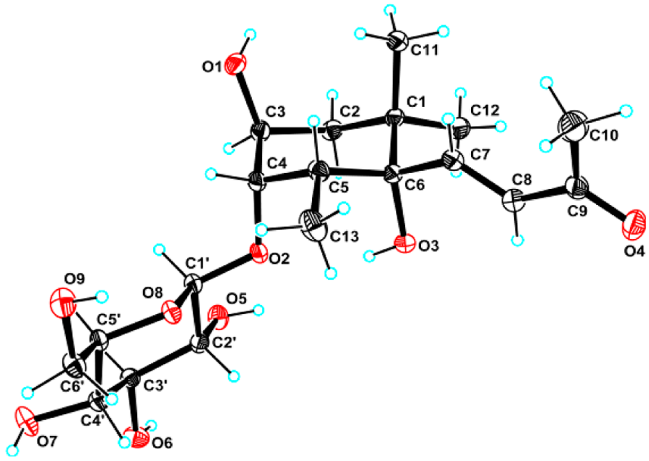


Figure 9. X-ray ORTEP drawing of compound **16**.

Compounds **1**–**9** and **13**–**19** were evaluated for cytotoxicity against five human cancer cell lines, including myeloid leukemia HL-60, hepatocellular carcinoma SMMC-7721, lung cancer A-549, breast cancer MCF-7, and colon cancer SW-480 cells, as well as the immortalized noncancerous Beas-2B human bronchial epithelial cell line. The results (Table S1) were notable for compound **13**, which exhibited IC_{50} values of 5.0, 3.1, 2.5, 3.4, and 12 μM, respectively, higher potency than *cis*-platin. Compound **13** was nontoxic to the Beas-2B cell line at the highest concentration tested, resulting in selectivity indices as high as >16 against the cancer-derived cells. The other compounds tested showed no significant cytotoxicity (IC_{50} >10 μM). Lauroside B,[18] a megastigmane glycoside isolated from the leaves of *Laurus nobilis* (Lauraceae), was reported to suppress the proliferation of human melanoma cell lines by inducing apoptosis, and the mechanism is the inhibition of NF-κB activation. The mechanism by which **13** exhibits cytotoxicity is likely similar to that of lauroside B, due to their structural similarity.

Selected compounds were also tested for in vitro immunomodulation. Immune cells play a pivotal role in the pathogenesis of cell-mediated autoimmune diseases and chronic inflammatory disorders such as rheumatoid arthritis and multiple sclerosis. Concanavalin A (ConA) and lipopolysaccharide (LPS) are specific stimuli for T and B cells, respectively. Compounds **1**–**4**, **6**, **9**, **13**–**17**, and **19** were evaluated in the ConA/LPS-induced splenocyte proliferation assay.[19] (Due to the exhaustion of supply by the modified Mosher's analysis, compounds **5**, **7**, **8**, **10**–**12**, and **18** were not tested.) Results (Tables S2–4) showed that compounds **1**, **2**, **9**, and **17** inhibited the proliferation of ConA-induced murine T cells, and compounds **9**, **14**, and **17** inhibited the proliferation of LPS-induced murine B cells. Interestingly, compound **19** significantly promoted the proliferation of both ConA-induced murine T cells and LPS-induced murine B cells. The cytotoxity assay (Tables S2–4) demonstrated that these active com-

dx.doi.org/10.1021/np4002493 | *J. Nat. Prod.* 2013, 76, 1303–1312

pounds are nontoxic to murine lymphocytes. Therefore, the antiproliferative activities against ConA-induced murine T cells and LPS-induced murine B cells of **1**, **2**, **9**, **14**, and **17** are not involved with the general cytotoxity.

Megastigmane sesquiterpenoids are degradation products of β-carotene in the biosynthetic pathway and are reported to show antielastase activity,[20] cytotoxicity against human melanoma cell lines,[18] mushroom tyrosinase inhibitory activity,[21] phytotoxicity on lettuce and tomato,[22] and promotion activity on HO-1 and SIRT1.[23] Although there are 2500 species in the family of Lauraceae, there are only four reports of the isolation of megastigmane sesquiterpenoids from this family.[13,18,24,25] This study implies that megastigmane derivatives may be more prevalent in Lauraceae species. These megastigmane compounds and the plant material *C. wilsonii* may have value as a source of a targeted compound library for investigating structure−activity relationships of megastigmane pharmacophores for potential molecular drug targets that may emerge from ongoing and future biological screening of megastigmane sesquiterpenoids.

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points (uncorrected) were measured on a Beijing Tech X-5 microscopic melting point apparatus. Optical rotations were determined in MeOH, at concentrations indicated, on a Perkin-Elmer 341 polarimeter. UV and FT-IR spectra were determined using Varian Cary 50 and Bruker Vertex 70 instruments, respectively. NMR spectra were recorded on a Bruker AM-400 spectrometer, and the ^{1}H and ^{13}C NMR chemical shifts were referenced to the solvent or solvent impurity peaks for $CDCl_3$ at δ_H 7.24 and δ_C 77.23, for DMSO-d_6 at δ_H 2.50 and δ_C 39.51, and for CD_3OD at δ_H 3.31 and δ_C 49.15. High-resolution electrospray ionization mass spectra (HRESIMS) were carried out in the positive-ion mode on a Thermo Fisher LC-LTQ-Orbitrap XL spectrometer. The X-ray diffraction experiments were carried out on a Bruker SMART APEX-II CCD diffractometer equipped with graphite-monochromatized Cu Kα radiation (λ = 1.541 78 Å). HPLC was carried out on an Agilent 1200 quaternary system with a UV detector using a reversed-phased C_{18} column (5 μm, 10 × 250 mm, YMC-pack ODS-A). Column chromatography was performed using silica gel (Qingdao Marine Chemical Inc., China), ODS (50 μm, YMC Co. Ltd., Japan), and Sephadex LH-20 (GE Healthcare Bio-Sciences AB, Sweden). Thin-layer chromatography (TLC) was performed with silica gel 60 F254 (Yantai Chemical Industry Research Institute) and RP-C_{18} F254 plates (Merck, Germany).

Plant Material. The leaves of *C. wilsonii* were collected at Wuxi, Sichuan Province, People's Republic of China, in July 2010. The plant material was identified by Prof. Changgong Zhang of the School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology. A voucher specimen (No. 2010-0701) was deposited in the herbarium of Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, Tongji Medical College, Huazhong University of Science and Technology.

Extraction and Isolation. The air-dried leaves of *C. wilsonii* (50.6 kg) were extracted with 95% EtOH at room temperature (3 × 200 L) and afforded a crude extract of 1.5 kg after evaporation of the solvent under vacuum. The extract was suspended in H_2O (10 L) and partitioned sequentially with petroleum ether (6 × 15 L), EtOAc (6 × 15 L), and *n*-BuOH (6 × 15 L). The EtOAc-soluble portion (102 g) was fractionated via silica gel column chromatography (CC) eluting with $CHCl_3$−MeOH (55:1 to 5:1) to yield six fractions, A1−A6, on the basis of TLC analysis. Fraction A1 (eluted by $CHCl_3$−MeOH, 55:1) was chromatographed on a Sephadex LH-20 column (MeOH) to give compounds **18** (2.4 mg) and **19** (4.8 mg). Fraction A2 (eluted by $CHCl_3$−MeOH, 45:1) was further separated using RP-C_{18} CC (MeOH−H_2O, 30:70 to 100:0) to afford four subfractions (A2-1 to A2-4). Repeated crystallization of subfraction A2-1 (eluted by 30% MeOH) in $CHCl_3$ containing a small amount of MeOH yielded **5** (7.2 mg). Subfraction A2-2 (eluted by 40% MeOH) was further purified by HPLC (MeOH−H_2O, 30:70) to afford **17** (7.2 mg) and **14** (9.3 mg). Fraction A5 (eluted with $CHCl_3$−MeOH, 20:1) was passed through an RP C_{18} column eluted with MeOH−H_2O (20:80 to 100:0) to give five subfractions (A5-1 to A5-5). Repeated crystallization of subfraction A5-1 yielded **1** (56 mg). Subfraction A5-2 was chromatographed on a Sephadex LH-20 column (MeOH) to give compounds **2** (7.3 mg) and **6** (6.6 mg). Subfraction A5-3 was further purified by semipreparative HPLC (MeOH−H_2O, 30:70) to afford **15** (7.8 mg) and **4** (4.7 mg). Subfraction A5-4 was further purified by semi-preparative HPLC (CH_3CN−H_2O, 16:84) to afford **9** (6.2 mg), **12** (2.6 mg), **10** (8.1 mg), and **11** (2.6 mg). The *n*-BuOH extract (300 g) was divided into five fractions (B1−B5) by silica gel CC eluted with $CHCl_3$−MeOH (30:1 to 2:1). Fraction B2 (eluted with $CHCl_3$−MeOH, 20:1) was further separated using RP-C_{18} CC (MeOH−H_2O, 10:90 to 100:0) to afford seven subfractions (B2-1 to B2-7). Repeated crystallization of B2-1 yielded **16** (23.0 mg). Subfraction B2-3 was separated on Sephadex LH-20 (MeOH) to yield **8** (5.4 mg) and **13** (7.5 mg). Subfraction B2-6 was further purified on Sephadex LH-20 (MeOH) to furnish **3** (27.0 mg) and **7** (5.6 mg).

*Wilsonol A (**1**):* colorless needle crystals; mp 101−102 °C; $[\alpha]^{25}_D$ −38 (*c* 1.87, MeOH); ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 267.1553 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_4Na$, 267.1572).

*Wilsonol B (**2**):* colorless block crystals; mp 102−103 °C; $[\alpha]^{25}_D$ −34 (*c* 0.24, MeOH); ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 267.1560 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_4Na$, 267.1572).

*Wilsonol C (**3**):* colorless block crystals; mp 171−172 °C; $[\alpha]^{25}_D$ −57 (*c* 0.55, MeOH); UV (MeOH) λ_{max} (log ε) 231 (4.97) nm; IR (KBr) ν_{max} 3467, 1670, 1641, 1385, 1270, 1100, 1058 cm^{-1}; ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 265.1406 $[M + Na]^+$ (calcd for $C_{13}H_{22}O_4Na$, 265.1416).

*Wilsonol D (**4**):* colorless block crystals; mp 153−155 °C; $[\alpha]^{25}_D$ −30 (*c* 0.07, MeOH); ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 251.1611 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_3Na$, 251.1623).

*Wilsonol E (**5**):* colorless needle crystals; mp 164−165 °C, $[\alpha]^{25}_D$ −12 (*c* 0.15, MeOH); ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 253.1767 $[M + Na]^+$ (calcd for $C_{13}H_{26}O_3Na$, 253.1780).

*Wilsonol F (**6**):* white powder; $[\alpha]^{25}_D$ −13 (*c* 0.80, MeOH); ^{1}H NMR data see Table 1, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 253.1770 $[M + Na]^+$ (calcd for $C_{13}H_{26}O_3Na$, 253.1780).

*Wilsonol G (**7**):* white powder; $[\alpha]^{25}_D$ −5 (*c* 0.29, MeOH); ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 267.1562 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_4Na$, 267.1572).

*Wilsonol H (**8**):* white powder; $[\alpha]^{25}_D$ −19 (*c* 0.47, MeOH); ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 283.1501 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_5Na$, 283.1521).

*Wilsonol I (**9**):* white powder; $[\alpha]^{25}_D$ −33 (*c* 0.15, MeOH); ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 251.1603 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_3Na$, 251.1623).

*Wilsonol J (**10**):* white powder; $[\alpha]^{25}_D$ −4 (*c* 0.27, MeOH); ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 251.1607 $[M + Na]^+$ (calcd for $C_{13}H_{24}O_3Na$, 251.1623).

*Wilsonol K (**11**):* white powder; $[\alpha]^{25}_D$ −52 (*c* 0.06, MeOH); UV (MeOH) λ_{max} (log ε) 233 (3.59), 282 (3.51) nm; ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 249.1453 $[M + Na]^+$ (calcd for $C_{13}H_{22}O_3Na$, 249.1467).

*Wilsonol L (**12**):* white powder; $[\alpha]^{25}_D$ −64 (*c* 0.05, MeOH); UV (MeOH) λ_{max} (log ε) 226 (3.62), 280 (3.64) nm; ^{1}H NMR data see Table 2, and ^{13}C NMR data see Table 3; HRESIMS *m*/*z* 249.1456 $[M + Na]^+$ (calcd for $C_{13}H_{22}O_3Na$, 249.1467).

Preparation of (*S*)- and (*R*)-MTPA Ester Derivatives of 2 (ref 10). Compound **2** (1.0 mg) was dissolved in 1 mL of anhydrous CH_2Cl_2. Dimethylaminopyridine (30 mg), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (37 mg) and (*S*)-MTPA (46 mg) were then added in sequence. The reaction mixture

was stirred at room temperature for 2 h. After addition of CH_2Cl_2 (1 mL), the solution was successively washed with H_2O (1 mL), 5% HCl (1 mL), $NaHCO_3$-saturated H_2O (1 mL), and brine (1 mL). The organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The residue was passed through a small silica gel column using $CHCl_3$−MeOH (50:1) as the eluent to furnish the (*S*)-MTPA ester of **2** (**2a**, 1.4 mg). The (*R*)-MTPA derivative (**2b**, 1.3 mg) was prepared with (*R*)-MTPA and purified in the same manner.

*(S)-MTPA derivative of **2** (**2a**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.34 (5H, overlap, aromatic protons), 5.65 (1H, d, J = 15.7 Hz, H-7), 5.57 (1H, dd, J = 15.7, 6.0 Hz, H-8), 5.61 (1H, dq, J = 6.3, 6.0 Hz, H-9), 4.03 (1H, ddd, J = 3.2, 2.8, 1.2 Hz, H-3α), 3.64 (1H, dd, J = 2.8, 2.5 Hz, H-4β), 3.55 (3H, s, OCH_3), 2.21 (1H, dq, J = 7.2, 2.5 Hz, H-5β), 2.04 (1H, dd, J = 15.0, 3.2 Hz, H-2α), 1.42 (3H, d, J = 6.3 Hz, H-10), 1.35 (1H, dd, J = 15.0, 1.2 Hz, H-2β), 1.07 (3H, s, H-11), 0.95 (3H, d, J = 7.2 Hz, H-13), 0.76 (3H, s, H-12); HRESIMS m/z 483.1953 $[M + Na]^+$ (calcd for $C_{23}H_{31}O_6F_3Na$, 483.1970).

*(R)-MTPA derivative of **2** (**2b**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.34 (5H, overlap, aromatic protons), 5.77 (1H, d, J = 15.7 Hz, H-7), 5.67 (1H, dd, J = 15.7, 6.0 Hz, H-8), 5.61 (1H, dq, J = 6.3, 6.0 Hz, H-9), 4.04 (1H, ddd, J = 3.2, 2.8, 1.2 Hz, H-3α), 3.66 (1H, dd, J = 2.8, 2.5 Hz, H-4β), 3.51 (3H, s, OCH_3), 2.26 (1H, dq, J = 7.2, 2.5 Hz, H-5β), 2.06 (1H, dd, J = 15.0, 3.2 Hz, H-2α), 1.37 (3H, d, J = 6.3 Hz, H-10),1.36 (1H, dd, J = 15.0, 1.2 Hz, H-2β), 1.12 (3H, s, H-11), 0.98 (3H, d, J = 7.2 Hz, H-13), 0.79 (3H, s, H-12); HRESIMS m/z 483.1947 $[M + Na]^+$ (calcd for $C_{23}H_{31}O_6F_3Na$, 483.1970).

Preparation of (*S*)- and (*R*)-MTPA Ester Derivatives of 6−12 (ref 10). Wilsonol F (**6**) (1.0 mg) was dissolved in 2 mL of anhydrous CH_2Cl_2. Dimethylaminopyridine (32 mg), triethylamine, and (*R*)-MTPA chloride (26 μL) were then added in sequence. The reaction mixture was stirred for 1 h at room temperature and then quenched by the addition of 0.5 mL of aqueous MeOH. The solvents were removed under vacuum, and the residue was passed through a small silica gel column using $CHCl_3$−MeOH (100:1) as the eluent to provide the (*S*)-MTPA ester of **6** (**6a**, 1.4 mg). The (*R*)-MTPA derivative (**6b**, 1.6 mg) was prepared with (*S*)-MTPA chloride and purified in the same manner. The same procedure was used to prepare the MTPA esters of compounds **7** (**7a**, **7b**), **8** (**8a**, **8b**), **9** (**9a**, **9b**), **10** (**10a**, **10b**), **11** (**11a**, **11b**), and **12** (**12a**, **12b**).

*(S)-MTPA derivative of **6** (**6a**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.55−7.40 (10H, overlap, aromatic protons), 5.13 (1H, dddd, J = 12.1, 12.1, 4.6, 4.5 Hz, H-3β), 5.07 (1H, m, H-9), 3.57 (3H, s, OCH_3), 3.52 (3H, s, OCH_3), 1.88 (1H, m, H-5β), 1.83 (1H, dd, J = 12.1, 12.1 Hz, H-2α), 1.67 (2H, overlap, H-8), 1.62 (1H, m, H-4β), 1.48 (2H, overlap, H-7), 1.47 (1H, overlap, H-4α), 1.42 (1H, ddd, J = 12.1, 4.6, 2.1 Hz, H-2β), 1.36 (3H, d, J = 6.3 Hz, H-10), 0.91 (3H, s, H-11), 0.88 (3H, s, H-12), 0.84 (3H, d, J = 7.1 Hz, H-13); HRESIMS m/z 685.2549 $[M + Na]^+$ (calcd for $C_{33}H_{40}O_7F_6Na$, 685.2576).

*(R)-MTPA derivative of **6** (**6b**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.53−7.40 (10H, overlap, aromatic protons), 5.17 (1H, dddd, J = 12.1, 12.1, 4.6, 4.5 Hz, H-3β), 5.07 (1H, m, H-9), 3.53 (3H, s, OCH_3), 3.52 (3H, s, OCH_3), 1.98 (1H, m, H-5β), 1.77 (2H, overlap, H-8), 1.76 (1H, dd, J = 12.1, 12.1 Hz, H-2α), 1.73 (1H, m, H-4β), 1.65 (1H, overlap, H-4α), 1.64 (2H, overlap, H-7), 1.37 (1H, ddd, J = 12.1, 4.6, 2.1 Hz, H-2β), 1.27 (3H, d, J = 6.3 Hz, H-10), 1.04 (3H, s, H-11), 0.95 (3H, s, H-12), 0.94 (3H, d, J = 7.1 Hz, H-13); HRESIMS m/z 685.2545 $[M + Na]^+$ (calcd for $C_{33}H_{40}O_7F_6Na$, 685.2576).

*(S)-MTPA derivative of **7** (**7a**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62−7.29 (15H, overlap, aromatic protons), 5.68 (1H, dd, J = 15.6, 10.2 Hz, H-7), 5.53 (1H, dq, J = 6.7, 6.5 Hz, H-9), 5.34 (1H, dd, J = 15.6, 6.7 Hz, H-8), 5.03 (1H, dd, J = 3.0, 2.9 Hz, H-4β), 4.87 (1H, dd, J = 12.5, 4.0 Hz, H-2α), 3.59 (3H, s, OCH_3), 3.53 (3H, s, OCH_3), 3.52 (3H, s, OCH_3), 2.36 (1H, ddd, J = 12.5, 12.5, 2.9 Hz, H-3α), 2.16 (1H, ddd, J = 12.5, 4.0, 3.0 Hz, H-3β), 1.68 (1H, d, J = 10.2 Hz, H-6β), 1.38 (3H, d, J = 6.5 Hz, H-10), 0.90 (3H, s, H-13), 0.82 (3H, s, H-11), 0.57 (3H, s, H-12); HRESIMS m/z 915.2731 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_{10}F_9Na$, 915.2767).

*(R)-MTPA derivative of **7** (**7b**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55−7.33 (15H, overlap, aromatic protons), 5.83 (1H, dd, J = 15.6, 10.2 Hz, H-7), 5.54 (1H, dq, J = 6.7, 6.5 Hz, H-9), 5.47 (1H, dd, J = 15.6, 6.7 Hz, H-8), 4.92 (1H, dd, J = 3.0, 2.9 Hz, H-4β), 4.81(1H, dd, J = 12.5, 4.0 Hz, H-2α), 3.55 (3H, s, OCH_3), 3.49 (3H, s, OCH_3), 3.46 (3H, s, OCH_3), 2.23 (1H, ddd, J = 12.5, 12.5,2.9 Hz, H-3α), 2.12 (1H, ddd, J = 12.5, 4.0, 3.0 Hz, H-3β), 1.75 (1H, d, J = 10.2 Hz, H-6), 1.35 (3H, d, J = 6.5 Hz, H-10), 1.00 (3H, s, H-13), 0.93 (3H, s, H-11), 0.68 (3H, s, H-12); HRESIMS m/z 915.2735 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_{10}F_9Na$, 915.2767).

*(S)-MTPA derivative of **8** (**8a**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.64−7.39 (10H, overlap, aromatic protons), 6.28 (1H, d, J = 15.6 Hz, H-7), 5.76 (1H, dd, J = 15.6, 7.1 Hz, H-8), 5.68 (1H, dq, J = 7.1, 6.4 Hz, H-9), 5.38 (1H, ddd, J = 12.5, 9.5, 4.6 Hz, H-3α), 3.66 (1H, d, J = 9.5 Hz, H-4β), 3.61 (3H, s, OCH_3), 3.55 (3H, s, OCH_3), 1.75 (1H, dd, J = 12.5, 12.5 Hz, H-2β), 1.49 (1H, dd, J = 12.5, 4.6 Hz, H-2α), 1.47 (3H, d, J = 6.4 Hz, H-10), 1.24 (3H, s, H-11), 1.15 (3H, s, H-13), 0.77 (3H, s, H-12); HRESIMS m/z 715.2287 $[M + Na]^+$ (calcd for $C_{33}H_{38}O_9F_6Na$, 715.2318).

*(R)-MTPA derivative of **8** (**8b**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.60−7.39 (10H, overlap, aromatic protons), 6.36 (1H, d, J = 15.6 Hz, H-7), 5.86 (1H, dd, J = 15.6, 7.1 Hz, H-8), 5.69 (1H, dq, J = 7.1, 6.4 Hz, H-9), 5.44 (1H, ddd, J = 12.5, 9.5, 4.6 Hz, H-3α), 3.42 (1H, d, J = 9.5 Hz, H-4β), 3.54 (3H, s, OCH_3), 3.53 (3H, s, OCH_3), 1.97 (1H, dd, J = 12.5, 12.5 Hz, H-2β), 1.61 (1H, dd, J = 12.5, 4.6 Hz, H-2α), 1.40 (3H, d, J = 6.4 Hz, H-10), 1.29 (3H, s, H-11), 1.16 (3H, s, H-13), 0.86 (3H, s, H-12); HRESIMS m/z 715.2278 $[M + Na]^+$ (calcd for $C_{33}H_{38}O_9F_6Na$, 715.2318).

*(S)-MTPA derivative of **9** (**9a**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.56−7.36 (15H, overlap, aromatic protons), 5.14 (1H, m, H-3α), 5.12 (1H, m, H-9), 4.72 (2H, overlap, H-13), 3.53 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.46 (3H, s, OCH_3), 2.31 (1H, ddd, J = 16.0, 5.3, 2.4 Hz, H-4α), 2.15 (2H, overlap, H-7), 2.06 (1H, dd, J = 16.0, 10.0 Hz, H-4β), 1.74 (1H, ddd, J = 12.0, 3.6, 2.4 Hz, H-2β), 1.63 (2H, overlap, H-8), 1.48 (1H, dd, J = 12.0, 12.0 Hz, H-2α), 1.28 (3H, d, J = 6.3 Hz, H-10),1.07 (3H, s, H-11), 0.98 (3H, s, H-12); HRESIMS m/z 899.2800 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_9F_9Na$, 899.2818).

*(R)-MTPA derivative of **9** (**9b**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.55−7.38 (15H, overlap, aromatic protons), 5.16 (1H, m, H-3α), 5.09 (1H, m, H-9), 4.72 (2H, overlap, H-13), 3.58 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.49 (3H, s, OCH_3), 2.33 (1H, ddd, J = 16.0, 5.3, 2.4 Hz, H-4α), 2.12 (2H, overlap, H-7), 1.92 (1H, dd, J = 16.0, 10.0 Hz, H-4β), 1.79 (1H, ddd, J = 12.0, 3.6, 2.4 Hz, H-2β), 1.57 (1H, dd, J = 12.0, 12.0 Hz, H-2α), 1.55 (2H, overlap, H-8), 1.33 (3H, d, J = 6.3 Hz, H-10), 0.94 (3H, s, H-11), 0.93 (3H, s, H-12); HRESIMS m/z 899.2784 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_9F_9Na$, 899.2818).

*(S)-MTPA derivative of **10** (**10a**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.32 (15H, overlap, aromatic protons), 5.15 (1H, m, H-3α), 5.09 (1H, m, H-9), 4.74 (1H, d, J = 12.0 Hz, H-13a), 4.54 (1H, d, J = 12.0 Hz, H-13b), 3.54 (3H, s, OCH_3), 3.51 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 2.28 (1H, ddd, J = 16.1, 5.2, 2.4 Hz, H-4α), 2.16 (1H, m, H-7a), 2.04 (1H, dd, J = 16.1, 10.0 Hz, H-4β), 1.94 (1H, m, H-7b), 1.72 (1H, ddd, J = 12.0, 3.6, 2.4 Hz, H-2α), 1.56 (2H, overlap, H-8), 1.47 (1H, dd, J = 12.0, 12.0 Hz, H-2β), 1.32 (3H, d, J = 6.3 Hz, H-10), 1.03 (3H, s, H-11), 0.91 (3H, s, H-12); HRESIMS m/z 899.2800 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_9F_9Na$, 899.2818).

*(R)-MTPA derivative of **10** (**10b**):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.30 (15H, overlap, aromatic protons), 5.17 (1H, m, H-3α), 5.07 (1H, m, H-9), 4.68 (2H, overlap, H-13), 3.50 (3H, s, OCH_3), 3.49 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 2.33 (1H, ddd, J = 16.1, 5.2, 2.4 Hz, H-4α), 2.23 (1H, m, H-7a), 2.03 (1H, m, H-7b), 1.96 (1H, dd, J = 16.1, 10.0 Hz, H-4β), 1.80 (1H, ddd, J = 12.0, 3.6, 2.4 Hz, H-2α), 1.59 (1H, dd, J = 12.0, 12.0 Hz, H-2β), 1.58 (2H, overlap, H-8), 1.24 (3H, d, J = 6.3 Hz, H-10), 1.06 (3H, s, H-11), 1.00 (3H, s, H-12); HRESIMS m/z 899.2784 $[M + Na]^+$ (calcd for $C_{43}H_{45}O_9F_9Na$, 899.2818).

*(S)-MTPA derivative of **11** (**11a**):* ^{1}H NMR (MeOD, 400 MHz) δ 7.53−7.34 (15H, overlap, aromatic protons), 6.30 (1H, d, J = 15.6 Hz, H-7), 5.60 (1H, dq, J = 7.5, 6.4 Hz, H-9), 5.50 (1H, dd, J = 15.6, 7.5 Hz, H-8), 5.23 (1H, m, H-3α), 4.94 (1H, d, J = 11.3 Hz, H-13a), 4.77 (1H, d, J = 11.3 Hz, H-13b), 3.52 (3H, s, OCH_3), 3.51 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 2.49 (1H, dd, J = 17.0, 5.3 Hz, H-4β), 2.19 (1H, ddd, J = 17.0, 9.3, 2.1 Hz, H-4α), 1.81 (1H, ddd, J = 12.0, 3.6, 2.1 Hz,

dx.doi.org/10.1021/np4002493 | *J. Nat. Prod.* 2013, 76, 1303−1312

H-2α), 1.54 (1H, dd, J = 12.0, 12.0 Hz, H-2β), 1.36 (3H, d, J = 6.4 Hz, H-10), 1.10 (3H, s, H-11), 0.95 (3H, s, H-12); HRESIMS m/z 897.2614 [M + Na]$^+$ (calcd for $C_{43}H_{43}O_9F_9Na$, 897.2661).

(R)-MTPA derivative of ***11*** *(****11b****):* ^{1}H NMR (MeOD, 400 MHz) δ 7.54−7.34 (15H, overlap, aromatic protons), 6.13 (1H, d, J = 15.6 Hz, H-7), 5.61 (1H, dq, J = 7.5, 6.4 Hz, H-9), 5.35 (1H, dd, J = 15.6, 7.5 Hz, H-8), 5.22 (1H, m, H-3α), 4.79 (1H, d, J = 11.3 Hz, H-13a), 4.69 (1H, d, J = 11.3 Hz, H-13b), 3.56 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 2.44 (1H, dd, J = 17.0, 5.3 Hz, H-4β), 2.04 (1H, ddd, J = 17.0, 9.3, 2.1 Hz, H-4α), 1.87 (1H, ddd, J = 12.0, 3.6, 2.1 Hz, H-2α), 1.65 (1H, dd, J = 12.0, 12.0 Hz, H-2β), 1.42 (3H, d, J = 6.4 Hz, H-10), 1.05 (3H, s, H-11), 0.96 (3H, s, H-12); HRESIMS m/z 897.2623 [M + Na]$^+$ (calcd for $C_{43}H_{43}O_9F_9Na$, 897.2661).

(S)-MTPA derivative of ***12*** *(****12a****):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.32 (15H, overlap, aromatic protons), 6.08 (1H, d, J = 15.7 Hz, H-7), 5.57 (1H, dq, J = 6.9, 6.5 Hz, H-9), 5.34 (1H, dd, J = 15.7, 6.9 Hz, H-8), 5.19 (1H, m, H-3α), 4.77 (1H, d, J = 11.6 Hz, H-13a), 4.70 (1H, d, J = 11.6 Hz, H-13b), 3.53 (3H, s, OCH_3), 3.49 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 2.44 (1H, dd, J = 16.8, 5.7 Hz, H-4β), 2.14 (1H, ddd, J = 16.8, 9.3, 2.1 Hz, H-4α), 1.77 (1H, ddd, J = 12.3, 3.0, 2.1 Hz, H-2α), 1.51 (1H, dd, J = 10.3, 10.3 Hz, H-2β), 1.39 (3H, d, J = 6.5 Hz, H-10), 1.00 (3H, s, H-12), 0.93 (3H, s, H-11); HRESIMS m/z 897.2623 [M + Na]$^+$ (calcd for $C_{43}H_{43}O_9F_9Na$, 897.2661).

(R)-MTPA derivative of ***12*** *(****12b****):* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.30 (15H, overlap, aromatic protons), 6.19 (1H, d, J = 15.7 Hz, H-7), 5.56 (1H, dq, J = 6.9, 6.5 Hz, H-9), 5.38 (1H, dd, J = 15.7, 6.9 Hz, H-8), 5.21 (1H, m, H-3α), 4.70 (1H, d, J = 11.6 Hz, H-13a), 4.66 (1H, d, J = 11.6 Hz, H-13b), 3.51 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 2.43 (1H, dd, J = 16.8, 5.7 Hz, H-4β), 2.03 (1H, ddd, J = 16.8, 9.3, 2.1 Hz, H-4α), 1.85 (1H, ddd, J = 12.3, 3.0, 2.1 Hz, H-2α), 1.61 (1H, dd, J = 10.3, 10.3 Hz, H-2β), 1.34 (3H, d, J = 6.5 Hz, H-10), 1.04 (3H, s, H-12), 1.00 (3H, s, H-11); HRESIMS m/z 897.2626 [M + Na]$^+$ (calcd for $C_{43}H_{43}O_9F_9Na$, 897.2661).

Single-Crystal X-ray Diffraction Analysis and Crystallographic Data of 1−5 and 16. The intensity data for **1**−**5** and **16** were collected on a Bruker SMART APEX-II CCD diffractometer equipped with graphite-monochromatized Cu Kα radiation (λ = 1.54178 Å). Data reduction was subsequently performed with Bruker SAINT. Structure solution and refinement were performed with SHELXS-97, and all non-hydrogen atoms were refined anisotropically using the full-matrix least-squares method. All hydrogen atoms were fixed at calculated positions. The final structures of **1**−**5** and **16** are shown in Figures 2, 4−7, and 9, respectively.

Crystallographic data of ***1****:* two independent molecules of **1** and two H_2O molecules in the asymmetric unit, $C_{13}H_{24}O_4{\cdot}H_2O$, M = 262.34, monoclinic, $P2_1$, a = 6.0818(2) Å, b = 19.4319(7) Å, c = 12.9792(4) Å, α = γ = 90°, β = 90.883(2)°, V = 1533.71(9) Å^3, T = 296(2) K, Z = 4, D_{calcd} = 1.136 Mg/m^3, crystal size 0.12 × 0.10 × 0.10 mm^3, F(000) = 576. The final R_1 value is 0.0324 (wR_2 = 0.0907) for 36 185 reflections [$I > 2\sigma(I)$]. Flack structure parameter: −0.04(11).

Crystallographic data of ***2****:* one independent molecule of **2** and half a H_2O molecule in the asymmetric unit, $C_{13}H_{24}O_4{\cdot}0.5H_2O$, M = 253.33, orthorhombic, $P2_12_12$, a = 13.0378(15) Å, b = 17.163(3) Å, c = 6.2782(9) Å, α = γ = β = 90°, V = 1404.9(3) Å^3, T = 296(2) K, Z = 4, D_{calcd} = 1.198 Mg/m^3, crystal size 0.12 × 0.10 × 0.10 mm^3, F(000) = 556. The final R_1 value is 0.0495 (wR_2 = 0.1256) for 5027 reflections [$I > 2\sigma(I)$]. Flack structure parameter: −0.3(4).

Crystallographic data of ***3****:* $C_{13}H_{22}O_4$, M = 242.31, orthorhombic, $P2_12_12_1$, a = 8.0315(2) Å, b = 10.5320(2) Å, c = 15.8116(3) Å, α = γ = β = 90°, V = 1337.47(5) Å^3, T = 296(2) K, Z = 4, D_{calcd} = 1.203 Mg/m^3, crystal size 0.23 × 0.20 × 0.20 mm^3, F(000) = 528. The final R_1 value is 0.0386 (wR_2 = 0.1000) for 7922 reflections [$I > 2\sigma(I)$]. Flack structure parameter: 0.0(2).

Crystallographic data of ***4****:* $C_{13}H_{24}O_3$, M = 228.32, orthorhombic, $P2_12_12_1$, a = 8.6241(2) Å, b = 9.7034(2) Å, c = 15.9697(3) Å, α = γ = β = 90°, V = 1336.39(5) Å^3, T = 296(2) K, Z = 4, D_{calcd} = 1.135 Mg/m^3, crystal size 0.15 × 0.12 × 0.10 mm^3, F(000) = 504. The final R_1 value is 0.0299 (wR_2 = 0.0858) for 12 226 reflections [$I > 2\sigma(I)$]. Flack structure parameter: 0.07(17).

Crystallographic data of ***5****:* $C_{13}H_{26}O_3$, M = 230.34, monoclinic, P2, a = 6.7617(3) Å, b = 7.8646(3) Å, c = 12.6936(5) Å, α = γ = 90°, β = 102.866(2)°, V = 658.07(5) Å^3, T = 298(2) K, Z = 2, D_{calcd} = 1.162 Mg/m^3, crystal size 0.20 × 0.10 × 0.10 mm^3, F(000) = 256. The final R_1 value is 0.0398 (wR_2 = 0.1108) for 5901 reflections [$I > 2\sigma(I)$]. Flack structure parameter: 0.2(3).

Crystallographic data of ***16****:* one independent molecule of **16** and two H_2O molecules in the asymmetric unit, $C_{19}H_{32}O_9{\cdot}2H_2O$, M = 440.48, monoclinic, $P2_1$, a = 11.2174(2) Å, b = 5.98460(10) Å, c = 16.7692(4) Å, α = γ = 90°, β = 98.3540(10)°, V = 1113.80(4) Å^3, T = 298(2) K, Z = 2, D_{calcd} = 1.313 Mg/m^3, crystal size 0.20 × 0.10 × 0.10 mm^3, F(000) = 476. The final R_1 value is 0.0286 (wR_2 = 0.0741) for 9701 reflections [$I > 2\sigma(I)$]. Flack structure parameter: 0.01(15).

Crystallographic data for the structures of **1**−**5** and **16** have been deposited with the Cambridge Crystallographic Data Centre (deposit number CCDC 927650, 927651, 927652, 927653, 927654, and 927655). Copies of the data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

Cytotoxicity Assay. Five human cancer cell lines (HL-60, SMMC-7721, A-549, MCF-7, and SW-480), together with one noncancerous cell line, Beas-2B human bronchial epithelial, were used in the cytotoxic activity assay. All cells were cultured in DMEM or RPMI-1640 medium (Hyclone, Logan, UT, USA), supplemented with 10% fetal bovine serum (Hyclone) at 37 °C in a humidified atmosphere with 5% CO_2. Cell viability was assessed by conducting colorimetric measurements of the amount of insoluble formazan formed in living cells based on the reduction of MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2*H*-tetrazolium) (Sigma, St. Louis, MO, USA).[26] Briefly, 100 μL of adherent cells was seeded into each well of the 96-well culture plates and allowed to adhere for 12 h before addition of test compounds, while suspended cells were seeded just before the addition of the drug with initial density of 1 × 10^5 cells/mL. Each tumor cell line was exposed to the test compound at concentrations of 0.0625, 0.32, 1.6, 8, and 40 μM in triplicate for 48 h, with DDP (*cis*-platin, Sigma) and Taxol (Sigma) as positive controls. After incubation, 20 μL of MTS (5 mg/mL) was added to each well, and the incubation continued for 4 h at 37 °C. The cells were next lysed with 200 μL of 10% SDS after removing the medium. The optical density of the lysate was measured at 595 nm in a 96-well microtiter plate reader (Bio-Rad 680). The IC_{50} value of each compound was calculated using the method of Reed and Muench.[27]

Lymphocyte Proliferation Test. Splenic lymphocytes were prepared as previously described by Kawaguchi et al.[28] with a slight modification. The prepared spleen cells (2.5 × 10^6 cells) were seeded into each well of a 96-well microplate, and various concentrations of compounds and 5 μg/mL of concanavalin A (Con A, from *Canavalia ensiformis* Type III, Sigma), for selective stimuli on T cells, or lipopolysaccharide (LPS, from *Escherichia coli*, Sigma), for selective stimuli on B cells, were added. The plates were cultured at 37 °C with 5% CO_2 in a humidified atmosphere for 48 h. For the last 4 h, 20 μL of CCK-8 (Beyotime Institute of Biotechnology, Haimen, Jiangsu, P. R. China) was added according to the technical manual. Absorbance at 450 nm with a 600 nm reference was measured with a microtiter plate reader (Bio-Rad 680). All optical density (OD) values shown are the mean of triplicate sample ± SD. Controls with and without ConA and LPS were used to establish the baseline proliferation for stimulated and unstimulated cells. Proliferation was assessed in terms of optical density [(compounds (OD_{450}) − positive control (OD_{450})/(positive control (OD_{450})] × 100. The inhibitory or enhancement rate of >10% is acceptable and considered active. In order to control for potential compound toxicity to splenocytes, the assay was repeated (at cell densities of 5 × 10^6 cells/200 μL/well) in the absence of both ConA and LPS. Cell viability (%) was determined as [compounds (OD_{450})/background (OD_{450})] × 100. All OD values shown are the mean of triplicate sample ± SD. Statistical analysis was carried out by the Student *t*-test.

■ ASSOCIATED CONTENT

Supporting Information

HRESIMS and 1D and 2D NMR spectra for compounds **1**−**12** and the MTPA ester derivatives of **2** and **6**−**12**, IR spectrum of **3**, UV spectra of **3**, **11**, and **12**, crystal packing of compounds **1**−**5** and **16**, X-ray crystallographic data (CIF files) for compounds **1**−**5** and **16**, cytotoxicity of compounds **1**−**9** and **13**−**19** against five cancer cell lines and one noncancerous human Beas-2B cell line, cytotoxicity against murine lymphocytes and immunomodulatory activity on murine lymphocyte proliferation induced by concanavalin A (5 μg/mL) or lipopolysaccharide (10 μg/mL) of compounds **1**−**4**, **6**, **9**, **13**−**17**, and **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Prof. F. D. Horgen at Hawaii Pacific University for his critical reading of the manuscript, and we are grateful to Prof. C.-G. Zhang at Huazhong University of Science and Technology for the authentification of the plant material and Dr. X.-G. Meng at Central China Normal University for the single-crystal X-ray data collection and analysis. This work was financially supported by Scientific Research Foundation for the Returned Oversea Chinese Scholars, State Education Ministry of China (2010-1561, 40th, to G.Y.), Program for Youth Chutian Scholar of Hubei Province of China (2011-6, to G.Y.), and Program for New Century Excellent Talents in University, State Education Ministry of China (NCET-2008-0224, to Y.Z.).

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