Phenolic Glycosides and Pyrrolidine Alkaloids from *Codonopsis tangshen*

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Chemical examination of the *n*-butanol extract of the root of *Codonopsis tangshen* led to the isolation of four new compounds named codonosides A (1) and B (2) and codonopyrrolidiums A (3) and B (4), with seven known compounds [(*Z*)-2-(*β*-glucopyranosyloxy)-3-phenylpropenoic acid (5), lobetyolin (6), lobetyol (7), luteolin (8), friedelin (9), 5,6,9-trihydroxy-octadec-7-enoic acid (10), and adenosine (11)]. Based on spectroscopic evidence, the structures of codonosides A (1) and B (2) were established as phenolic glycosides, and those of codonopyrrolidiums A (3) and B (4) as pyrrolidines. The relative configuration of 3 was determined by X-ray crystallographic analysis.

Key words *Codonopsis tangshen*; Campanulaceae; codonoside A; codonoside B; codonopyrrolidium A; codonopyrrolidium B

Chuan–Danshen [the root of *Codonopsis tangshen* OLIV. (Campanulaceae)] is a well-known traditional Chinese medicine sometimes used as a substitute for ginseng. It is used mainly as a tonic agent to treat general weakness.[1)] Phenolic glucosides, neolignan glycoside, alkyl glycosides, and diyne compounds have been isolated from this plant.[2,3)] As a part of our studies on tonic Chinese medicine, a chemical investigation was conducted on the root of *C. tangshen*. Here we report the isolation and structural elucidation of four new compounds (Fig. 1), two phenolic glycosides (**1**, **2**) and two pyrrolidine alkaloids (**3**, **4**), with seven known compounds from the root of the *C. tangshen*.

Results and Discussion

The ethanol extract of the dried roots of *C. tangshen* was partitioned between water and *n*-hexane, followed by water and *n*-BuOH. Purification of the *n*-BuOH fraction by passage on a series of column chromatography resulted in the isolation of 11 compounds. Seven were identified as [(*Z*)-2-(*β*-glucopyranosyloxy)-3-phenyl-propenoic acid (**5**),[4)] lobetyolin (**6**),[5)] lobetyol (**7**),[5)] luteolin (**8**),[6)] friedelin (**9**),[7)] 5,6,9-trihydroxy-octadec-7-enoic acid (**10**), and adenosine (**11**)].

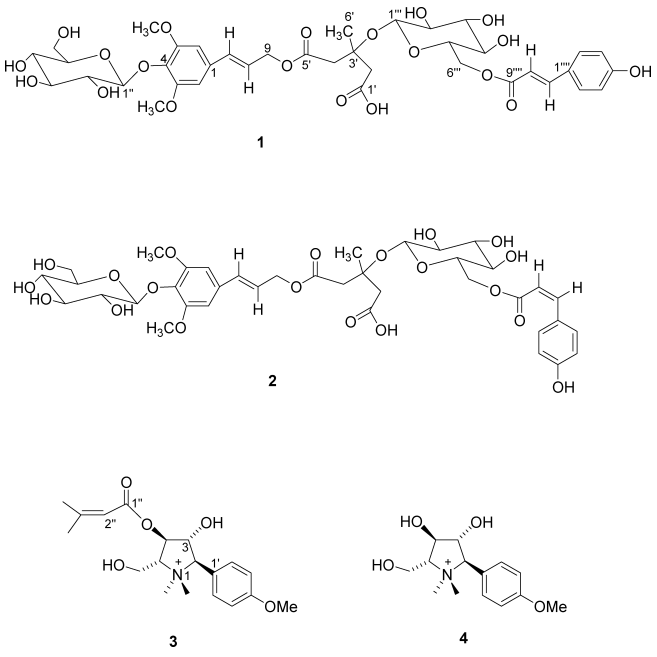

Fig. 1. Structures of Compounds **1**—**4**

Codonoside A (**1**) has the molecular formula $C_{38}H_{48}O_{20}$ based on HR-FAB-MS *m/z*: 847.2642 $[M+Na]^+$. The IR (ν_{max} 3410, 1733, 1717, 1700, 1558, 1540, 1506 cm^{-1}) and UV (λ_{max} 221, 274, 308 nm) spectra showed hydroxyl, aromatic ring, carbonyl, and α,β-unsaturated absorption systems. In the ^{1}H-NMR spectrum of **1**, signals at δ 4.67 (totally 3H, two were assigned as H_2-9 and the other was assigned as H-1‴), δ 6.24 (1H, dt, J=16.0, 6.0 Hz, H-8), δ 6.57 (1H, d, J=16.0 Hz, H-7), and δ 6.72 (2H, s, H-2, 6) suggested the presence of a 3,4,5-trisubstituted *trans*-cinnamoyl moiety. Significant cross peaks were observed between H-7 and H-8, and H-8 and H-9 in the ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum, indicating the connectivity of H-7, H-8, and H-9. Furthermore, signals of A_2B_2 aromatic protons at δ 7.41/6.79 (each d, J=8.5 Hz, H-2⁗, 6⁗/-3⁗, 5⁗) and *trans*-α,β-unsaturated protons at δ 7.62/6.32 (each d, J=15.5 Hz, H-7⁗/-8⁗) were assigned to the *trans*-*p*-coumaroyl group. The ^{1}H-NMR spectrum of **1** (CD_3OD) showed two anomeric protons at δ 4.67 (d, J=7.0 Hz, H-1‴) and 4.89 (H-1″). Due to overlapping, signal patterns were unclear. To clarify the signal patterns of H-1‴, H-1″, and H_2-9, another ^{1}H-NMR spectrum was recorded in DMSO-d_6. The ^{1}H-NMR spectrum of **1** measured in DMSO-d_6 was consistent with the above observation (measured in CD_3OD), with two anomeric protons at δ 4.52 (d, J=7.5 Hz, H-1‴) and 4.91 (d, J=7.0 Hz, H-1″), and methylene protons at δ 4.46 (d, J=6.0 Hz, H_2-9), suggesting the presence of two β-glucosyl units and an oxygenated methylene. The assignments of chemical shifts arising from the respective glucosyl units were conducted based on ^{1}H–^{1}H COSY, 1D-total correlation spectroscopy (TOCSY), and heteronuclear multiple quantum coherence (HMQC) experiments. In the 1D-TOCSY experiment (Fig. 2B), the anomeric proton at δ 4.67 (H-1‴) was irradiated, giving responses from H-2‴, H-3‴, H-4‴, H-5‴, and both H-6‴. The other set of glucosyl unit was subjected to ^{1}H–^{1}H COSY and HMQC experiments, and the data are summarized in Table 1. In addition, two aromatic methoxy methyls (δ 3.85, s, OMe-3/-5), two sets of methylene protons (δ 2.94,

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Table 1. ^{1}H-, ^{13}C-NMR Data of Compounds **1**, **2**[a)]

	No.	**1**		**2**	
		δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H
Cinnamoyl	1	134.5 (s)	—	134.5 (s)	—
	2/6	105.6 (d)	6.72 (2H, s)	105.7 (d)	6.76 (2H, s)
	3/5	154.3 (s)	—	154.4 (s)	—
	4	136.2 (s)	—	136.2 (s)	—
	7	134.9 (d)	6.57 (1H, d, 16.0)	135.0 (d)	6.62 (1H, d, 15.5)
	8	124.3 (d)	6.24 (1H, dt, 16.0, 6.0)	124.3 (d)	6.29 (1H, dt, 15.5, 6.0)
	9	66.0 (t)	4.67 (2H, d, 6.0)	66.1 (t)	4.72 (2H, d, 6.0)
	3/5-OCH_3	57.0 (q)	3.85 (6H, s)	57.1 (q)	3.85 (6H, s)
	1′	172.3 (s)	—	174.7 (s)	—
	2′	44.5 (t)	2.94[b)]	44.3 (t)	2.77/2.88 (each 1H, d, 15.5)
	3′	77.8 (s)	—	77.6 (s)	—
	4′	44.5 (t)	2.94[b)]	44.2 (t)	2.90 (2H)
	5′	172.3 (s)	—	172.3 (s)	—
	6′	25.3 (q)	1.52 (3H, s)	25.1 (q)	1.48 (3H, s)
p-Coumaroyl	1′′′′	127.1 (s)	—	127.6 (s)	—
	2′′′′/6′′′′	131.2 (d)	7.41 (2H, d, 8.5)	133.8 (d)	7.62 (2H, d, 8.5)
	3′′′′/5′′′′	116.8 (d)	6.79 (2H, d, 8.5)	115.9 (d)	6.75 (2H, d, 8.5)
	4′′′′	161.2 (s)	—	160.1 (s)	—
	7′′′′	146.7 (d)	7.62 (1H, d, 15.5)	145.4 (d)	6.81 (1H, d, 13.0)
	8′′′′	115.0 (d)	6.32 (1H, d, 15.5)	116.3 (d)	5.79 (1H, d, 13.0)
	9′′′′	169.0 (s)	—	168.1 (s)	—
Glucosyl-1	1′′	105.3 (d)	4.89[b)]	105.3 (d)	4.89[b)]
	2′′	75.7 (d)	3.49[b)]	75.7 (d)	3.49[b)]
	3′′	78.0 (d)	3.43[b)]	77.9 (d)	3.42[b)]
	4′′	71.3 (d)	3.41[b)]	71.3 (d)	3.42[b)]
	5′′	78.3 (d)	3.23[b)]	78.3 (d)	3.22[b)]
	6′′	62.5 (t)	3.79 (1H, dd, 12.0, 2.0)/ 3.68 (1H, dd, 12.0, 5.0)	62.6 (t)	3.79 (1H, d, 12.5)/ 3.67 (1H, dd, 12.5, 5.5)
Glucosyl-2	1′′′	98.4 (d)	4.67 (1H, d, 7.0)	98.4 (d)	4.61 (1H, d, 8.0)
	2′′′	75.1 (d)	3.23[b)]	75.1 (d)	3.20 (1H, t, 8.5)
	3′′′	77.8 (d)	3.43[b)]	77.8 (d)	3.42[b)]
	4′′′	71.8 (d)	3.30 (1H, t, 9.0)	71.7 (d)	3.26 (1H, t, 9.5)
	5′′′	75.2 (d)	3.55 (1H, t, 8.0)	75.1 (d)	3.49[b)]
	6′′′	64.9 (t)	4.48 (1H, d, 11.0)/ 4.24 (1H, dd, 11.0, 7.0)	64.6 (t)	4.43 (1H, d, 11.0)/ 4.19 (1H, dd, 11.0, 6.5)

a) Measured in MeOH-d_4; multiplicity and coupling constant (J in Hz) assigned in parentheses. *b*) Signal patterns are unclear due to overlapping.

H-2′/-4′), and a tertiary methyl (δ 1.52, s, H-6′) were also observed in the spectrum. This information suggested that **1** is a "tangshenoside-type" phenylpropanoid derivative.[2)] The connection of the above units was established in NOESY and HMBC (Fig. 3) experiments. The NOESY spectrum of **1** showing the correlation of H-2/-6 with H-7 and OMe-3/-5, and of H-1″ with OMe-3/-5, and the HMBC spectrum showing the correlation of H-1″ with C-4, and H-2/6, H-7, and H-8 with C-1 indicates a 3,5-dimethoxy-4-β-*O*-glucosyl-*trans*-cinnamoyl moiety. HMBC correlations of **1** between H-9 and H-4′ with C-5′, between H-2′, -4′, and H-1‴ with C-3′, between H-2′ and H-4′ with C-6′, and between H-2′ and C-1′ indicate the linkages of cinnamoyl and 3-*O*-β-glucosyl-3-methylglutarate. A down-field shift was observed at C-6‴ (δ 64.9) compared with that on tangshenoside I,[2)] suggesting an acyl-substitution at this position. HMBC correlations between H-6‴, H-8′′′′, and H-7′′′′ with C-9′′′′, and between H-3′′′′/5′′′′ and H-8′′′′ with C-1′′′′ confirmed the linkage of C-6‴ and the *trans*-*p*-coumaroyl group. Thus codonoside A (**1**) is 6‴-*trans*-*p*-coumaroyl-tangshenoside I, although the absolute configuration at C-3′ could not be confirmed because of the scarcity of the compound.

Codonoside B (**2**) was separated from the mixture of **1** and **2** using semipreparative HPLC. The UV and ESI-MS spectra of **2** were consistent with those of **1**, indicating that **2** is also a tangshenoside-type phenylpropanoid derivative. Comparison of the ^{1}H and ^{13}C spectra of **2** with those of **1** suggested that the main differences lie in the region of the *trans*-*p*-coumaroyl group of **1** (Table 1). In the ^{1}H-NMR spectrum of **2**, signals of A_2B_2 aromatic protons at δ 7.62/6.75 (each d, J=8.5 Hz, H-2′′′′, 6′′′′/-3′′′′, 5′′′′) and *cis*-α, β-unsaturated protons at δ 6.81/5.79 (each d, J=13.0 Hz, H-7′′′′/-8′′′′) were assigned to the *cis*-*p*-coumaryl group that replaced the *trans*-*p*-coumaroyl group of **1**. HMBC correlations between H-6‴ (δ 4.19/4.43) and H-7′′′′ with C-9′′′′ (δ 168.1) and between H-3′′′′/5′′′′ and H-8′′′′ with C-1′′′′ (δ 127.6) indicated the linkage of C-6‴ and the *cis*-*p*-coumaroyl group. Thus **2** was characterized as 6‴-*cis*-*p*-coumaroyl-tangshenoside I.

Codonopyrrolidium A (**3**), a colorless crystal (MeOH), was positive to Dragendoff's reagent (orange coloration). The molecular formula of **3** was consistent with $C_{19}H_{28}O_5N$ from the HR-FAB-MS spectrum m/z: 350.1964 $[M]^+$. The ^{1}H-NMR spectrum of **3** showed an A_2B_2 aromatic proton at δ 7.60 (d, J=8.5 Hz, H-2′, 6′), and δ 7.11 (d, J=8.5 Hz, H-3′, 5′), suggesting that a 1,4-disubstituted benzene ring was present. Signals at δ 4.95 (d, J=10.5 Hz, H-2), 5.07 (dd, J=10.5, 4.5 Hz, H-3), 5.42 (br s, H-4), and 3.90 (br s, H-5) were assigned to a 2,3,4,5-tetrasubstituted pyrrolidine moi-

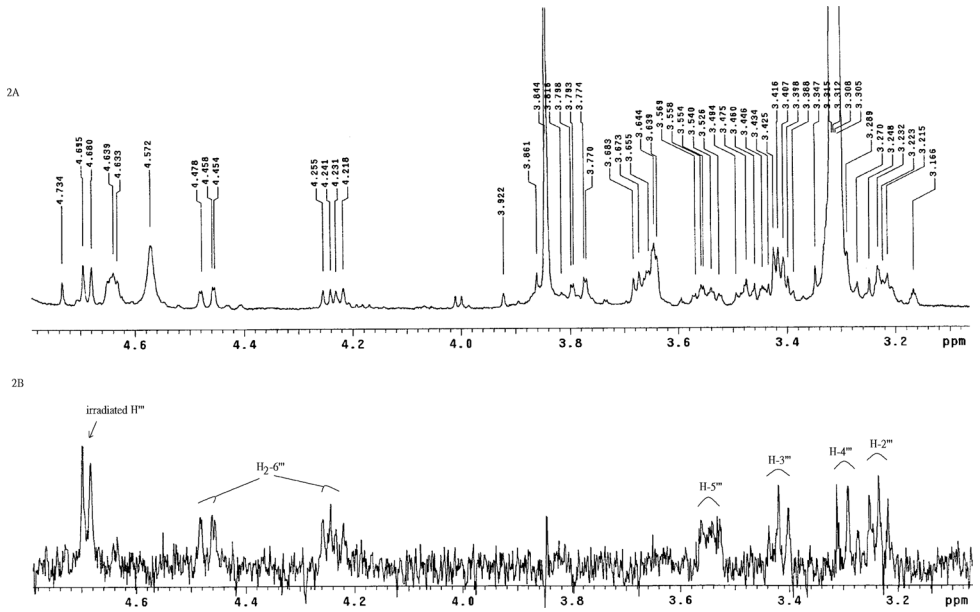

Fig. 2. (A) Expanded Region of Normal ^{1}H-NMR Spectrum of Compound **1**, (B) 1D TOCSY Spectrum of Compound **1**, Irradiated at δ 4.67 (H-1‴) with Mixing Time of 0.20 s

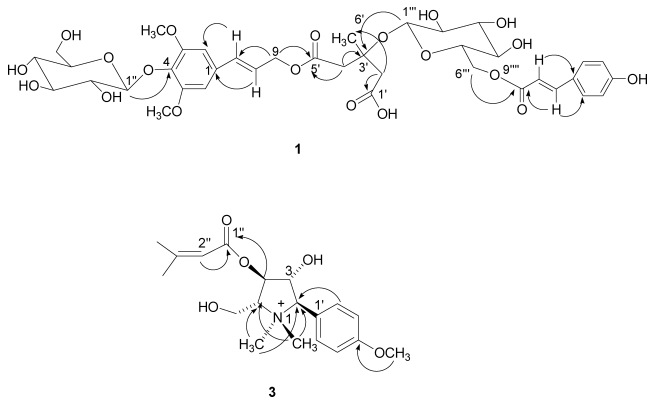

Fig. 3. Selected HMBC (H→C) Correlations of Compounds **1** and **3**

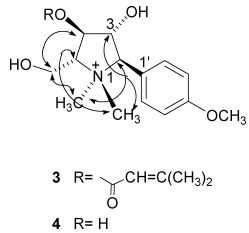

Fig. 4. Selected NOESY Correlations of Compounds **3** and **4**

ety, as confirmed by COSY and TOCSY experiments. A 3-methyl-but-2 enoic acid group was indicated by the signals at δ 1.98/2.23 (each 3H, s) and δ 5.87 (1H, s). The finding of a 3-methyl-but-2 enoic acid group was consistent with the ^{13}C-NMR signals at δ 167.2 (s, C-1″), 115.5 (d, C-2″), 161.6 (s, C-3″) 27.6 (q, C-4″), and 20.6 (q, C-5″). In addition, one set of oxygenated methylene protons (δ 4.29, H_2-6), one aromatic methoxy methyl (δ 3.86), and two nitrogen methyls (δ 2.88/3.11) were also observed in the spectrum. The TOCSY spectrum revealed the connection of H-5 and an oxygenated methylene moiety. The HMBC spectrum (Fig. 3) revealed correlations between –OC$\underline{H}_3$ (δ 3.86), H-3′/5′, and H-2′/6′ with C-4′, between H-3′/5′ and H-2 with C-1′, and between H-2′/6′ and C-2, indicating the linkage of C-2 and 4′-methoxy-phenyl group. Correlations between H-4 and H-2″ with C-1″ indicated that the 3-methyl-but-2 enoic acid ester is located at C-4. Other correlations between –N(C$\underline{H}_3$)$_2$ (δ 2.88/3.11) and C-2, and between –N(C$\underline{H}_3$)$_2$ and C-5 confirmed the 1,1-dimethyl pyrrolidine structure. Therefore the structure of **3** was proposed to be 3-methyl-but-2-enoic acid 3-hydroxy-5-hydroxymethyl-2-(4-methoxy-phenyl)-1,1-dimethyl-pyrrolidine-4-yl ester. NOESY data (Fig. 4) showed that the four asymmetric carbons are with substitutes *trans*-relative to each other. NOE correlations between –N(C$\underline{H}_3$) (δ 3.11) and H-2 and H-6 and between H-6 and H-4 indicate these hydrogen are in a *cis* relationship. Other correlations from –N(C$\underline{H}_3$) (δ 2.88) to H-3 and H-5 showed that these hydrogens are in the same direction. The X-ray analysis of **3**·HCl confirmed the proposed structure of **3**. Determination of the absolute configuration was not conducted, but the relative configurations were consistent with those of (−)-codonopsinine (2*R*, 3*R*, 4*R*, 5*R*), which was isolated from *Codonopsis clematidea*, and the absolute configuration was established by total synthesis.[8] An ORTEP drawing of **3**·HCl is shown in Fig. 5 in which the absolute configuration follows that of (−)-codonopsinine.

Codonopyrrolidium B (**4**) was positive to Dragendoff's reagent with orange coloration. The ^{1}H-NMR spectrum of **4** revealed the presence of a 1,4-disubstituted benzene ring [δ 7.55 (d, J=8.5 Hz, H-2′, 6′), and δ 7.08 (d, J=8.5 Hz, H-3′, 5′)], a 2,3,4,5-tetrasubstituted 1,1-dimethyl pyrrolidine moiety [δ 2.79/3.18 (N–(C$\underline{H}_3$)$_2$), 4.64 (d, J=9.0 Hz, H-2), 4.69 (dd, J=9.0, 5.0 Hz, H-3), 4.29 (t, J=5.5 Hz, H-4), and 3.65 (m, H-5)], a set of oxygenated methylene protons (δ 4.08/4.17), and an aromatic methoxy methyl (δ 3.85). The ^{1}H- and ^{13}C-NMR spectral data of **4** were very similar to those of **3**, except for the lack of a 3-methyl-but-2 enoic acid ester group. These findings were consistent with the molecular formula $C_{14}H_{22}O_4N$ derived from the HR-FAB-MS spec-

Table 2. ^{1}H-, ^{13}C-NMR Data of Compounds **3**, **4**[a)]

	3		**4**	
No.	δ ^{13}C	δ ^{1}H	δ ^{13}C	δ ^{1}H
2	81.5 (d)	4.95 (1H, d, 10.5)	83.2 (d)	4.64 (1H, d, 9.0)
3	75.2 (d)	5.07 (1H, dd, 4.5, 10.5)	77.6 (d)	4.69 (1H, dd, 5.0, 9.5)
4	79.0 (d)	5.42 (1H, br s)	76.3 (d)	4.29 (1H, t, 5.5)
5	81.0 (d)	3.90 (1H, br s)	81.7 (d)	3.65 (1H, m)
6	60.0 (t)	4.29 (2H, br s)	59.3 (t)	4.08 (1H, br d, 13.5); 4.17 (1H, d, 13.5)
1′	119.8 (s)	—	121.1 (s)	—
2′/6′	134.6 (d)	7.60 (2H, d, 8.5)	134.4 (d)	7.55 (2H, d, 8.5)
3′/5′	115.8 (d)	7.11 (2H, d, 8.5)	115.8 (d)	7.08 (2H, d, 8.5)
4′	163.4 (s)	—	163.3 (s)	—
1″	167.2 (s)	—	—	—
2″	115.5 (d)	5.87 (1H, s)	—	—
3″	161.6 (s)	—	—	—
4″	27.6 (q)	1.98 (3H, s)	—	—
5″	20.6 (q)	2.23 (3H, s)	—	—
N–$(CH_3)_2$	48.2 (q)	3.11 (3H, s)	49.0 (q)	3.18 (3H, s)
	50.5 (q)	2.88 (3H, s)	52.1 (q)	2.79 (3H, s)
OCH_3	56.0 (q)	3.86 (3H, s)	56.0 (q)	3.85 (3H, s)

a) Measured in MeOH-d_4; multiplicity and coupling constant (J in Hz) assigned in parentheses.

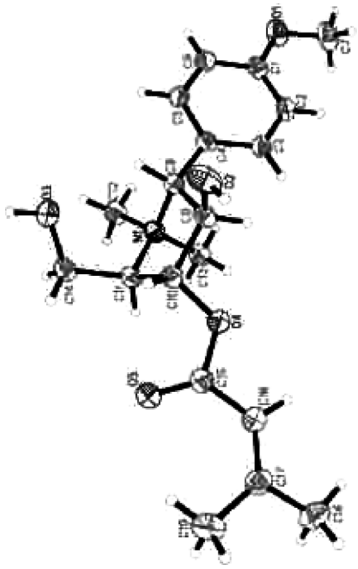

Fig. 5. ORTEP Drawing of Compound **3**

trum *m/z*: 268.1552 $[M]^+$. The TOCSY spectrum revealed the connection of H-5 of pyrrolidine and the oxygenated methylene moiety. The HMBC spectrum revealed correlations between –OC$\underline{H}_3$ (δ 3.86), H-3′/5′, and H-2′/6′ with C-4′; H-3′/5′ and H-2 with C-1′; and H-2′/6′ with C-2, indicating the linkage of C-2 and the 4′-methoxy-phenyl group. Other correlations between –N(C$\underline{H}_3$)$_2$ (δ 2.79/3.18) and C-2, and between –N(C$\underline{H}_3$)$_2$ and C-5 confirmed the 1,1-dimethyl pyrrolidine structure. Therefore the structure of **4** was proposed to be 5-hydroxymethyl-2-(4-methoxy-phenyl)-1,1-dimethyl-pyrrolidine-3,4-diol. An NOESY experiment (Fig. 4) performed on **4** showed interactions between –N(C$\underline{H}_3$) (δ 3.18) and H-2 and H-6, and between –N(C$\underline{H}_3$) (δ 2.79) and H-3 and H-5. These indicated that –N(C$\underline{H}_3$) (δ 3.18), H-2, and H-6 are in a *cis* relationship; –N(C$\underline{H}_3$) (δ 2.79), H-3, and H-5 are also in a *cis* relationship. The four asymmetric carbons of **4** are with substitutes *trans* relative to each other like compound **3**.

Experimental

Apparatus IR spectra were obtained on a Nicolet Avatar 320 IR spectrometer. UV spectra were measured on a Hitachi U-3200 spectrophotometer in MeOH. Optical rotations were measured on a JASCO DIP-370 polarimeter. ^{1}H-, ^{13}C-, and 2D-NMR spectra were measured with a Varian Inova-500 spectrometer with deuterated solvents as an internal standard. ESI-MS and HR-FAB-MS were recorded on Finnigan LCQ and Finnigan/Thermo Quest MAT spectrometers, respectively. HPLC analysis was performed using a Shimadzu LC-8A or LC-10AT vp pump and SPD-10A vp UV–Vis detector. The X-ray data were acquired on a Nonius, Kappa CCD Single Crystal XRD.

Plant Material The roots of *C. tangshen* were purchased from a drugstore in Taipei, Taiwan, and verified by Mr. Ching-Song Shyu, director of Chia Huei Co., Inc., Taipei, Taiwan, based on comparisons of the external appearance of the roots with the figures drawn in the literature.[9)] A voucher specimen is deposited in the National Research Institute of Chinese Medicine, Taipei, Taiwan.

Extraction and Isolation The roots of *C. tangshen* (8.5 kg) were crushed and extracted with ethanol (60 l×3) under reflux. The ethanolic extract was evaporated to dryness and then partitioned between *n*-hexane and water to give the *n*-hexane extract. The aqueous layer was further extracted with *n*-BuOH (1.5 l×3) to give the *n*-BuOH extract. The *n*-BuOH extract (240 g) was subjected to column chromatography on a Sephadex LH-20 (10×120 cm, GE Healthcare Biosciences AB, Sweden), with a gradient of MeOH in H_2O, and 5 fractions (fr. 1—5) were collected. Fr. 2 (40 g) was rechromatographed on a Dianion HP-20 column (Nippon Rensui, Tokyo, Japan) using H_2O, 20% MeOH/H_2O, and MeOH to give three main fractions. Fr. 2-2 (3.7 g) was repeatedly chromatographed on a Sephadex LH-20 column (MeOH) to give **5** (47.9 mg) and **11** (33.9 mg). Fr. 2-3 (6.6 g) was purified with silica gel (EtOAc/butanone/formic acid//H_2O=15 : 3 : 1 : 1) and semipreparative HPLC [column: Cosmosil 5C18-AR-II, 20×250 mm, 5 μm (Nacalai Tesque, Kyoto, Japan); solvent, 15% ACN/H_2O; flow rate, 17 ml/min] to give **3** (392.9 mg) and **4** (39.1 mg). Fr. 3 (1.3 g) was chromatographed on a Sephadex LH-20 column (MeOH) and on a silica gel column (12—26 μm, Eurochrom, Knauer) with 2% MeOH/$CHCl_3$ eluted repeatedly to give **6** (5.5 mg), **7** (6.8 mg), **10** (34.1 mg), and subfraction 3-4. Subfraction 3-4 yielded **1** (14.8 mg) and **2** (9.4 mg) after being purified on a semipreparative HPLC [column: Develosil C30-UG-5, 10×250 mm, 5 μm (Nomura chemical, Kyoto, Japan); solvent; 28% ACN/H_2O; flow rate, 2 ml/min]. **8** (6.2 mg) and **9** (2.3 mg) were purified from Fr. 5 on a silica gel column (*n*-hexane/EtOAc) and Sephadex LH-20 column (MeOH).

Codonoside A (**1**): Syrup; UV (MeOH) λ_{max} (log ε): 221 (4.64), 274 (4.38), 308 (4.30) nm; $[\alpha]_D^{24}$ −13.3° (c=0.23, MeOH); IR (neat) ν_{max} 3410, 1733, 1717, 1700, 1558, 1540, 1506 cm^{-1}; ^{1}H-NMR (CD_3OD, 500 MHz); ^{13}C-NMR (CD_3OD, 125 MHz): see Table 1; ESI-MS *m/z*: 847 $[M+Na]^+$; HR-FAB-MS *m/z*: 847.2642 $[M+Na]^+$ (Calcd for $C_{38}H_{48}O_{20}Na$, 847.2636).

Codonoside B (**2**): Syrup; UV (MeOH) λ_{max} (log ε): 221 (4.40), 274

(4.14), 308 (4.05) nm; $[\alpha]_D^{24}$ −26.4° (c=0.23, MeOH); IR (neat) ν_{max} 3411, 1730, 1714, 1700, 1605, 1584, 1514 cm^{-1}; ^{1}H-NMR (CD_3OD, 500 MHz); ^{13}C-NMR (CD_3OD, 125 MHz): see Table 1; ESI-MS m/z: 847 $[M+Na]^+$; HR-FAB-MS m/z: 847.2636 $[M+Na]^+$ (Calcd for $C_{38}H_{48}O_{20}Na$, 847.2636).

Codonopyrrolidium A (**3**): UV (MeOH) λ_{max} (log ε): 231 (4.05) nm; $[\alpha]_D^{24}$ −7.0° (c=0.57, MeOH); IR (KBr) ν_{max} 3268, 1711, 1611, 1518, 1367, 1357,1142, 1078 cm^{-1}; ^{1}H-NMR (CD_3OD, 500 MHz); ^{13}C-NMR (CD_3OD, 125 MHz): see Table 2; ESI-MS m/z: 350 $[M]^+$; HR-FAB-MS m/z: 350.1964 $[M]^+$ (Calcd for $C_{19}H_{28}O_5N$, 350.1967).

X-ray structure analysis of **3**: A suitable colorless crystal (0.25×0.20×0.15 mm^3), grown by slow evaporation of MeOH solution, was mounted on a Nonius CCD diffractometer equipped with Mo radiation (λ=0.71073 Å). Crystal data: $C_{19}H_{29}ClNO_5$, M_r=386.88 g/mol, monoclinic, $P2_1$, a=7.5086(2), b=12.2451(2), c=11.5924(2) Å, β=108.8470(10)°, V=1008.70(4) $Å^3$, Z=2, D_{calc}=1.274 mg/m^3, F(000)=414. A total of 7310 reflections were collected (4160 unique, R_{int}=0.0247) in the range 1.86°<θ<27.46°. The structure was resolved using direct methods and refined using the full-matrix least-squares method on F^2 values. The nonhydrogen atoms were refined anisotropically. All hydrogen atoms were fixed at calculated positions. The final indices were R_1=0.0463, wR_2=0.1222, with goodness-of-fit=1.098.

Codonopyrrolidium B (**4**): UV (MeOH) λ_{max} (log ε): 233 (3.82) nm; $[\alpha]_D^{24}$ 16.7° (c=0.3, MeOH); IR (KBr) ν_{max} 3411, 1597, 1518, 1383, 1352, 1260, 1184 cm^{-1}; ^{1}H-NMR (CD_3OD, 500 MHz); ^{13}C-NMR (CD_3OD, 125 MHz): see Table 2; ESI-MS m/z: 268 $[M]^+$; HR-FAB-MS m/z: 268.1552 $[M]^+$ (Calcd for $C_{14}H_{22}O_4N$, 268.1549).

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