JOURNAL OF NATURAL PRODUCTS

Article

pubs.acs.org/jnp

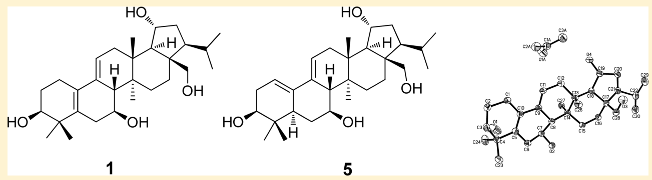
Structure and Bioassay of Triterpenoids and Steroids Isolated from *Sinocalamus affinis*

Liang Xiong, Mei Zhu, Chenggeng Zhu, Sheng Lin, Yongchun Yang, and Jiangong Shi*

State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China

Supporting Information

ABSTRACT: Five triterpenoids with a new 25-norfern carbon skeleton (**1**−**5**), a lupane triterpenoid (**6**), and four 20-hydroxyprogesterone acyl esters (**7**−**10**), together with 23 known compounds, were isolated from the stem (with skin removed) of *Sinocalamus affinis*. The absolute configuration of compound **1** was confirmed by single-crystal X-ray crystallographic analysis using anomalous scattering of Cu Kα radiation. Compounds **1**−**5** exhibited inhibitory activity against protein tyrosine phosphatase 1B.



Sinocalamus affinis (Rendle) McClure (Poaceae) is widely distributed and cultivated in southwestern China.[1] Slices of the stem (with skin removed), named "ci zhu ru" in Chinese, are commonly used to treat various symptoms such as cough and phlegm.[1,2] Our previous study on the EtOAc-soluble portion of an EtOH extract of "ci zhu ru" reported 36 lignans and neolignans and their absolute configurations.[3] During the continued examination of the same extract, six triterpenoids (**1**−**6**) and four 20-hydroxyprogesterone acyl esters (**7**−**10**), together with 23 known compounds, were characterized. Compounds **1**−**5** are triterpenoids with a new 25-norfern carbon skeleton. This paper describes the isolation, structure elucidation, and bioassay of these isolates.

■ RESULTS AND DISCUSSION

Compound **1** showed IR absorptions for hydroxy (3627, 3472, and 3406 cm^{-1}) and olefinic (3043 and 1466 cm^{-1}) functionalities. The molecular formula $C_{29}H_{46}O_4$ of **1**, with seven hydrogen deficiencies, was indicated by HRESIMS and NMR data. The ^{1}H NMR spectrum of **1** displayed resonances attributable to (a) four tertiary [δ_H 1.01 (H_3-24 and H_3-27), 1.04 (H_3-23), and 1.06 (H_3-26)] and two secondary [δ_H 0.83 (d, J = 6.6 Hz, H_3-30) and 0.95 (d, J = 6.6 Hz, H_3-29)] methyl groups; (b) an isolated oxymethylene group [δ_H 3.82 (brd, J = 11.4 Hz, H-28a) and 3.72 (d, J = 11.4 Hz, H-28b)]; (c) three oxymethines [δ_H 3.46 (dd, J = 7.8 and 2.4 Hz, H-3), 3.70 (dt, J = 4.8 and 10.2 Hz, H-7), and 4.40 (dt, J = 3.0 and 10.2 Hz, H-19)]; and (d) an olefinic methine group [δ_H 5.60 (dd, J = 6.0 and 3.0 Hz, H-11)]. In addition, it showed resonances assignable to four exchangeable hydroxy protons (Table 1) and partially overlapped resonances ascribable to several aliphatic methylenes and methines between δ_H 1.20 and 2.50. The ^{13}C NMR and DEPT spectra of **1** revealed 29 carbon resonances (Table 2) corresponding to the above protonated units and seven quaternary carbons (three olefinic, δ_C 127.3, 136.4, and 137.6). These data suggested that **1** was an unusual pentacyclic nortriterpenediene with substitution of four hydroxy groups; this conjecture was confirmed by 2D NMR data analysis. The gHSQC spectrum of **1** furnished assignments of the proton-bearing carbon and corresponding proton resonances in the NMR spectra (Table 1). In the ^{1}H−^{1}H gCOSY spectrum of **1**, the homonuclear coupling correlations of H_2-1/H_2-2/H-3; H_2-6/H-7/H-8; H-11/H_2-12; H_2-15/H_2-16; H-18/H-19/H_2-20/H-21/H-22/H_3-29; and H-22/H_3-30 revealed the presence of structural units containing the vicinally coupled protons. In the HMBC spectrum, two- and three-bond correlations of H_2-1/C-3 and C-5; H_2-6/C-4, C-5, C-7, C-8, and C-10; H-11/C-8, C-10, C-12, and C-13; H_3-23 and H_3-24/C-3, C-4, and C-5; H_3-26/C-12, C-13, C-14, and C-18; H_3-27/C-8, C-13, C-14, and C-15; H_2-28/C-16, C-17, C-18, and C-21; and H_3-29 and H_3-30/C-21 and C-22, in combination with the shifts of these proton and carbon resonances, indicated a gross structure of 25-norfern-5(10),9(11)-diene-3,7,19,28-tetraol for **1**. In the ROESY spectrum of **1**, correlations of H_2-28/H-19, H_3-26, and H_3-30 and of H_3-26/H-8 and H-19 indicated that these protons were cofacial. ROESY correlations of H_3-27/H-6a, H-7, and H-18 and H_3-23/H-3 and H-6a demonstrated that these protons were located on the opposite side of the ring system. This result was corroborated by the splitting patterns and coupling constants of H-3, H-7, H-18, and H-19, indicating that these protons had pseudoaxial orientations. The electronic circular dichroism (ECD) spectrum of **1** displayed a positive Cotton effect at 235 nm ($\Delta\varepsilon$ +3.66), which corresponded to the π−π* transition of the conjugated diene chromophore. On the basis of the allylic axial chirality rule for conjugated *s-trans* dienes,[4] the 8*S*,13*R*,14*S* configuration was assigned to **1**. This was confirmed by single-crystal X-ray crystallographic analysis using the anomalous scattering of Cu Kα radiation. An ORTEP drawing, with the atom numbering indicated, is shown in

Received: April 7, 2012
Published: June 12, 2012

Table 1. ^{1}H NMR Data for Compounds 1−6^{a}

no.	1	2	3	4	5	6^{b}
1a	2.16 m	2.16 m	2.17 m	2.18 m	5.56 dd (3.0, 2.4)	1.64 m
1b	2.16 m	2.16 m	2.17 m	2.18 m		0.98 m
2a	1.80 m	1.81 m	1.82 m	1.81 m	2.14 m	1.63 m
2b	1.70 m	1.70 m	1.71 m	1.67 m	1.91 m	1.57 m
3	3.46 dd (7.8, 2.4)	3.46 dd (7.8, 2.4)	3.46 dd (7.8, 2.4)	3.88 dd (10.2, 3.0)	3.34 dd (11.2, 5.4)	4.47 dd (11.0, 5.5)
5					1.86 m	0.79 brd (10.0)
6a	2.42 dd (16.2, 4.8)	2.43 dd (16.2, 4.8)	2.43 dd (16.8, 4.8)	2.43 dd (16.2, 4.8)	2.01 dt (12.0, 3.6)	1.51 m
6b	2.10 dd (16.2, 10.2)	2.12 dd (16.2, 10.2)	2.07 dd (16.8, 10.2)	2.13 dd (16.2, 10.2)	1.33 m	1.40 m
7a	3.70 dt (4.8, 10.2)	3.70 dt (4.8, 10.2)	3.69 dt (4.8, 10.2)	3.75 dt (4.8, 10.2)	3.70 m	1.38 m
7b						1.04 m
8	2.02 d (10.2)	2.02 d (10.2)	2.01 d (10.2)	2.01 d (10.2)	1.85 d (10.2)	
9						1.31 m
11a	5.60 dd (6.0, 3.0)	5.60 dd (5.4, 2.4)	5.61 dd (6.0, 2.4)	5.58 dd (6.0, 3.0)	5.69 dt (5.4, 2.4)	1.40 m
11b						1.20 m
12a	2.15 dd (18.0, 3.0)	2.08 dd (18.0, 2.4)	2.79 dd (18.0, 6.0)	2.13 dd (18.0, 3.0)	2.15 m	1.61 m
12b	2.05 dd (18.0, 6.0)	1.98 dd (18.0, 5.4)	1.84 dd (18.0, 2.4)	2.05 dd (18.0, 6.0)	2.02 m	1.06 m
13						1.62 m
15a	2.37 dt (14.4, 3.6)	2.39 dt (13.8, 3.6)	2.46 dt (14.4, 3.6)	2.35 dt (14.4, 3.6)	2.27 dt (14.4, 3.6)	1.69 m
15b	1.57 dt (3.6, 14.4)	1.61 dt (3.6, 13.8)	2.14 dt (3.6, 14.4)	1.55 dt (3.6, 14.4)	1.51 dt (3.6, 14.4)	1.07 m
16a	1.70 dt (14.4, 3.6)	1.52 dt (13.8, 3.6)	1.64 m	1.72 dt (14.4, 3.6)	1.70 dt (13.2, 3.0)	1.92 m
16b	1.39 dt (3.6, 14.4)	1.44 dt (13.8, 3.6)	1.64 m	1.39 dt (3.6, 14.4)	1.36 dt (13.2, 3.0)	1.30 m
18	1.85 d (10.2)	1.75 d (10.8)	2.23 s	1.86 d (10.2)	1.85 d (9.6)	1.59 m
19	4.40 dt (3.0, 10.2)	4.19 brd (10.8)		4.41 dt (3.0, 10.2)	4.39 brt (9.6)	2.39 m
20a	2.12 m	3.83 dd (7.2, 1.8)	2.15 m	2.13 m	2.11 m	1.94 m
20b	1.61 m		2.08 m	1.60 m	1.60 m	1.42 m
21a	1.32 m	1.25 t (7.2)	1.54 m	1.32 m	1.30 m	1.86 m
21b						1.04 m
22	1.78 m	1.89 m	1.90 m	1.78 m	1.78 m	
23a	1.04 s	1.04 s	1.04 s	3.67 brd (10.2)	0.99 s	0.84 s
23b				3.50 dd (10.2)		
24	1.01 s	1.02 s	1.01 s	0.95 s	0.72 s	0.84 s
25						0.85 s
26	1.06 s	1.11 s	1.15 s	1.07 s	1.04 s	1.02 s
27	1.01 s	1.02 s	1.01 s	1.01 s	1.03 s	0.98 s
28a	3.82 brd (11.4)	3.94 brd (11.4)	4.02 brd (11.4)	3.83 brd (11.4)	3.80 (11.4, 4.2)	3.80 d (10.5)
28b	3.72 brd (11.4)	3.52 brd (11.4)	3.76 brd (11.4)	3.74 brd (11.4)	3.72 (11.4, 3.6)	3.33 d (10.5)
29a	0.95 d (6.6)	0.98 d (6.6)	1.00 d (6.6)	0.94 d (6.6)	0.93 d (6.6)	4.68 brs
29b						4.58 brs
30	0.83 d (6.6)	0.94 d (6.6)	0.91 d (7.2)	0.83 d (6.6)	0.82 d (6.6)	1.69 s
OH-3	3.48 d (6.0)	3.53 brs	3.64 brs	3.52 d (4.2)	3.56 brs	
OH-7	3.38 d (6.0)	3.45 brs	3.46 brs	3.34 d (6.0)	3.35 d (6.0)	
OH-19	3.07 d (6.0)	3.52 brs		3.08 d (6.6)	3.09 brd (6.0)	
OH-20		3.83 brs				
OH-23				3.55 t (5.4)		
OH-28	3.27 t (4.2)	4.75 brs	3.29 brs	3.27 t (4.2)	3.27 brt (4.2)	

^{a}Data were measured at 600 MHz for **1**−**5** in acetone-d_6 and 500 MHz for **6** in $CDCl_3$. Coupling constants (J) in Hz are given in parentheses, and coupling constants with hydroxy proton were ignored for the OH geminated protons. The assignments were based on DEPT, ^{1}H−^{1}H COSY, HSQC, and HMBC experiments. ^{b}Data for the myristoyl unit in **6**: δ 2.29 (2H, t, J = 7.5 Hz), 1.62 (2H, m), 1.40 (2H, m) 1.28−1.25 (18H, m), 0.88 (3H, t, J = 7.5 Hz).

Figure 1. Therefore, compound **1** was deduced to be (+)-(3*S*,7*S*,8*S*,13*R*,14*S*,17*R*,18*R*,19*R*,21*S*)-25-norfern-5(10),9-(11)-diene-3,7,19,28-tetraol.

Compound **2** had spectroscopic data similar to those of **1**. The HRESIMS data indicated that it had the molecular formula $C_{29}H_{46}O_5$ with one more oxygen atom than **1**. Comparison of the NMR data of **2** and **1** indicated replacement of a methylene group in **1** by a hydoxymethine [δ_H 3.83 (dd, J = 7.2 and 1.8 Hz, H-20) and 3.83 (brs, O*H*-20) and δ_C 82.8] functionality in **2**. In addition, the H-28a and C-19 and C-21 resonances in **2** were deshielded by $\Delta\delta_H$ +0.12 and $\Delta\delta_C$ +10.2 and +3.5 ppm, respectively, unlike those of **1**, whereas the H-19 and H-28b and C-18 and C-22 resonances were shielded by $\Delta\delta_H$ −0.21 and −0.20 and $\Delta\delta_C$ −2.5 and −5.0 ppm, respectively. This revealed that **2** was the 20-OH analogue of **1**, which was proved by 2D NMR experiments on **2** that amended the assignments of the NMR data. In the ROESY spectrum of **2**, correlations of H-18 with H-20, H-21, and H_3-27 demonstrated that the 20-OH group was β-oriented. The ECD spectrum of **2** showed a positive Cotton effect at 245 nm ($\Delta\varepsilon$ +1.94), similar to that of

Table 2. ^{13}C NMR Data for Compounds 1−6[a]

no.	1	2	3	4	5	6[b]
1	24.0	24.0	24.0	25.7	118.3	38.4
2	27.5	27.5	27.4	27.8	38.7	23.7
3	74.8	74.8	74.7	70.1	74.3	80.6
4	40.0	40.0	40.0	45.5	37.2	37.8
5	136.4	136.5	136.6	134.5	46.2	55.4
6	38.2	38.2	38.1	37.6	37.8	18.2
7	70.6	70.6	70.5	70.2	71.3	34.2
8	50.9	51.0	50.1	50.9	52.9	40.9
9	137.6	137.5	137.8	137.8	139.5	50.3
10	127.3	127.3	127.2	130.0	141.5	37.1
11	120.8	120.7	120.1	121.1	124.1	20.8
12	38.5	38.2	36.0	38.5	33.1	25.2
13	38.2	38.0	37.3	38.1	38.6	37.3
14	40.1	40.3	39.6	40.1	40.1	42.7
15	32.2	32.6	31.9	32.2	32.7	27.0
16	33.5	35.1	33.3	33.5	33.4	29.2
17	49.2	49.1	47.2	49.2	49.2	47.8
18	59.8	57.3	61.6	59.8	59.9	48.7
19	70.9	81.1	213.0	70.9	70.9	47.8
20	43.3	82.8	43.9	43.4	43.3	29.7
21	58.3	61.8	55.8	58.2	58.3	34.0
22	31.0	26.0	30.6	31.0	31.0	150.5
23	26.7	26.7	26.7	67.2	25.0	28.0
24	22.2	22.2	22.2	16.7	14.4	16.0
25						16.6
26	17.5	17.0	16.9	17.4	16.8	16.2
27	15.2	15.2	15.2	15.3	16.2	14.7
28	63.3	63.7	63.7	63.3	63.3	60.6
29	23.4	22.7	23.1	23.4	23.4	109.7
30	23.6	23.2	23.3	23.6	23.6	19.1

[a] ^{13}C NMR data (δ) were measured at 125 MHz for 1−5 in acetone-d_6 and for 6 in $CDCl_3$. The assignments were based on DEPT, ^{1}H−^{1}H COSY, HSQC, and HMBC experiments. [b] Data for the myristoyl unit in 6: δ 173.7 (C-1′), 34.9 (C-2′), 31.9 (C-13′), 29.7−29.2 (C-4′−C-11′), 25.2 (C-3′), 22.7 (C-12′), 14.1 (C-14′).

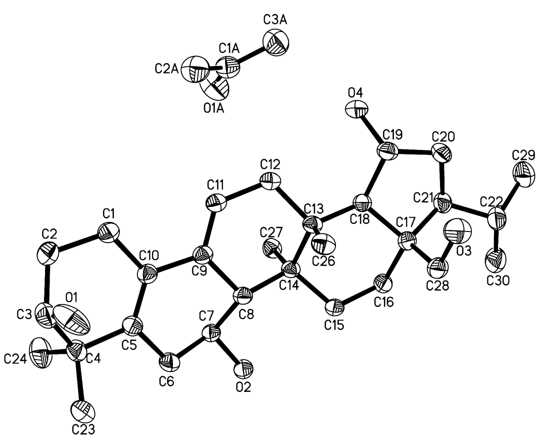
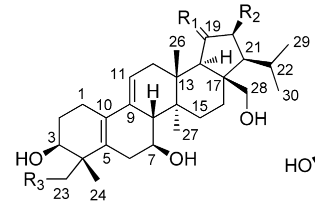
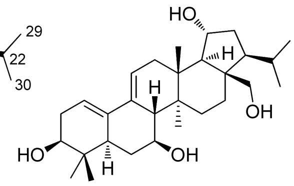


Figure 1. ORTEP diagram of compound 1 cocrystallizing with acetone.

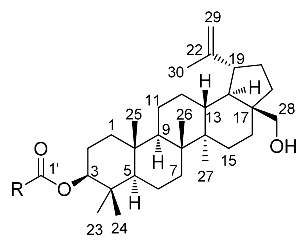
1, which indicated that the absolute configuration around the *s-trans* diene chromophore of 2 was identical to that of 1. Therefore, compound 2 was determined to be (+)-(3*S*,7*S*,8*S*,13*R*,14*S*,17*R*,18*R*,19*S*,20*S*,21*S*)-25-norfern-5(10),9(11)-diene-3,7,19,20,28-pentaol.



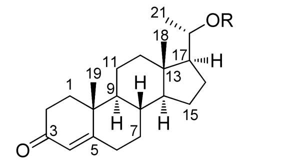
1 R_1 = β-H, α-OH; R_2 = R_3 = H
2 R_1 = β-H, α-OH; R_2 = OH; R_3 = H
3 R_1 = O; R_2 = H; R_3 = H
4 R_1 = β-H, α-OH; R_2 = H; R_3 = OH



5



6 R = $(CH_2)_{12}CH_3$



7 R = $OC(CH_2)_{12}CH_3$
7a R = H
8 R = $OC(CH_2)_{10}CH_3$
9 R = $OC(CH_2)_8CH_3$
10 R = $OC(CH_2)_6CH_3$

The spectroscopic data of 3 (Tables 1 and 2 and Experimental Section) showed that it was another analogue of 1 with the molecular formula $C_{29}H_{44}O_4$, as indicated by HRESIMS data. Comparison of the NMR data of 3 with those of 1 indicated replacement of one hydroxymethine unit in 1 by a carbonyl group (δ_C 213.0) in 3. In addition, the H-18 doublet in 1 was deshielded and changed into a singlet (δ_H 2.23) in 3, and the C-18 and C-20 resonances in 3 were deshielded by $\Delta\delta_C$ +1.8 and +0.6, respectively. In contrast, the C-13, C-17, and C-21 resonances were shielded by $\Delta\delta_C$ −0.9, −2.0, and −2.5. This revealed that 3 was the 19-oxo derivative of 1, a conclusion that was supported by the presence of a carbonyl absorption at 1728 cm^{-1} in the IR spectrum of 3 and confirmed by 2D NMR and ECD data. In particular, the ECD spectrum of 3 showed Cotton effects, positive at 241 nm and negative at 286 nm, arising from the $\pi\rightarrow\pi^*$ transition of the conjugated *s-trans* diene chromophore and the n$\rightarrow\pi^*$ transition of the cyclopentone chromophore, respectively. Applying the allylic axial chirality rule to the conjugated *s-trans* diene chromophore[4] and the octant rule to the cyclopentone chromophore,[5] the observed Cotton effects predicted that the absolute configuration of 3 was consistent with that of 1. Therefore, compound 3 was assigned as (+)-(3*S*,7*S*,8*S*,13*R*,14*S*,17*R*,18*R*,21*S*)-25-norfern-5(10),9(11)-diene-19-oxo-3,7,28-triol.

The spectroscopic data of compound 4 indicated that it was an isomer of 2. Comparison of the NMR data of 4 and 2 demonstrated replacement of the secondary 20-OH group in 2 by a primary OH group in 4. In addition, the H-3 and C-4 and C-10 resonances in 4 were deshielded by $\Delta\delta_H$ +0.42 and $\Delta\delta_C$ +5.5 and +2.7, respectively. In contrast, the C-3, C-5, and C-24 resonances were shielded by $\Delta\delta_C$ −4.7, −2.0, and −5.5. This indicated that the primary OH group was located at C-23 in 4, which was supported by the HMBC correlations of H_3-24/C-3, C-4, C-5, and C-23, in combination with the shifts of these proton and carbon resonances. This regiochemistry was confirmed by the correlations of H-7 (pseudoaxial)/H-6a (pseudoequatorial)/H_2-23 in the NOESY spectrum of 4. The ECD spectrum of 4 displayed a positive Cotton effect at 235 nm ($\Delta\varepsilon$ +6.50), similar to that of 2, suggesting that the absolute configuration around the *s-trans* diene chromophore of

4 was identical with that of 2. Therefore, compound 4 was determined as (+)-(3*S*,4*R*,7*S*,8*S*,13*R*,14*S*,17*R*,18*R*,19*R*,21*S*)-25-norfern-5(10),9(11)-diene-3,7,19,23,28-pentaol.

Compound **5** was an isomer of **1**, as indicated by spectroscopic data. Comparison of the NMR data of **5** and **1** indicated the presence of a trisubstituted double bond [δ_H 5.56 (dd, J = 3.0 and 2.4 Hz, H-1), δ_C 118.3 (C-1) and 141.5 (C-10)] and a methine group [δ_H 1.86 (m, H-5), δ_C 46.2 (C-5)] in **5**, replacing the tetrasubstituted double bond and one methylene group (CH_2-1) in **1**, respectively. This suggested that the C-5−C-10 double bond in **1** shifted to C-1 and C-10 in **5**. The suggestion was confirmed by the 2D NMR data, particularly by HMBC correlations from H-1 to C-3, C-5, and C-9, combined with their shifts. In the NOESY spectrum, correlations of H-3/H_3-23/H-5/H-7/H_3-27/H-18/H-21 demonstrated an α-orientation of H-5. Therefore, compound **5** was assigned as (+)-(3*S*,5*S*,7*S*,8*S*,13*R*,14*S*,17*R*,18*R*,19*R*,21*S*)-25-norfern-1(10),9(11)-diene-3,7,19,28-tetraol, and the absolute configuration was supported by a positive $\pi \rightarrow \pi^*$ Cotton effect at 236 nm in the ECD spectrum, based on the *s-cis* diene allylic axial chirality rule.[4,6]

Compound **6** possessed the molecular formula $C_{44}H_{76}O_3$, as indicated by spectroscopic data. The NMR data of **6** showed that it was an analogue of the co-occurring 3-*O*-palmitoylbetulin[7] except for substitution of the palmitoyl unit by a myristoyl unit. This was proven by the 2D NMR analysis and alkaline hydrolysis of **6** to afford betulin.[8] Specifically, the location of the myristoyl unit at C-3 was confirmed by a correlation of H-3/C-1′ in the HMBC spectrum of **6**. Thus, compound **6** was defined as 3-*O*-myristoylbetulin.

Compound **7** showed IR absorptions for OH (3435 cm^{-1}) and carbonyl (1730 and 1669 cm^{-1}) groups. The molecular formula, $C_{35}H_{58}O_3$, was indicated by HRESIMS and NMR data. The NMR spectra of **7** displayed resonances characteristic of a sterol ester (Table 2). Alkaline hydrolysis of **7** liberated **7a**, having ^1H NMR and EIMS data consistent with those of 20-hydroxypregn-4-en-3-one.[9] This revealed that **7** was 20-*O*-myristoylpregn-4-en-3-one, which was confirmed by the HMBC correlations of H_3-21/C-17 and C-20 and H-20/C-1′. The ECD spectrum of **7** showed Cotton effects at 235 ($\Delta\varepsilon$ +5.78) and 322 ($\Delta\varepsilon$ −1.21) nm, corresponding to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the conjugated 4-en-3-one chromophore, indicating that the tetracyclic nucleus of **7** possessed the same absolute configuration as the common pregn-4-en-3-one analogues on the basis of the octant rule.[10] Comparison of the ^1H NMR data of **7a** with those of the 20*S* and 20*R* epimers of 20-hydroxypregn-4-en-3-one,[11] especially the shifts of H_3-19 and H_3-21, demonstrated that the data of **7a** were in agreement with those of the 20*S* epimer. This suggested that **7** had a 20*S* configuration. Therefore, compound **7** was defined as (+)-(20*S*)-20-*O*-myristoylpregn-4-en-3-one.

Compound **8** possessed the molecular formula $C_{33}H_{54}O_3$, with two fewer CH_2 units than **7**, as indicated by HRESIMS and NMR data. Comparison of the NMR data between **8** and **7** indicated that the myristoyl unit in **7** was substituted by a lauroyl unit in **8**. Thus, compound **8** was assigned as (+)-(20*S*)-20-*O*-lauroylpregn-4-en-3-one. This conclusion was confirmed by alkaline hydrolysis, 2D NMR, and ECD experiments.

The spectroscopic data of compound **9** were similar to those of **8**, except that the HRESIMS of **9** indicated the molecular formula $C_{31}H_{50}O_3$ for **9** with two fewer CH_2 units than **8**. Thus, compound **9** was determined as (+)-(20*S*)-20-*O*-caprinoyl-pregn-4-en-3-one.

Compound **10** was (+)-(20*S*)-20-*O*-capryloylpregn-4-en-3-one, as determined by HRESIMS at m/z 443.3564 $[M + H]^+$ (calculated for $C_{29}H_{47}O_3$, 443.3520) and as indicated by NMR and CD data.

The known compounds were identified by comparison of their spectroscopic data with reported data. They were friedelin,[12] maytensifolin B,[13] 3,21-dioxofriedelane,[14] epifriedelanol,[15] 29-norlupan-3,20-dione,[16] 3-*O*-palmitoylbetulin,[7] 3-*O*-lauroylbetulin, 28-*O*-lauroylbetulin,[17] *trans*-phytol,[18] α-tocoquinone,[19] 2,3-epoxy-α-tocoquinone,[20] (*E*)-4-oxo-β-ionone,[21] (*E*)-4-oxo-β-dihydroionone,[22] (3*S*,5*R*,6*S*)-3-acetoxy-5,6-epoxy-5,6-dihydro-β-ionone,[23] (22*E*)-ergosta-6,9,22-triene-3β,5α,8α-triol,[24] (22*E*)-ergosta-6,22-diene-3β,5α,8α-triol,[25] (22*E*)-ergosta-7,22-dien-3β-ol,[26] ergosta-7,24(24^1)-dien-3β-ol,[27] (24*R*)-5α-stigmast-3,6-dione,[28] (24*R*)-stigmast-4-en-3-one,[29] cholest-4-ene-3,24-dione,[30] β-sitosterol,[31] and β-daucosterol.[32]

In the in vitro bioassays, compounds **1**−**5** showed inhibitory activity against protein tyrosine phosphatase 1B (PTP1B)[33] with IC_{50} values of 6.8−16.6 μM. The positive control in this assay was oleanolic acid (IC_{50}, 5.6 μM). However, compounds **1**−**10** and the other known compounds, at a concentration of 10 μM, were inactive in the assays against nitric oxide production in mouse peritoneal macrophages,[3] HIV-1 replication,[34] Fe^{2+}-cystine-induced rat liver microsomal lipid peroxidation,[35] and DL-galactosamine-induced WB-F344 cell damage,[36] as well as cytotoxicity against several human cancer cell lines.[37]

■ EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. UV spectra were measured on a Cary 300 spectrometer. ECD spectra were recorded on a JASCO J-815 ECD spectrometer. IR spectra were recorded on a Nicolet 5700 FT-IR microscope instrument (FT-IR microscope transmission). NMR spectra were obtained at 300, 500, or 600 MHz for ^1H, and 125 or 150 MHz for ^{13}C, on a Varian Mecury-300 MHz or INOVA 500 MHz or SYS 600 MHz spectrometer with solvent peaks used as references. ESIMS data were measured with a Q-Trap LC/MS/MS (turbo ionspray source) spectrometer. HRESIMS data were measured using an Agilent Technologies 6520 Accurate Mass Q-ToF LC/MS spectrometer. Column chromatography was performed using silica gel (200−300 mesh, Qingdao Marine Chemical Inc., China) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala Sweden). HPLC separation was performed on an instrument consisting of a Waters 600 controller, a Waters 600 pump, and a Waters 2487 dual λ absorbance detector with an Alltima (250 × 10 mm) preparative column packed with C_{18} (5 μm). TLC was carried out on precoated silica gel GF_{254} plates. Spots were visualized under UV light (254 or 356 nm) or by spraying with 7% H_2SO_4 in 95% EtOH followed by heating.

Plant Material. The skin-removed stems of *Sinocalamus affinis* were collected at Pingle Town, Sichuan Province, China, in August 2008. Plant identification was verified by Dr. Yan Ren (Chengdu University of TCM, Sichuan 610075, China). A voucher specimen (No. ID-S-2326) was deposited at the Herbarium of the Department of Medicinal Plants, Institute of Materia Medica, Beijing 100050, China.

Extraction and Isolation. Air-dried slices of the skin-removed stem of *S. affinis* (6 kg) were powdered and extracted with 95% EtOH (3 × 40 L) at rt for 3 × 72 h. The EtOH extract was evaporated under reduced pressure to yield a dark brown residue (330 g). The residue was suspended in H_2O (2500 mL) and then partitioned with EtOAc (6 × 2500 mL). After the removal of the solvent, the EtOAc fraction (120 g) was applied to a silica gel column. Successive elution with a gradient of increasing acetone (0−100%) in petroleum ether afforded 10 fractions (F_1−F_{10}) based on TLC analysis. F_2 was recrystallized in

Table 3. NMR Data (δ) for Compounds 7−10 in $CDCl_3$[a]

	7[b]		**8**[c]		**9**[d]		**10**[e]	
no.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1a	2.02 m	35.7	2.02 m	35.7	2.02 m	35.7	2.03 m	35.7
1b	1.71 m		1.71 m		1.71 m		1.71 m	
2a	2.44 m	33.9	2.43 m	34.0	2.43 m	34.0	2.44 m	34.0
2b	2.34 m		2.33 m		2.34 m		2.34 m	
3		199.6		199.6		199.6		199.5
4	5.73 s	123.8	5.73 s	123.8	5.73 s	123.8	5.73 s	123.9
5		171.3		171.3		171.3		171.2
6a	2.39 m	32.9	2.39 m	32.8	2.39 m	32.9	2.40 m	32.9
6b	2.29 m		2.29 m		2.29 m		2.29 m	
7a	1.83 m	32.0	1.83 m	31.9	1.83 m	32.0	1.84 m	32.0
7b	1.03 m		1.03 m		1.03 m		1.03 m	
8	1.55 m	35.3	1.54 m	35.3	1.55 m	35.3	1.54 m	35.3
9	0.95 m	53.7	0.95 m	53.7	0.95 m	53.7	0.95 m	53.8
10		38.6		38.6		38.6		38.6
11a	1.55 m	20.7	1.55 m	20.7	1.56 m	20.7	1.54 m	20.7
11b	1.42 m		1.42 m		1.42 m		1.41 m	
12a	1.91 m	38.6	1.91 m	38.6	1.91 m	38.6	1.92 m	38.6
12b	1.17 m		1.18 m		1.16 m		1.18 m	
13		41.7		41.7		41.7		41.7
14	1.05 m	55.7	1.05 m	55.7	1.06 m	55.7	1.08 m	55.7
15a	1.68 m	24.0	1.69 m	24.0	1.69 m	24.0	1.68 m	24.0
15b	1.17 m		1.17 m		1.18 m		1.17 m	
16a	1.83 m	25.5	1.83 m	25.5	1.83 m	25.5	1.84 m	25.5
16b	1.48 m		1.48 m		1.47 m		1.47 m	
17	1.56 m	55.5	1.55 m	55.5	1.57 m	55.5	1.58 m	55.5
18	1.18 s	17.4	1.18 s	17.4	1.18 s	17.4	1.19 s	17.4
19	0.72 s	12.5	0.73 s	12.5	0.72 s	12.5	0.73 s	12.5
20	4.95 m	72.6	4.95 m	72.6	4.95 m	72.6	4.95 m	72.6
21	1.22 d (6.5)	20.6	1.22 d (6.0)	20.6	1.22 d (6.0)	20.6	1.22 d (6.0)	20.6

[a]Data were measured at 500 for ^1H and 125 for ^{13}C, respectively. Coupling constants (J) in Hz are given in parentheses. The assignments were based on $^1H-^1H$ COSY, HSQC, and HMBC experiments of **7** and **8**. [b]Data for the myristoyl unit in **7**: δ 2.26 (2H, t, J = 7.5 Hz), 1.59 (2H, m), 1.30 (2H, m), 1.28−1.25 (18H, m), 0.88 (3H, t, J = 7.5 Hz); δ_C 173.3 (C-1′), 34.9 (C-2′), 31.9 (C-13′), 29.6−29.1 (C-4′−C-11′), 25.1 (C-3′), 22.7 (C-12′), 14.1 (C-14′). [c]Data for the lauroyl unit in **8**: δ 2.25 (2H, t, J = 7.0 Hz), 1.60 (2H, m), 1.30 (2H, m), 1.28−1.25 (14H, m), 0.88 (3H, t, J = 7.5 Hz); δ_C 173.3 (C-1′), 34.9 (C-2′), 31.9 (C-11′), 29.6−29.1 (C-4′−C-9′), 25.1 (C-3′), 22.7 (C-10′), 14.1 (C-12′). [d]Data for the caprinoyl unit in **9**: δ 2.24 (2H, t, J = 7.0 Hz), 1.57 (2H, m), 1.30 (2H, m), 1.28−1.25 (10H, m), 0.88 (3H, t, J = 7.5 Hz); δ_C 173.3 (C-1′), 34.9 (C-2′), 31.8 (C-9′), 29.7−29.2 (C-4′−C-7′), 25.1 (C-3′), 22.7 (C-8′), 14.1 (C-10′). [e]Data for the capryloyl unit in **10**: δ 2.25 (2H, t, J = 7.5 Hz), 1.54 (2H, m), 1.30 (2H, m), 1.29−1.26 (8H, m), 0.89 (3H, t, J = 7.5 Hz); δ_C 173.3 (C-1′), 34.9 (C-2′), 31.8 (C-7′), 29.4−29.2 (C-4′−C-5′), 25.1 (C-3′), 22.7 (C-6′), 14.1 (C-8′).

petroleum ether−Me_2CO (5:1) to yield friedelin (2.3 g). β-Sitosterol (2.1 g) was crystallized from F_3 in petroleum ether−Me_2CO (5:1). The remaining mixture of F_3 (15.0 g) was subjected to CC over silica gel with a gradient of increasing EtOAc (0−50%) in petroleum ether, to yield subfractions $F_{3\text{-}1}$−$F_{3\text{-}6}$. $F_{3\text{-}1}$ was chromatographed over Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1), followed by recrystallization in petroleum ether−Me_2CO (5:1), to give epifriedelanol (438 mg). $F_{3\text{-}2}$ (0.8 g) was repeatedly chromatographed over silica gel (petroleum ether−EtOAc, 50:1−10:1) to yield *trans*-phytol (45.0 mg). The successive separation of $F_{3\text{-}3}$ (2.1 g) with Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1) and with RP semipreparative HPLC (98% MeOH in H_2O) yielded **6** (10.0 mg), (24*R*)-stigmast-4-en-3-one (36 mg), 3-*O*-palmitoylbetulin (3.0 mg), 3-*O*-lauroylbetulin (2.5 mg), and 28-*O*-lauroylbetulin (1.6 mg). $F_{3\text{-}4}$ was separated with Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1) to give $F_{3\text{-}4\text{-}1}$−$F_{3\text{-}4\text{-}5}$. Separation of $F_{3\text{-}4\text{-}3}$ with semipreparative HPLC (MeOH−H_2O, 96:4) gave maytensifolin B (3.5 mg), 3,21-dioxofriedelane (2.0 mg), and 29-norlupan-3,20-dione (4.1 mg). (24*R*)-5α-Stigmast-3,6-dione (1.4 g) was crystallized from $F_{3\text{-}4\text{-}4}$ in petroleum ether−Me_2CO (5:1), while the remaining mixture was isolated with CC over silica gel (petroleum ether−EtOAc, 50:1−10:1), followed by RP semipreparative HPLC purification (MeOH−H_2O, 95:5), to yield α-tocoquinone (86.5 mg), 2,3-epoxy-α-tocoquinone (3.1 mg), (22*E*)-ergosta-7,22-dien-3β-ol (3.6 mg), and ergosta-7,24(24[1])-dien-3β-ol (2.2 mg). $F_{3\text{-}5}$ (2.5 g) was fractioned via Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 5:5:1) followed by RP semipreparative HPLC (96% MeOH in H_2O) purification to yield **7** (5.5 mg), **8** (3.7 mg), **9** (2.0 mg), **10** (1.6 mg), and cholest-4-ene-3,24-dione (0.8 mg). $F_{3\text{-}6}$ (1.6 g) was repeatedly separated by CC over silica gel (petroleum ether−EtOAc, 50:1−3:1), followed by RP semipreparative HPLC (94% MeOH in H_2O) purification to yield (*E*)-4-oxo-β-dihydroionone (1.8 mg), (3*S*,5*R*,6*S*)-3-acetoxy-5,6-epoxy-5,6-dihydro-β-ionone (1.5 mg), (22*E*)-ergosta-6,9,22-triene-3β,5α,8α-triol (3.6 mg), and (22*E*)-ergosta-6,22-diene-3β,5α,8α-triol (5.0 mg). F_6 (21.0 g) was separated by flash chromatography over MCI gel, to give $F_{6\text{-}1}$−$F_{6\text{-}11}$. Separation of $F_{6\text{-}7}$ (3.6 g) by chromatography over Sephadex LH-20 (petroleum ether−$CHCl_3$−MeOH, 2:2:1) and RP semipreparative HPLC (60% MeOH in H_2O) yielded **1** (31.9 mg), **2** (1.8 mg), **3** (2.0 mg), **4** (4.1 mg), and **5** (3.4 mg). β-Daucosterol (23.2 mg) was precipitated as a white, amorphous powder from $F_{6\text{-}8}$ in MeOH−$CHCl_3$ (10:1).

*(+)-(3S,7S,8S,13R,14S,17R,18R,19R,21S)-25-Norfern-5(10),9(11)-diene-3,7,19,28-tetraol (**1**):* colorless needles, mp 234−236 °C (acetone); $[\alpha]^{20}_D$ +23 (c 0.5, MeOH); UV (MeOH) λ_{max} (log ε) 244 (1.46) nm; ECD (MeOH) 235 ($\Delta\varepsilon$ +3.66) nm; IR ν_{max} 3472, 3406, 2927, 1466, 1433, 1380, 1286, 1241, 1186, 1125, 1094, 1062, 1007, 963, 932, 889, 811, 794 cm^{-1}; ^1H NMR (acetone-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (acetone-d_6, 125 MHz) data, see Table 2;

(+)-ESIMS m/z 481 $[M + Na]^+$; (+)-HRESIMS m/z 481.3292 $[M + Na]^+$ (calcd for $C_{29}H_{46}O_4Na$, 481.3288).

*X-ray Crystallography of Compound **1**.* $C_{29}H_{46}O_4$, M = 458.68, monoclinic, $P2_1$, a = 14.374(6) Å, b = 7.464(6) Å, c = 15.053(7) Å, β = 116.02(1)°, V = 1451.3(2) Å^3, Z = 2, D_{calcd} = 1.183 g·cm^{-3}, 4310 reflections independent, 3717 reflections observed ($|F|^2 \geq 2\sigma|F|^2$), R_1 = 0.0489, wR_2 = 0.1312, S = 1.060.

The data were collected on a Rigaku MicroMax 002+ diffractometer with Cu Kα radiation using the ω and κ scan technique to a maximum 2θ value of 144.56°. The crystal structures were solved by direct methods using SHELXS-97, and all non-hydrogen atoms were refined anisotropically using the least-squares method. All hydrogen atoms were positioned by geometrical calculations and a difference Fourier overlapping calculation. The absolute configuration was determined on the basis of the Flack parameter of 0.0(3). Crystallographic data for the structure of **1** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 842894. Copies of these 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).

*(+)-(3S,7S,8S,13R,14S,17R,18R,19S,20S,21S)-25-Norfern-5(10),9(11)-diene-3,7,19,20,28-pentaol (**2**):* white, amorphous powder; $[\alpha]^{20}_D$ +59.4 (c 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 244 (1.49) nm; ECD (MeOH) 245 ($\Delta\varepsilon$ +1.94) nm; IR ν_{max} 3397, 2924, 2855, 1655, 1595, 1464, 1378, 1279, 1211, 1178. 1129, 1060, 973 cm^{-1}; ^{1}H NMR (acetone-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (acetone-d_6, 125 MHz) data, see Table 2; (+)-ESIMS m/z 497 $[M + Na]^+$; (+)-HRESIMS m/z 497.3231 $[M + Na]^+$ (calcd for $C_{29}H_{46}O_5Na$, 497.3237).

*(+)-(3S,7S,8S,13R,14S,17R,18R,21S)-25-Norfern-5(10),9(11)-diene-19-oxo-3,7,28-triol (**3**):* white, amorphous powder; $[\alpha]^{20}_D$ +55.6 (c 0.08, MeOH); UV (MeOH) λ_{max} (log ε) 245 (1.52) nm; ECD (MeOH) 241 ($\Delta\varepsilon$ +3.38), 286 ($\Delta\varepsilon$ −2.19) nm; IR ν_{max} 3441, 2934, 2890, 1728, 1631, 1469, 1443, 1384, 1375, 1267, 1228, 1188, 1102, 1063, 1032, 999, 967 cm^{-1}; ^{1}H NMR (acetone-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (acetone-d_6, 125 MHz) data, see Table 2; (+)-ESIMS m/z 457 $[M + H]^+$; (+)-HRESIMS m/z 457.3302 $[M + H]^+$ (calcd for $C_{29}H_{45}O_4$, 457.3312), 479.3118 $[M + Na]^+$ (calcd for $C_{29}H_{44}O_4Na$, 479.3132).

*(+)-(3S,4R,7S,8S,13R,14S,17R,18R,19R,21S)-25-Norfern-5(10),9(11)-diene-3,7,19,23,28-pentaol (**4**):* white, amorphous powder; $[\alpha]^{20}_D$ +32.5 (c 0.3, MeOH); UV (MeOH) λ_{max} (log ε) 202 (1.93), 241 (2.05) nm; ECD (MeOH) 235 ($\Delta\varepsilon$ +6.50) nm; IR ν_{max} 3389, 2935, 1643, 1458, 1443, 1376, 1283, 1186, 1085, 1040, 968, 947, 887 cm^{-1}; ^{1}H NMR (acetone-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (acetone-d_6, 125 MHz) data, see Table 2; (+)-HRESIMS m/z 497 $[M + Na]^+$; (+)-HRESIMS m/z 497.3253 $[M + Na]^+$ (calcd for $C_{29}H_{46}O_5Na$, 497.3237).

*(+)-(3S,5S,7S,8S,13R,14S,17R,18R,19R,21S)-25-Norfern-1(10),9(11)-diene-3,7,19,28-tetraol (**5**):* white, amorphous powder; $[\alpha]^{20}_D$ +28 (c 0.05, MeOH); UV (MeOH) λ_{max} (log ε) 236 (1.48) nm; ECD (MeOH) 236 ($\Delta\varepsilon$ +2.69) nm; IR ν_{max} 3192, 2921, 2850, 1647, 1470, 1421, 1380, 1127, 1037 cm^{-1}; ^{1}H NMR (acetone-d_6, 600 MHz) data, see Table 1; ^{13}C NMR (acetone-d_6, 125 MHz) data, see Table 2; (+)-ESIMS m/z 481 $[M + Na]^+$; (+)-HRESIMS m/z 481.3300 $[M + Na]^+$ (calcd for $C_{29}H_{46}O_4Na$, 481.3288).

*3-O-Myristoylbetulin (**6**):* white, amorphous powder; $[\alpha]^{20}_D$ +31.5 (c 0.08, $CHCl_3$); IR ν_{max} 2926, 2854, 1731, 1466, 1375, 1248, 1178, 1035, 980, 881, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) data, see Table 1; ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 2; EIMS m/z 652 $[M]^{+\bullet}$; HREIMS m/z 652.5783 $[M]^{+\bullet}$ (calcd for $C_{44}H_{76}O_3$ 652.5794).

*(+)-(20S)-20-O-Myristoylpregn-4-en-3-one (**7**):* colorless gum; $[\alpha]^{20}_D$ +38 (c 0.03, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 211 (2.42), 240 (1.65) nm; ECD (MeOH) 235 ($\Delta\varepsilon$ +5.78), 322 ($\Delta\varepsilon$ −1.21) nm; IR ν_{max} 2927, 2854, 1730, 1669, 1459, 1379, 1175, 1076, 948, 866 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 3; (+)-ESIMS m/z 527 $[M + H]^+$, 549 $[M + Na]^+$; (+)-HRESIMS m/z 527.4484 $[M + H]^+$ (calcd for $C_{35}H_{59}O_3$, 527.4459).

*(+)-(20S)-20-O-Lauroylpregn-4-en-3-one (**8**):* colorless gum; $[\alpha]^{20}_D$ +38.2 (c 0.03, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 204 (2.28), 240 (1.67) nm; ECD (MeOH) 233 ($\Delta\varepsilon$ +5.77), 323 ($\Delta\varepsilon$ −1.14) nm; ^{1}H NMR ($CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 3; (+)-ESIMS m/z 499 $[M + H]^+$, 521 $[M + Na]^+$; (+)-HRESIMS m/z 499.4164 $[M + H]^+$ (calcd for $C_{33}H_{55}O_3$, 499.4146).

*(+)-(20S)-20-O-Caprinoylpregn-4-en-3-one (**9**):* colorless gum; $[\alpha]^{20}_D$ +38.6 (c 0.06, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 210 (2.57), 240 (1.64) nm; ECD (MeOH) 232 ($\Delta\varepsilon$ +5.24), 325 ($\Delta\varepsilon$ −1.07) nm; ^{1}H NMR ($CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 3; (+)-ESIMS m/z 471 $[M + H]^+$, 493 $[M + Na]^+$; (+)-HRESIMS m/z 471.3903 $[M + H]^+$ (calcd for $C_{31}H_{51}O_3$, 471.3833).

*(+)-(20S)-20-O-Capryloylpregn-4-en-3-one (**10**):* colorless gum; $[\alpha]^{20}_D$ +38.2 (c 0.06, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 210 (2.61), 240 (1.66) nm; ECD (MeOH) 235 ($\Delta\varepsilon$ +5.37), 323 ($\Delta\varepsilon$ −1.09) nm; ^{1}H NMR ($CDCl_3$, 500 MHz) data, see Table 3; ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 3; (+)-ESIMS m/z 443 $[M + H]^+$, 465 $[M + Na]^+$; (+)-HRESIMS m/z 443.3564 $[M + H]^+$ (calcd for $C_{29}H_{47}O_3$, 443.3520).

*Hydrolysis of **6**−**10**.* Compound **6** (7.0 mg) was stirred with KOH (10 mg) in methanol (3 mL) for 2 h. The reaction solution was partitioned between H_2O (25 mL) and $CHCl_3$ (25 mL). The $CHCl_3$ phase was evaporated under reduced pressure to give a residue that was separated by PTLC using petroleum ether−EtOAc (5:1) to afford betulin with $[\alpha]^{20}_D$ +18.5 (c 0.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) and (+)-ESIMS data were identical with reported data.[8] Similarly, compounds **8**−**10** were hydrolyzed to afford (20S)-20-hydroxypregn-4-en-3-one with $[\alpha]^{20}_D$ +99.5 (c 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) data were identical with reported data.[11]

■ ASSOCIATED CONTENT

Supporting Information

Copies of IR, MS, and 1D and/or 2D NMR for compounds **1**−**10** and ECD spectra for **1**−**5** and **7**−**10**. This can be accessed free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: 86-10-83154789. Fax: 86-10-63017757. E-mail: shijg@imm.ac.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Natural Sciences Foundation of China (NNSFC; grant nos. 30825044 and 20932007), the Program for Changjiang Scholars and Innovative Research Team in University (PCSIRT, grant no. IRT1007), and the National Science and Technology Project of China (no. 2011ZX09307-002-01) is acknowledged.

■ REFERENCES

(1) Jiangsu New Medical College. *Dictionary of Traditional Chinese Medicine*; Shanghai Science and Technology Publishing House: Shanghai, 1986; p 2514.

(2) Jia, H. H.; Wu, X. D. *Zhong Yao Cai* **1992**, *15*, 35−36.

(3) Xiong, L.; Zhu, C. G.; Li, Y. R.; Tian, Y.; Lin, S.; Yuan, S. P.; Hu, J. F.; Hou, Q.; Chen, N. H.; Yang, Y. C.; Shi, J. G. *J. Nat. Prod.* **2011**, *74*, 1188−1200.

(4) Gawronski, J. K.; Walborsky, H. M. In *Circular Dichroism Principles and Applications*; Nakanishi, K.; Berova, N.; Woody, R. W., Ed.; Wiley-VCH, Inc.: New York, 1994; Chapter 11, pp 301−330.

(5) Lightner, D. A. In *Circular Dichroism Principles and Applications*; Nakanishi, K.; Berova, N.; Woody, R. W., Ed.; Wiley-VCH, Inc.: New York, 1994; Chapter 10, pp 259−299.
(6) Burgstahler, A. W.; Barkhurst, R. C. *J. Am. Chem. Soc.* **1970**, *92*, 7601−7603.
(7) Toriumi, Y.; Kakuda, R.; Kikuchi, M.; Yaoita, Y.; Kikuchi, M. *Chem. Pharm. Bull.* **2003**, *51*, 89−91.
(8) Alakurtti, S.; Heiska, T.; Kiriazis, A.; Sierra, N. S.; Jaffe, C. L.; Kauhaluoma, J. Y. *Bioorg. Med. Chem.* **2010**, *18*, 1573−1582.
(9) Monsalve, L. N.; Rada, M. Y. M.; Ghini, A. A.; Baldessari, A. *Tetrahedron* **2008**, *64*, 1721−1730.
(10) Snatzke, G.; Laurent, H.; Wiechert, R. *Tetrahedron* **1969**, *25*, 761−769.
(11) (a) Kirk, D. N.; Toms, H. C.; Douglas, C.; White, K. A. *J. Chem. Soc., Perkin Trans.* **1990**, *2*, 1567−1594. (b) Farooq, A.; Hanson, J. R.; Iqbal, Z. *Phytochemistry* **1994**, *37*, 723−726.
(12) Akihisa, T.; Yamamoto, K. *Chem. Pharm. Bull.* **1992**, *40*, 789−791.
(13) Nozaki, H.; Suzuki, H.; Hirayama, T.; Kasai, R.; Wu, R. Y.; Lee, K. H. *Phytochemistry* **1986**, *25*, 479−485.
(14) Patra, A.; Mukhopadhyay, A. K.; Mitra, A. K. *Org. Magn. Reson.* **1981**, *17*, 166−168.
(15) Li, T. L.; Yin, X. H.; Pang, W. D.; Yang, J.; Liang, G. Y. *Zhong Yao Cai* **2010**, *33*, 55−57.
(16) Cole, B. W.; Bentley, M. D.; Hua, Y.; Bu, L. *J. Wood Chem. Technol.* **1991**, *11*, 209−223.
(17) Era, V.; Jaaskelainen, P. *J. Am. Oil Chem. Soc.* **1981**, *58*, 20−23.
(18) Brown, G. D. *Phytochemistry* **1994**, *36*, 1553−1554.
(19) Ling, T. J.; Ling, W. W.; Chen, Y. J.; Wan, X. C.; Xia, T.; Du, X. F.; Zhang, Z. Z. *Molecules* **2010**, *15*, 8469−8477.
(20) Liebler, D. C.; Baker, F. P.; Kaysen, K. L. *J. Am. Chem. Soc.* **1990**, *112*, 6995−7000.
(21) Becher, E.; Albrecht, R.; Bernhard, K.; Leuenberger, H. G. W.; Mayer, H.; Müller, R. K.; Schüep, W.; Wagner, H. P. *Helv. Chim. Acta* **1981**, *64*, 2419−2435.
(22) Rosenberger, M.; McDougal, P.; Bahr, J. *J. Org. Chem.* **1982**, *47*, 2130−2134.
(23) Buchecker, R.; Marti, U.; Eugster, C. H. *Helv. Chim. Acta* **1984**, *67*, 2043−2056.
(24) Ponce, M. A.; Ramirez, J. A.; Galagovsky, L. R.; Gros, E. G.; Erra-Balsells, R. *Photochem. Photobiol. Sci.* **2002**, *1*, 749−756.
(25) Rivera, A.; Benavides, O. L.; Rios-Motta, J. *Nat. Prod. Res.* **2009**, *23*, 293−300.
(26) Keller, A. C.; Maillard, M. P.; Hostettmann, K. *Phytochemistry* **1996**, *41*, 1041−1046.
(27) Shirane, N.; Takenaka, H.; Ueda, K.; Hashimoto, Y.; Katoh, K.; Ishii, H. *Phytochemistry* **1996**, *41*, 1301−1308.
(28) Lim, J. C.; Park, J. H.; Budesinsky, M.; Kasal, A; Han, Y. H.; Koo, B. S.; Lee, S. I.; Lee, D. U. *Chem. Pharm. Bull.* **2005**, *53*, 561−564.
(29) Gaspar, E. M.; Neves, H. J. *Phytochemistry* **1993**, *34*, 523−527.
(30) Ochi, K.; Matsunaga, I.; Shindo, M.; Kaneko, C. *Chem. Pharm. Bull.* **1978**, *26*, 2386−2390.
(31) Zhang, X.; Geoffroy, P.; Miesh, M.; Julien-David, D.; Raul, F.; Aoude-Werner, D.; Marchioni, E. *Steroids* **2005**, *70*, 886−895.
(32) Bayoumi, S. A. L.; Rowan, M. G.; Beeching, J. R.; Blagbrough, I. S. *Phytochemistry* **2010**, *71*, 598−604.
(33) Xu, W.; Zhu, C.; Cheng, W.; Fan, X.; Chen, X.; Yang, S.; Guo, Y.; Ye, F.; Shi, J. *J. Nat. Prod.* **2009**, *72*, 1620−1626.
(34) Fan, X. N.; Zi, J. C.; Zhu, C. G.; Xu, W. D.; Cheng, W.; Yang, S.; Guo, Y.; Shi, J. G. *J. Nat. Prod.* **2009**, *72*, 1184−1190.
(35) Wang, Y.; Shang, X. Y.; Wang, S. J.; Mo, S. Y.; Li, S.; Yang, Y. C.; Ye, F.; Shi, J. G.; He, L. *J. Nat. Prod.* **2007**, *70*, 296−299.
(36) Cheng, W.; Zhu, C. G.; Xu, W. D.; Fan, X. N.; Yang, Y. C.; Li, Y.; Chen, X. G.; Wang, W. J.; Shi, J. G. *J. Nat. Prod.* **2009**, *72*, 2145−2152.
(37) Mo, S. Y.; Wang, S. J.; Zhou, G. X.; Yang, Y. C.; Li, Y.; Chen, X. G.; Shi, J. G. *J. Nat. Prod.* **2004**, *67*, 823−828.