C_{19}-Diterpenoid Alkaloids from *Aconitum hemsleyanum* var. *circinatum*

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Seven new C_{19}-diterpenoid alkaloids, circinasines A−G (**1**−**7**), together with six known compounds, talatisamine, yunaconitine, senbusine A, sachaconitine, hemsleyanisine, and isohemsleyanisine, were isolated from the roots of *Aconitum hemsleyanum* var. *circinatum*. The structures of **1**−**7** were determined by the interpretation of spectroscopic data and by the single-crystal X-ray crystallographic analysis of **6** and the acetonide derivative of **1**. In addition, the structures of hemsleyanisine and isohemsleyanisine were revised from **8** and **9** to **10** and **11**, respectively.

There is a long and fascinating history of the use of various species of *Aconitum* sources of medicines in various civilizations. *Aconitum* preparations have been used as cardiotonics, febrifuges, sedatives, and anodynes.[1] The diterpenoid alkaloids from *Aconitum* plants are believed to be the main bioactive compounds. The plant *A. hemsleyanum* var. *circinatum* W. T. Wang (Ranunculaceae)[2,3] is a species endemic to the Emei Mountains of Sichuan Province in mainland China and has been used as a folk remedy for the treatment of arthritic pain.[4] In the present investigation on this plant, seven new C_{19}-diterpenoid alkaloids, circinasines A−G (**1**−**7**), together with six known compounds were isolated. In this paper, we report the separation and structure elucidation of these new alkaloids.

The NMR and MS spectra of compounds **1**−**7** showed that they are all aconitine-type C_{19}-diterpenoid alkaloids.[5]

Circinasine A (**1**) was isolated as a white, amorphous powder. The HREIMS peak at *m*/*z* 439.2736 corresponded to the protonated molecular ion $[M]^+$ ($C_{23}H_{37}NO_7$). The NMR spectra of **1** showed the presence of one NCH_2CH_3 group (δ_H 1.03, 3H, t, J = 7.2 Hz; δ_C 13.5 q, 49.1 t) and two methoxyl groups (δ_H 3.24, 3.33, each 3H, s; δ_C 56.3 q, 59.5 q). A one-proton doublet signal (J = 4.8 Hz) at δ_H 4.20 could be assigned to H-14β, suggesting the presence of an OH-14α group and substitution of H-9 or H-13.[5] Two methoxyl groups could be located at C-1 and C-18 from a set of $^1H-^{13}C$ long-range HMBC correlations between the CH_3O-1 (δ_H 3.24 s), CH_3O-18 (δ_H 3.33 s), and the related carbons C-1 (δ_C 83.6 d) and C-18 (δ_C 78.5 t). The ^1H NMR spectrum revealed a doublet signal (J = 8.8 Hz) at δ_H 3.73, which showed HMBC correlations with C-13 (δ_C 76.6 s), C-14 (δ_C 79.5 d), and C-15 (δ_C 43.7 t), implying the presence of a hydroxyl group at C-16. The remaining hydroxyl groups could be assigned at C-5, C-8, and C-13, respectively, by the careful analysis of the 2D-NMR correlations (Figure 1). Therefore, the structure of circinasine A could be assigned initially as **1a**, a rare C_{19}-diterpenoid alkaloid containing an OH group at C-16. In general, most C_{19}-diterpenoid alkaloids possess methoxyl groups at C-16 with β-orientation, and the hydroxyl group is of indefinite configuration. Thus, treatment of **1** (200 mg) with acetone (20 mL) and 2 drops of HCl at room temperature for 48 h produced **1b** quantitively (Table S1, Supporting Information). The structure of **1b** was confirmed by X-ray analysis, and the configuration of the hydroxyl group at C-16 was determined as having a β-orientation (Figure 2). The structure of circinasine A was thus determined as **1**.

In the present investigation, we isolated two previously known alkaloids, hemsleyanisine and isohemsleyanisine,[6] which have been obtained in earlier work.[2] Their ^{13}C NMR data are very similar to those of circinasine A (**1**) (Table 2). Accordingly, it is presumed

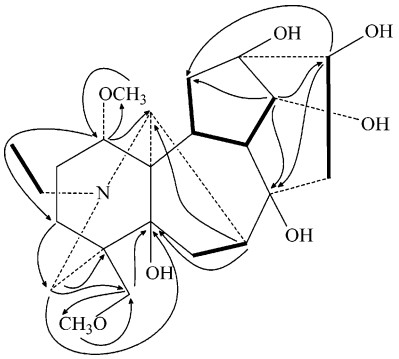

Figure 1. Key $^1H-^1H$ COSY (bold lines) and HMBC (curved arrows) correlations of **1**.

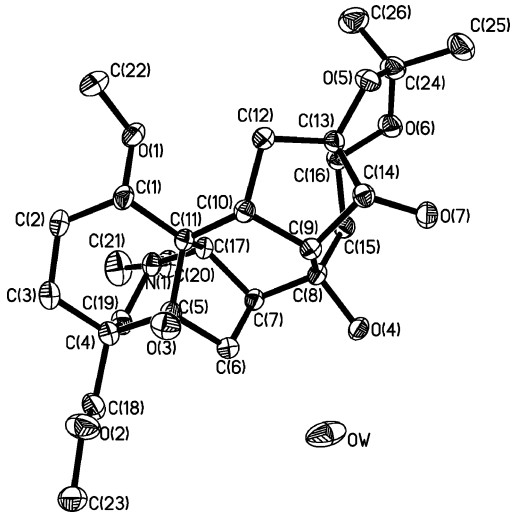

Figure 2. ORTEP diagram for **1b**.

that the structures of these two compounds are incorrect. Comparison by co-TLC (silica gel, 95:5 chloroform−methanol, 1:1 ether−acetone) and the NMR data of their hydrolytic products with circinasine A (**1**) has shown that the structures of hemsleyanisine and isohemsleyanisine should be revised from **8** and **9**[6] to **10** and **11**, respectively.

The HRFABMS of circianasine B (**2**) exhibited a protonated molecular ion peak at *m*/*z* 590.2969 (calcd 590.2965), corresponding to a molecular formula of $C_{31}H_{43}NO_{10}$ (16 mass units more than that of **10** and **11**), suggesting that **2** has an additional hydroxyl group. In the ^1H NMR spectrum of **2**, a one-proton double doublet signal (J = 12.0, 6.0 Hz) at δ_H 4.31 could be assigned to H-3β, implying that the additional hydroxyl group is located at C-3.[5] Thus, the structure of circinasine B was deduced as **2**.

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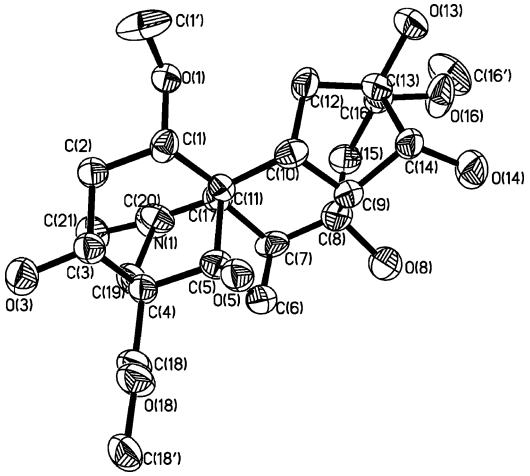


Figure 3. ORTEP diagram for circinasine F (**6**).

Circinasine C (**3**), obtained as a white, amorphous powder, showed the same HREIMS experimental result (M^+ *m*/*z* 573.2991, calcd 573.2937) as isohemsleyanisine (**11**). The analysis of all spectra measured revealed that the structure of circinasine C is very similar to **11** except for the location of a hydroxyl group. This hydroxyl group could be assigned at C-3 rather than C-5 in **11** by the HMBC correlations of H-3 (δ_H 3.85) with C-1 (δ_C 82.9), C-2 (δ_C 34.0), C-4 (δ_C 43.5), and C-18 (δ_C 77.2) (Figure S1, Supporting Information). Furthermore, the α-orientation of OH-3 was established by a large coupling constant (J = 12.0 Hz) between H-3β and H-2α.[5] Accordingly, the structure of circinasine C was elucidated as **3**.

Circinasine D (**4**), an amorphous powder, was also indicated to be an aconitine-type diterpenoid alkaloid by the analysis of its 1D-NMR spectra, with the molecular formula, $C_{31}H_{43}NO_8$, determined by HREIMS (M^+ *m*/*z* 557.2960, calcd 557.2988). Careful analysis of its ^{1}H and ^{13}C NMR and 2D-NMR spectroscopic data determined that the structure of circinasine D was very similar to that of hemslyanisine (**10**). The C-13 oxymethine at δ_C 76.7 (s) in **10** was dehydroxylated as a methylene signal at δ_C 41.6 (d) in circinasine D, as supported by the HMBC correlations between the methylene signal (δ_C 41.6) and H-9 (δ_H 2.68), H-14 (δ_H 5.29), and H-15 (δ_H 2.01, 2.30) and the ^{1}H−^{1}H COSY correlations between the methylene proton (δ_H 2.47) and H-14 (δ_H 5.29) and H-16 (δ_H 3.80) (Figure S2, Supporting Information). On the basis of the above evidence, the structure of circinasine D was deduced as **4**.

Circinasine E (**5**) gave a molecular ion peak at *m*/*z* 423, corresponding to a molecular formula of $C_{23}H_{37}NO_6$, as confirmed by HREIMS (M^+ *m*/*z* 423.2620, calcd 423.2640). Its ^{13}C NMR data were very similar to those of circinasine D (**4**) (Table 2), with minor differences evident in the vicinity of C-14. On comparison by co-TLC (silica gel, 98:2 chloroform−methanol, 3:1 ether−acetone) and the NMR data of the hydrolytic product of **4** with circinasine E, the structure of circinasine E was established as **5**.

Circinasine F (**6**) was obtained as colorless, cubic crystals from Me_2CO with a molecular formula of $C_{24}H_{39}NO_8$, as indicated by the molecular ion peak at *m*/*z* 469.2672 in its HREIMS. The NMR spectra of **6** showed the presence of one NCH_2CH_3 group (δ_H 1.06, 3H, t, J = 7.2 Hz; δ_C 13.5 q, 49.0 t) and three methoxyl groups (δ_H 3.26, 3.37, 3.41, each 3H, s; δ_C 56.4 q, 57.7 q, 59.4 q), which could be assigned to C-1, C-16, and C-18 as a result of the HMQC data and the HMBC correlations of CH_3O-1 (δ_H 3.26), CH_3O-16 (δ_H 3.41), and CH_3O-18 (δ_H 3.37) with their geminal carbons C-1 (δ_C 81.6), C-16 (δ_C 84.7), and C-18 (δ_C 73.4), respectively. Five hydroxyl groups could be located at C-3, C-5, C-8, C-13, and C-14, respectively, also by the 2D-NMR correlations (Figure S3, Supporting Information). In addition, all the ^{1}H and ^{13}C NMR signals for **6** could be assigned unambiguously on the basis of 2D-NMR (HMQC, ^{1}H−^{1}H COSY, HMBC) data. Owing to the complex stereochemistry of circinasine F, single-crystal X-ray diffraction analysis was used to determine the structure and relative stereochemistry of circinasine F as **6**.

Circinasine G (**7**) was analyzed as $C_{30}H_{39}NO_{10}$ by HREIMS (*m*/*z* 573.2362, calcd 573.2388). However, there was no evidence giving a typical NCH_2CH_3 group, but a N=C (19) signal (δ_H 7.19, 1H, s; δ_C 163.0 d) was observed instead. Besides this difference between **7** and **6**, an additional anisoyl ester group could be assigned at C-14 due to the presence of a one-proton doublet signal (J = 4.8 Hz) at δ_H 5.22.[4] Therefore, the structure of circinasine G, containing a rare C=N imine group, was determined as **7**.

The other four known alkaloids isolated from this plant were identified as talatisamine,[7] yunaconitine,[8] senbusine A,[9] and sachaconitine,[10] respectively, by comparing their spectroscopic data with those reported in the literature.

Aconitum hemsleyanum is one of the most widely distributed and highly variable species of *Aconitum* that is native to China.[11] Four variations of *A. hemsleyanum* have been subjected to phytochemical research, *A. hemsleyanum* Pritz, *A. hemsleyanum* var. *leucanthus*, *A. hemsleyanum* var. *circinatum*, and *A. hemsleyanum* var. *pengshines*, and these have shown considerable differences in their alkaloidal profiles.[12−15]

Experimental Section

General Experimental Procedures. Melting points were determined on an XT-4 micro melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. IR spectra were obtained on a Nicolet FT-IR 200 SXV spectrophotometer. ^{1}H and ^{13}C NMR spectra were taken on a Varian Unity INOVA 400/45 NMR spectrometer in $CDCl_3$ with TMS as the internal standard. The ESIMS and HREIMS were recorded on a VG Auto Spec 3000 or Finnigan-MAT 90 instrument. Silica gel H (Qingdao Sea Chemical Factory, Qingdao, People's Republic of China) was used for column chromatography. Spots on TLC (silica gel G) were detected with modified Dragendorff's reagent. A polyvinyl sulfonic ion-exchange resin (H-form, cross-linking 1×1, Chemical Factory of Nankai University, Tianjin, People's Republic of China) was used in the extraction of the crude alkaloids.

Plant Material. *Aconitum hemsleyanium* var. *circinacum* W. T. Wang was collected in the Emei Mountains, Sichuan Province, People's Republic of China, in July 2001 and authenticated by Professor W. T. Wang of the Institute of Botany, Chinese Academy of Sciences, where a voucher specimen (01-7-4) was deposited.

Extraction and Isolation. According to a method reported in the literature,[16] powdered roots (4.0 kg) of *A. hemsleyanum* var. *circinatum* were percolated with 0.05 mol/L HCl (40 L). Wet resin (dry weight 4 kg) was added to the percolate, followed by repeated washing on a suction filter with deionized H_2O. The air-dried resin was then alkalized with 10% aqueous NH_4OH (1.8 L), continuously extracted with ether (5.0 L), and evaporated to give the total crude alkaloids (68.0 g) as a yellowish, amorphous powder substance. The crude alkaloids (38.2 g) were chromatographed over a silica gel column, eluting with a $CHCl_3$−MeOH (200:1 → 7:1) gradient system, to give hemsleyadine (2.6 g), fractions A (3.2 g), B (10.8 g), C (9.6 g), and D (6.2 g), and circinasine A (**1**, 1.4 g). Fraction C (9.6 g) was chromatographed on a silica gel column eluting with $CHCl_3$−CH_3OH (97:3), to afford fractions C-1 (800 mg), C-2 (1.2 g), hemsleyanisine (**10**, 1.2 g), isohemsleyanisine (**11**, 1.3 g), C-3 (2.3 g), and C-4 (1.5 g). Fraction C-1 was separated on a silica gel H column, eluting with ether−acetone (4:1), to give talatisamine (120 mg) and sachaconitine (32 mg). Fraction C-2 was chromatographed over a silica gel column with cyclohexane−acetone (4:1) to yield circinasine B (**2**, 26 mg), circinasine D (**4**, 35 mg), and fractions C-2-1 (200 mg) and C-2-2 (400 mg). Further silica gel chromatography of fraction C-2-2, eluting with $CHCl_3$−CH_3OH (97:3), produced senbusine A (20 mg), yunaconitine (60 mg), and circinasine C (**3**, 23 mg). Fraction C-3 was separated on a column of silica gel with petroleum−acetone (3:1) to give circinasine E (**5**, 800 mg). Fraction C-4 was chromatographed on a silica gel column with ether−acetone (2:1) to give a mixture of two alkaloids, which was

Table 1. ^{1}H NMR Spectroscopic Data for Compounds **1**, **3**, **4**, and **6** (400 MHz for ^{1}H, δ_H mult., J = Hz in $CDCl_3$)

position	**1**	**3**	**4**	**6**
1	3.16 m	3.10 m	3.24 m	3.23 m
2	1.82 m (β)	2.28 m (β)	2.03 m (β)	2.28 m (β)
	2.16 m (α)	2.34 m (α)	2.32 m (α)	2.32 m (α)
3	1.34 m (β)	3.85 dd	13.8 m (β)	4.30 dd
	2.23 m (α)	(12.0, 4.8)	2.22 m (α)	(12.0, 4.8)
5		1.58 m		
6	1.98 m (β)	1.54 d (8.0, β)	1.87 m (β)	1.98 m (β)
	2.15 m (α)	1.92 m (α)	2.16 m (α)	2.06 m (α)
7	2.03 m	2.17 d (8.0)	1.95 m	1.88 m
9	2.65 t (4.8)	2.42 m	2.68 m	2.68 t (5.2)
10	2.50 m	1.88 m	2.42 m	2.18 m
12	2.12 m (α)	1.93 m (α)	1.92 m (α)	1.94 m (α)
	2.55 m (β)	2.26 m (β)	2.21 m (β)	2.00 m (β)
13			2.47 m	
14	4.20 d (4.8)	4.10 d (4.8)	5.29 t (4.8)	4.08 t (4.8)
15	2.16 m (β)	2.22 m (β)	2.01 m (β)	2.36 m (β)
	2.80 m (α)	2.77 dd (α)	2.30 m (α)	2.40 m (α)
16	3.73 d (8.8)	5.24 d (9.2)	3.80 d (9.2)	3.45 m
17	3.16 br s	3.20 br s	3.03 br s	3.15 s
18	2.95 ABq (9.2)	3.16 hidden	2.95 ABq (9.2)	2.45 ABq (9.2)
	3.65 ABq (9.2)	3.33 hidden	3.65 ABq (9.2)	3.52 ABq (9.2)
19	1.76 hidden	1.79 ABq (9.2)	1.85 hidden	1.54 ABq (9.2)
	2.56 hidden	2.99 ABq (9.2)	2.55 hidden	2.93 ABq (9.2)
21	2.26 m	2.41 m	2.37 m	2.48 m
	2.56 m	2.54 m	2.52 m	2.53 m
22	1.03 t (7.2)	1.09 t (7.2)	1.04 t (7.2)	1.06 t (7.2)
CH_3O-1	3.24 s	3.25 s	3.27 s	3.26 s
CH_3O-16				3.41 s
CH_3O-18	3.33 s	3.32 s	3.32 s	3.37 s
2′, 6′		7.96 d (8.8)	7.95 d (8.8)	
3′, 5′		6.90 d (8.8)	6.91 d (8.8)	
Ar-OCH_3		3.85 s	3.84 s	

Table 2. ^{13}C NMR Spectroscopic Data for Compounds **1**−**7**, **10**, and **11** (100 MHz, in $CDCl_3$, δ ppm)

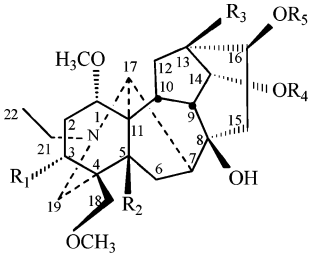
position	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**10**	**11**
1	83.6 d	81.9 d	82.9 d	83.7 d	84.0 d	81.6 d	81.2 d	83.6 d	83.6 d
2	25.7 t	34.9 t	34.0 t	26.2 t	25.8 t	34.7 t	34.9 t	25.9 t	25.8 t
3	28.2 t	65.2 d	71.8 d	28.3 t	28.3 t	65.2 d	66.1 d	28.3 t	28.2 t
4	41.3 s	46.2 s	43.5 s	41.1 s	41.1 s	46.3 s	56.9 s	41.0 s	41.0 s
5	84.6 s	84.9 s	43.8 d	84.3 s	84.9 s	85.1 s	81.0 s	84.2 s	84.4 s
6	34.4 t	35.2 t	24.8 t	34.6 t	34.3 t	35.0 t	35.0 t	34.5 t	34.4 t
7	45.0 d	45.5 d	45.5 d	45.7 d	46.6 d	44.7 d	45.7 d	45.5 d	45.6 d
8	73.6 s	74.0 s	73.2 s	73.8 s	73.6 s	73.1 s	73.0 s	74.0 s	73.5 s
9	48.6 d	47.6 d	48.0 d	45.1 d	45.2 d	49.6 d	53.7 d	49.0 d	48.4 d
10	36.9 t	36.5 t	42.0 t	39.0 t	39.7 t	36.2 t	36.5 t	36.8 t	36.4 t
11	50.5 s	50.4 s	48.2 s	50.6 s	50.6 s	50.3 s	49.7 s	50.4 s	50.5 s
12	35.4 t	36.2 t	36.9 t	28.0 t	27.7 t	35.1 t	35.7 t	36.4 t	36.9 t
13	76.6 s	76.8 s	77.5 s	41.6 d	40.9 d	77.0 s	76.3 s	76.7 s	77.4 s
14	79.5 d	81.4 d	78.5 d	76.8 d	75.7 d	79.5 d	79.9 d	81.8 d	78.4 d
15	43.7 t	43.5 t	41.6 t	43.3 t	42.6 t	39.6 t	40.7 t	43.5 t	41.8 t
16	75.5 d	74.2 d	76.0 d	72.5 d	72.5 d	84.7 d	83.3 d	74.2 d	76.0 d
17	63.7 d	62.7 d	62.4 d	63.1 d	63.8 d	63.1 d	63.8 d	63.2 d	63.5 d
18	78.5 t	73.3 t	77.2 t	78.9 t	78.7 t	73.4 t	71.2 t	78.7 t	78.6 t
19	55.5 t	48.2 t	46.7 t	55.5 t	55.5 t	48.2 t	163.0 d	55.3 t	55.4 t
21	49.1 t	48.9 t	49.2 t.	48.9 t	49.1 t	49.0 t		49.0 t	49.0 t
22	13.5 q	13.5 q	13.4 q	13.5 q	13.5 q	13.5 q		13.5 q	13.5 q
CH_3O-1	56.3 q	56.5 q	56.1 q	56.3 q	56.4 q	56.4 q	56.2 q	56.5 q	56.2 q
CH_3O-16						57.7 q	58.1 q		
CH_3O-18	59.5 q	59.5 q	59.4 q	59.5 q	59.5 q	59.4 q	59.5 q	59.8 q	59.4 q
ArCO		167.9 s	166.8 s	165.8 s			166.7 s	167.8 s	166.4 s
1′		121.3 s	122.2 s	122.6 s			122.3 s	121.8 s	121.4 s
2′, 6′		131.7 d	131.8 d	131.6 s			131.6 d	131.7 d	131.7 d
3′, 5′		113.7 d	113.8 d	113.8 s			113.6 d	113.6 d	113.5 d
4′		163.8 s	163.6 s	162.3 s			163.3 s	163.6 s	163.2 s
CH_3O-4′		55.4 q	55.4 q	55.5 q			55.2 q	55.3 q	55.2 q

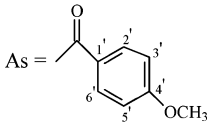
further separated with $CHCl_3$−CH_3OH (96:4) to give circinasines G (**7**, 16 mg) and F (**6**, 36 mg), in turn.

Circinasine A (1): white, amorphous powder; $[\alpha]_D^{20}$ −32.0 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3419, 2924, 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m*/*z* 440 $[M + H]^+$; HREIMS *m*/*z* 439.2736 $[M]^+$ (calcd for $C_{23}H_{37}NO_7$, 439.2758).

Single-Crystal X-ray Crystallography of 1b. 1b was produced by the treatment of **1** (200 mg) with acetone (20 mL) and 2 drops of HCl at room temperature for 48 h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24, 3.31 (each 3H, s, 2×OCH_3), 4.05 (1H, t, J = 4.8 Hz, H-14β), 1.03 (3H, t, J = 7.2 Hz, *N*-CH_2CH_3), 1.38, 1.51 (each 3H, s, $CH_3CO_2CH_3$), 2.95, 3.65 (each 1H, ABq system, J = 9.2 Hz, H_2-18); ^{13}C NMR (100 MHz, $CDCl_3$), see Table S1 (Supporting Information); ESIMS *m*/*z* 480 $[M + H]^+$.

The colorless sheet crystal of **1b** from acetone−cyclohexane was mounted on a P_4 four-circle diffractometer and exposed to graphite-monochromated Mo Kα irradiation. The unit cell parameters are a = 9.186(1) Å, b = 10.212(1) Å, c = 54.792(1) Å in space group $P2_12_12_1$ (Z = 4), D_x = 1.286 g·cm^{-3}. The structure was solved by direct methods with the program SHELX 97 and refined by full-matrix least-squares on F^2. The final R indices were R^1 = 0.0647 and wR^2 = 0.1397. CCDC 628273 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge via





1 $R_1 = R_4 = R_5 = H$ $R_2 = R_3 = OH$

2 $R_1 = R_2 = R_3 = OH$ $R_4 = As$ $R_5 = H$

3 $R_1 = R_3 = OH$ $R_2 = R_4 = H$ $R_5 = As$

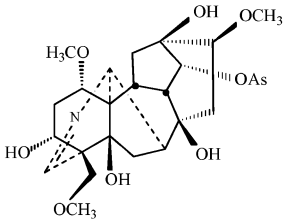
4 $R_1 = R_3 = R_5 = H$ $R_2 = OH$ $R_4 = As$

5 $R_1 = R_3 = R_4 = R_5 = H$ $R_2 = OH$

6 $R_1 = R_2 = R_3 = OH$ $R_4 = H$ $R_5 = CH_3$

10 $R_1 = R_5 = H$ $R_2 = R_3 = OH$ $R_4 = As$

11 $R_1 = R_4 = H$ $R_2 = R_3 = OH$ $R_5 = As$



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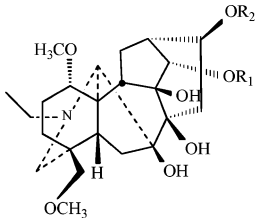
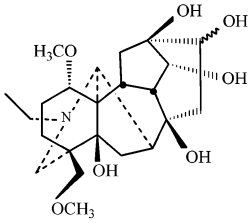
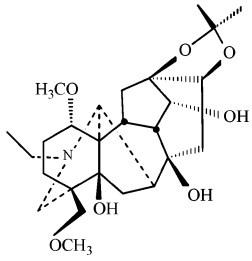


8 $R_1 = As$ $R_2 = H$

9 $R_1 = H$ $R_2 = As$



1a



1b

www.ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 IEZ, UK, fax: (+44) 1223-336-033.

Circinasine B (2): white, amorphous powder; $[\alpha]_D^{20}$ +52.3 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3445, 2925, 1699, 1606, 1511, 1459, 1285, 1257, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.27, 3.37, 3.84 (each 3H, s, 3×OCH_3), 5.24 (1H, d, J = 4.8 Hz, H-14β), 3.78 (1H, brd, J = 9.2 Hz, H-16α), 4.31(1H, dd, J = 12.0, 6.0 Hz, H-3β), 1.07 (3H, t, J = 7.2 Hz, *N*-CH_2CH_3), 6.94−7.95 (4H, AA′BB′ system, J = 8.8 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$), see Table 1; ESIMS *m*/*z* 590 $[M + H]^+$; HRESIMS *m*/*z* 590.2969 $[M + H]^+$ (calcd for $C_{31}H_{43}NO_{10}$, 590.2965).

Circinasine C (3): white, amorphous powder; $[\alpha]_D^{20}$ +43.8 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3432, 2915, 1699, 1598, 1523, 1459, 1265, 1244 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m*/*z* 574 $[M + H]^+$; HREIMS *m*/*z* 573.2991 $[M]^+$ (calcd for $C_{31}H_{43}NO_9$, 573.2937).

Circinasine D (4): white, amorphous powder; $[\alpha]_D^{20}$ +15.8 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3460, 2924, 1701, 1606, 1512, 1460, 1257, 1170, 1102 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m*/*z* 558 $[M + H]^+$; HREIMS *m*/*z* 557.2960 $[M]^+$ (calcd for $C_{31}H_{43}NO_8$, 557.2988).

Circinasine E (5): white, amorphous powder; $[\alpha]_D^{20}$ +36.5 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3420, 2924, 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.26, 3.34 (each 3H, s, 2×OCH_3), 4.33 (1H, t, J = 4.8 Hz, H-14β), 1.04 (3H, t, J = 7.2 Hz, *N*-CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$), see Table 1; ESIMS *m*/*z* 424 $[M + H]^+$; HREIMS *m*/*z* 423.2620 $[M]^+$ (calcd for $C_{23}H_{37}NO_6$, 423.2640).

Circinasine F (6): colorless, cubic crystals (Me_2CO); mp 239−240 °C; $[\alpha]_D^{20}$ +24.8 (1.0, $CHCl_3$); IR (KBr) ν_{max} 3415, 2930, 1085 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m*/*z* 470 $[M + H]^+$; HREIMS *m*/*z* 469.2672 M^+ (calcd for $C_{24}H_{39}NO_8$, 469.2675).

Single-Crystal X-ray Crystallography of 6. A colorless sheet crystal from acetone was mounted on a P_4 four-circle diffractometer and exposed to graphite-monochromated Mo Kα irradiation. The unit cell parameters are a = 13.491(1) Å, b = 15.501(2) Å, c = 21.975(2) Å in space group $C222_1$ (Z = 8), D_x = 1.357 g·cm^{-3}. The structure was solved by direct methods with the program SHELX 97 and refined by full-matrix least-squares on F^2. The final R indexes were $R^1 = 0.041$ and $wR^2 = 0.164$. CCDC 628274 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge via www.ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 IEZ, UK, fax: (+44) 1223-336-033.

Circinasine G (7): white, amorphous powder; $[\alpha]_D^{20}$ +43.6 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.25, 3.37, 3.42, 3.85 (each 3H, s, 4×OCH_3), 5.22 (1H, d, J = 4.8 Hz, H-14β), 6.81−7.96 (4H, AA′BB′ system, J = 8.8 Hz, Ar-H); 7.19 (1H, s, −N=*CH*); ^{13}C NMR (100 MHz, $CDCl_3$), see Table 1; ESIMS *m*/*z* 574 $[M + H]^+$; HREIMS *m*/*z* 573.2362 $[M]^+$ (calcd for $C_{30}H_{39}NO_{10}$, 573.2388).

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Supporting Information Available: Figures S1, S2, and S3 showing $^1H-^1H$ COSY and HMBC NMR correlations of **3**, **4**, and **6**. Table S1 showing the ^{13}C NMR spectroscopic data of **1b**. These materials are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Pelletier, S. W.; Mody, N. V.; Joshi, B. S.; Schramm L. C. In *The Alkaloids: Chemical and Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1983; Vol. 1, pp 153−210.
(2) Gao, F.; Wang, F. P. *Heterocycles* **2005**, *65*, 365−370.
(3) Gao, F.; Chen, D. L.; Wang, F. P. *Chem. Pharm. Bull.* **2006**, *54*, 117−118.
(4) Institute of Botany, Chinese Academy of Science and Institute of Materia Medica, Chinese Academy of Medical Science. In *Flora Reipublicae Popularis Sinicae*; Science Press: Beijing, 1979; Vol. 27, pp 235−236.
(5) Pelletier, S. W.; Mody, N. V.; Joshi, B. S.; Schramm L. C. In *The Alkaloids: Chemical and Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1984; Vol. 2, pp 206−264.
(6) Xu, Q. Y.; Li, Z. B.; Wang, F. P.; Che, C. T. *Heterocycles* **1996**, *43*, 1243−1250.
(7) Xie, G. B.; Wang, F. P. *Chem. J. Chin. Univ.* **2004**, *25*, 482−483.
(8) Chen, S. Y. *Acta Chim. Sin.* **1979**, *37*, 15−19.
(9) Konno, C.; Shirasaka, M.; Hikino, H. *J. Nat. Prod.* **1982**, *45*, 128−133.
(10) Pelletier, S. W.; Mody, N. V.; Katusi, N. *Tetrahedron Lett.* **1977**, *18*, 4027−4030.
(11) Yang, Q. E. *Acta Phytotaxon. Sin.* **1999**, *37*, 545−590.
(12) Zhou, X. L.; Jian, X. X.; Wang, F. P. *Nat. Prod. Res. Dev.* **2002**, *14*, 14−17.
(13) Lin, L. Y.; Chen, Q. H.; Zhou, X. L.; Chen, D. L.; Wang, F. P.; Che, C. T. *J. Nat. Prod.* **2003**, *66*, 269−271.
(14) Peng, C. S.; Wang, F. P.; Jian, X. X. *J. Asian Nat. Prod. Res.* **2000**, *2*, 245−249.
(15) Peng, C. S.; Wang, F. P.; Jian, X. X. *Chin. Chem. Lett.* **2002**, *13*, 133−136.
(16) Fang, Q. C.; Huo, Z. M. *Acta Pharm. Sin.* **1966**, *13*, 577−588. .

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