Six Novel 5α-Adynerin-Type Cardenolides from *Parepigynum funingense*

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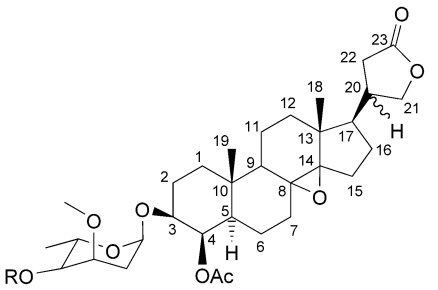
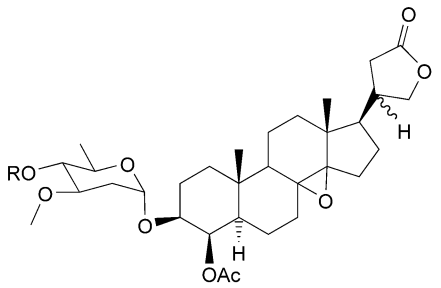
Six novel 5α-adynerin-type cardenolides, funingenosides K (**1**), L (**2**), M (**3**), N (**4**), O (**5**), and P (**6**), have been isolated from the roots of *Parepigynum funingense*. Their structures were elucidated on the basis of 1D- and 2D-NMR techniques.

Introduction. – *Parepigynum funingense* Tsiang et P. T. Li (Apocynaceae), a member of a monotypic genus, is distributed widely in Yunnan Province, China [1]. In a previous paper, we reported the structures of four steroidal glycosides [2]. Our continuing phytochemical investigation of this plant has now led to the isolation of six novel 5α-adynerin-type dihydrocardenolides, namely, funingenosides K–P (**1**–**6**).

Results and Discussion. – The dried roots (15 kg) of *P. funingense* were extracted with 75% aqueous EtOH. The EtOH extract was successively purified chromatographically on *HPD-100*, silica-gel, and *RP-18* columns to afford funingenosides K–P (**1**–**6**).

Funingenoside K (**1**) was obtained as white powder, and analyzed for $C_{44}H_{68}O_{19}$ by negative-ion HR-FAB-MS. Its IR spectrum exhibited absorption bands for OH (3441) and C=O groups (1783, 1737 cm^{-1}). The UV spectrum showed no significant absorptions. The ^{1}H- and ^{13}C-NMR spectra (see *Tables 1* and *2*) showed signals of an Ac group (δ_C 21.1 (*q*), 170.9 (*s*)), one C=O group (δ_C 177.6 (*s*)/177.0 (*s*)), and two angular Me groups [δ_C 15.9 (*q*)/15.8 (*q*), 15.2 (*q*)]. Also observed were signals of three anomeric C-atoms and their corresponding H-atoms (δ_C 94.9 (*d*), 101.7 (*d*), 105.5 (*d*); δ_H 5.16 (br. *s*), 4.96 (*d*, $J = 7.5$), 5.18 (*d*, $J = 7.7$)). In the negative FAB mass spectrum, significant peaks occurred at *m/z* 899 $[M-H]^-$, 737 $[M-H-162]^-$, 575 $[M-H-162-162]^-$, and 431 $[M-H-162-162-144]^-$, indicating the elimination of three hexose moieties. Comparison of the ^{1}H- and ^{13}C-NMR data of the aglycon with those of 5α-adynerin, 3β-(β-D-diginopyranosyloxy)-8,14β-epoxy-5α-card-20(22)-enolide [3] showed that the two aglycons were very similar. Compound **1** had one additional OH group, and the absence of the olefinic group, as well as the resonance of C(23) at δ_C 177.6/177.0, suggested that the C=O group of the five-membered lactone ring was not conjugated in **1**. This observation was confirmed by the IR absorption of the C=O group at 1783 cm^{-1} and the absence of any significant UV absorption. The downfield-shifted resonance of H–C(4) [δ_H 5.43 (br. *s*)] and correlations between both H–C(4) and H–C(3) [δ_H 3.76 (*m*)] and H–C(4) and H–C(5) [δ_H 1.29 (*m*)] in the ^{1}H,^{1}H-

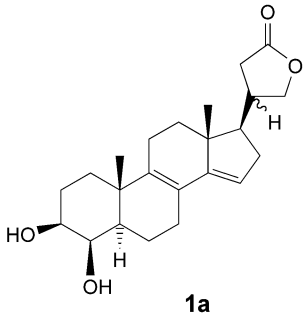




1 R = β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl **4**

2 R = β-D-glucopyranosyl **5**

3 R = β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl **6**



1a

COSY spectrum suggested that the additional OH group was attached at C(4). The 5α configuration of **1** was assigned based on the upfield-shifted Me(19) group at δ_C 15.2 [4]. Also, H–C(3) was determined to be α-oriented due to a ROESY correlation between H_α–C(5) and H–C(3), which indicated a *cis* relationship. The configuration at C(4) could be determined by the signal of H–C(4). For a chair-like conformation of the A-ring, when the substituent at C(4) is β-oriented, H_α–C(4) appears as a broad *s*, which was observed indeed. The β-orientation of AcO–C(4) was further supported by the absence of a correlation between H–C(4) and Me(19) in the corresponding ROESY spectrum. The configuration of H–C(17) was determined to be α based on the ROESY correlation between H_α–C(12) (δ_H 1.43) and H–C(17) (δ_H 1.33), which indicated their *cis* relationship. It is interesting to note that C(20), C(21), C(22), C(23), C(16), C(12), C(13), C(14), and Me(18) exhibited double peaks in the ^{13}C-NMR spectrum, indicating that **1** is a C(20)-epimeric mixture. The ratio of the two epimers is 1:1 in solvents such as C_5D_5N, MeOD, or D_2O according to the NMR spectra.

Acid hydrolysis of **1** with 1N HCl furnished two monosaccharides and the aglycon **1a**. The EI mass spectrum of **1a** showed the M^+ ion at *m*/*z* 372, compatible with the molecular formula $C_{23}H_{32}O_4$. Interestingly, the resonances of the two quaternary C-atoms C(8) and C(14), as well as the Ac group in the aglycon moiety, were absent, and

Table 1. *^{13}C-NMR Data* (100 MHz) *of Compounds* **1**–**6** (in C_5D_5N), *and of* **1a** (in $CDCl_3$). δ in ppm.

	1	**1a**	**2**	**3**	**4**	**5**	**6**
C(1)	37.0	36.3	37.0	37.0	37.0	36.9	37.1
C(2)	25.1	27.3	25.1	25.3	24.8	24.8	24.9
C(3)	75.3	72.5	75.4	75.4	73.9	73.9	74.1
C(4)	72.4	75.4	72.4	72.5	72.0	72.0	72.0
C(5)	47.1	45.2	47.2	47.2	47.0	47.2	47.1
C(6)	24.0	23.6	24.0	24.0	24.0	23.9	24.1
C(7)	32.3	35.6	32.3	32.4	32.4	32.3	32.4
C(8)	64.3	122.7	64.3	64.4	64.3	64.2	64.5
C(9)	51.1	142.9/143.0	51.1	51.1	51.1	51.1	51.2
C(10)	37.5	37.3	37.5	37.5	37.5	37.5	37.6
C(11)	16.2	21.5	16.2	16.3	16.3	16.2	16.4
C(12)	37.5/37.3	36.3/36.2	37.5/37.3	37.5/37.3	37.5/37.3	37.5/37.3	37.6/37.4
C(13)	41.2/40.9	45.2	41.2/41.0	41.2/41.0	41.2/40.9	41.2/40.9	41.3/41.0
C(14)	70.9/70.8	150.8	70.9/70.8	71.0/70.9	71.0/70.9	70.9/70.7	71.0/70.9
C(15)	27.6	116.9/116.7	27.7	27.7	27.7	27.6	27.8
C(16)	27.1/26.0	34.3	27.1/26.0	27.1/26.0	27.1/25.9	27.1/25.9	27.2/26.1
C(17)	54.7	55.2	54.7	54.7	54.7	54.7	54.8
Me(18)	15.9/15.8	16.7	16.0/15.8	16.0/15.9	16.0/15.9	15.9/15.8	16.1/16.0
Me(19)	15.2	22.2	15.2	15.3	15.2	15.1	15.3
C(20)	38.1/37.7	37.8/37.4	38.1/37.7	38.2/37.7	38.1/37.6	38.1/37.6	38.2/37.8
C(21)	72.9/72.5	72.9/72.5	72.9/72.6	73.0/72.6	73.0/72.6	72.9/72.5	73.0172.7
C(22)	34.2/34.1	34.5/34.3	34.2/34.1	34.3/34.2	34.2/34.1	34.2/34.1	34.4/34.3
C(23)	177.6/177.0	177.6/177.0	177.6/177.0	177.7/177.2	177.7/177.1	177.4/176.8	177.9/177.4
Ac	170.9		170.9	171.0	171.0	170.8	171.2
	21.1		21.1	21.2	21.1	21.0	21.2
Cymarosyl					Oleandrosyl		
C(1′)	94.9		94.9	95.0	94.9	94.9	95.1
C(2′)	31.8		31.7	31.8	35.1	35.1	35.2
C(3′)	73.2		73.3	73.3	79.2	79.0	79.3
C(4′)	78.4		78.4	78.4	82.0	82.0	82.2
C(5′)	65.1		65.01	65.2	68.1	67.9	68.2
C(6′)	18.6		18.5	18.7	19.0	18.8	19.1
OMe(3′)	56.4		56.4	56.4	56.9	56.8	57.0
Glucosyl							
C(1″)	101.7		101.9	101.8	104.9	105.1	105.0
C(2″)	75.3		75.5	75.2	75.8	76.0	75.2
C(3″)	78.5		78.6	78.5	78.5	78.4	78.4
C(4″)	71.7		71.8	71.7	71.7	71.7	71.7
C(5″)	77.8		78.6	78.4	77.3	78.4	78.3
C(6″)	70.3		63.0	70.1	70.7	63.1	70.1
Glucosyl							
C(1‴)	105.5			105.5	105.6	105.6	105.4
C(2‴)	75.3			75.1	75.3	75.3	75.1
C(3‴)	78.3			78.4	78.4		78.3
C(4‴)	71.7			71.5	71.8		71.8
C(5‴)	78.5			77.1	78.5		77.2
C(6‴)	62.8			70.3	62.9		70.6
Glucosyl							
C(1⁗)				105.5			105.5
C(2⁗)				75.4			75.8
C(3⁗)				78.5			78.3
C(4⁗)				71.7			71.5
C(5⁗)				77.7			77.1
C(6⁗)				62.8			62.8

Table 2. *^{1}H-NMR Data* (500 MHz) *of Compounds* **1**–**6** (in C_5D_5N), *and of* **1a** (in $CDCl_3$). δ in ppm, J in Hz.

	1	**1a**	**2**	**3**	**4**	**5**	**6**
H_α–C(1)	1.67 (*m*)	1.68 (*m*)	1.67 (*m*)	1.67 (*m*)	1.72 (*m*)	1.70 (*m*)	1.73 (*m*)
H_β–C(2)	1.01 (*m*)	1.05 (*m*)	1.02 (*m*)	1.01 (*m*)	1.06 (*m*)	1.04 (*m*)	1.06 (*m*)
H_α–C(2)	1.38[a])	1.41[a])	1.38[a])	1.39[a])	1.35[a])	1.34[a])	1.36[a])
H_β–C(2)	2.00 (*m*)	2.01 (*m*)	2.01 (*m*)	2.00 (*m*)	1.97 (*m*)	1.97 (*m*)	1.98 (*m*)
H–C(3)	3.76 (*m*)	3.82 (*m*)	3.77 (*m*)	3.77 (*m*)	3.78 (*m*)	3.78 (*m*)	3.78 (*m*)
H–C(4)	5.43 (br. *s*)	4.11 (br. *s*)	5.43 (br. *s*)	5.44 (br. *s*)	5.44 (br. *s*)	5.44 (br. *s*)	5.44 (br. *s*)
H–C(5)	1.29 (*m*)	1.21 (*m*)	1.29 (*m*)	1.29 (*m*)	1.31 (*m*)	1.30 (*m*)	1.31 (*m*)
H_α–C(6)	1.48[a])		1.47[a])	1.48[a])	1.46[a])	1.45[a])	1.47[a])
H_β–C(6)	1.82 (*m*)		1.82 (*m*)	1.82 (*m*)	1.82 (*m*)	1.82 (*m*)	1.84 (*m*)
H_α–C(7)	1.79 (*m*)		1.79 (*m*)	1.80 (*m*)	1.78 (*m*)	1.75 (*m*)	1.78 (*m*)
H_β–C(7)	1.35 (*m*)		1.36 (*m*)	1.36 (*m*)	1.35 (*m*)	1.34 (*m*)	1.35 (*m*)
H–C(9)	1.22 (*m*)		1.22 (*m*)	1.22 (*m*)	1.24 (*m*)	1.24 (*m*)	1.24 (*m*)
H_α–C(11)	0.98 (*m*)		0.97 (*m*)	0.98 (*m*)	0.98 (*m*)	0.98 (*m*)	0.99 (*m*)
H_β–C(11)	1.32 (*m*)		1.32 (*m*)	1.32 (*m*)	1.33 (*m*)	1.31 (*m*)	1.34 (*m*)
H_α–C(12)	0.93[a])		0.93[a])	0.93[a])	0.92[a])	0.92[a])	0.93[a])
H_β–C(12)	1.43 (*m*)		1.43 (*m*)	1.43 (*m*)	1.43 (*m*)	1.43 (*m*)	1.44 (*m*)
H_α–C(15)	1.80 (*m*)	5.38 (*m*)	1.81 (*m*)	1.80 (*m*)	1.79 (*m*)	1.77 (*m*)	1.80 (*m*)
H_β–C(15)	1.42[a])		1.42[a])	1.42[a])	1.42[a])	1.41[a])	1.41[a])
H_α–C(16)	1.58 (*m*)		1.59 (*m*)	1.58 (*m*)	1.57 (*m*)	1.57 (*m*)	1.58 (*m*)
H_β–C(16)	1.84 (*m*)		1.85 (*m*)	1.85 (*m*)	1.86 (*m*)	1.85 (*m*)	1.87 (*m*)
H–C(17)	1.33 (*m*)	1.73 (*m*)	1.33 (*m*)	1.33 (*m*)	1.38 (*m*)	1.38 (*m*)	1.38 (*m*)
Me(18)	0.89 (*s*)	0.80 (*s*)	0.90 (*s*)	0.90 (*s*)	0.90 (*s*)	0.88 (*s*)	0.91 (*s*)
Me(19)	1.22 (*s*)	1.48 (*s*)	1.22 (*s*)	1.23 (*s*)	1.23 (*s*)	1.21 (*s*)	1.23 (*s*)
H–C(20)	2.42/2.41 (*m*)	2.51/2.53 (*m*)	2.42/2.41 (*m*)	2.43/2.42 (*m*)	2.42/2.41 (*m*)	2.42/2.41 (*m*)	2.43/2.42 (*m*)
H_α–C(21)	3.88[a])	3.85[a])	3.89[a])	3.89[a])	3.89[a])	3.87[a])	3.89[a])
H_β–C(21)	4.43 (*m*)	4.45 (*m*)	4.43 (*m*)	4.43 (*m*)	4.44 (*m*)	4.42 (*m*)	4.44 (*m*)
H_α–C(22)	2.53/2.67 (*m*)	2.55/2.69 (*m*)	2.53/2.66 (*m*)	2.54/2.68 (*m*)	2.53/2.65 (*m*)	2.53/2.65 (*m*)	2.54/2.65 (*m*)
H_β–C(22)	2.30 (*m*)	2.30 (*m*)	2.30 (*m*)	2.31 (*m*)	2.31 (*m*)	2.30 (*m*)	2.31 (*m*)
Ac	2.07 (*s*)		2.07 (*s*)	2.07 (*s*)	2.05 (*s*)	2.04 (*s*)	2.06 (*s*)
H–C(1′)	5.16 (br. *s*)		5.16 (br. *s*)	5.14 (br. *s*)	5.33 (br. *s*)	5.32 (br. *s*)	5.33 (br. *s*)
H_α–C(2′)	1.87 (*m*)		1.82 (*m*)	1.85 (*m*)	2.28 (*m*)	2.29 (*m*)	2.30 (*m*)

Table 2 (cont.)

	1	**1a**	**2**	**3**	**4**	**5**	**6**
H_β–C(2′)	2.32 (*m*)		2.30 (*m*)	2.32 (*m*)	1.61 (*m*)	1.62 (*m*)	1.62 (*m*)
H–C(3′)	3.90[a])		3.91[a])	3.94[a])	3.93[a])	3.92[a])	3.92[a])
H–C(4′)	4.09 (*m*)		4.08 (*m*)	4.08 (*m*)	3.86 (*t*, *J* = 9.0)	3.79 (*t*, *J* = 9.0)	3.85 (*m*)
H–C(5′)	4.65 (*m*)		4.61 (*m*)	4.65 (*m*)	4.05 (*m*)	4.03 (*m*)	4.05 (*m*)
H–C(6′)	1.55 (*d*, *J* = 5.9)		1.48 (*d*, *J* = 5.5)	1.53 (*d*, *J* = 6.1)	1.72 (*d*, *J* = 6.0)	1.69 (*d*, *J* = 6.2)	1.71 (*d*, *J* = 5.7)
MeO(3′)	3.40 (*s*)		3.40 (*s*)	3.41 (*s*)	3.37 (*s*)	3.35 (*s*)	3.37 (*s*)
H–C(1″)	4.96 (*d*, *J* = 7.5)		5.01 (*d*, *J* = 7.5)	4.95 (*d*, *J* = 7.9)	5.22 (*d*, *J* = 7.7)	5.28 (*d*, *J* = 7.7)	5.17 (*d*, *J* = 7.5)
H–C(2″)	3.92[a])		3.94[a])	3.92[a])	3.93[a])	3.95[a])	3.92[a])
H–C(3″)	4.23[a])		4.24[a])	4.19[a])	4.22[a])	4.22[a])	4.21[a])
H–C(4″)	4.04[a])		4.09[a])	4.07[a])	4.14[a])	4.16[a])	4.14[a])
H–C(5″)	3.90[a])		3.92[a])	3.92[a])	3.92[a])	3.92[a])	3.93[a])
H_α–C(6″)	4.35[a])		4.34 (*dd*, *J* = 12.0, 5)	4.30	4.26 (*dd*, *J* = 11.7, 5)	4.34 (*dd*, *J* = 11.8, 5)	4.27
H_β–C(6″)	4.82 (*dd*, *J* = 12.0, 2)		4.56 (*dd*, *J* = 12.0, 2)	4.77 (*dd*, *J* = 11.5, 2)	4.78 (*dd*, *J* = 11.7, 2)	4.53 (*dd*, *J* = 11.8, 2)	4.72[a])
H–C(1‴)	5.18 (*d*, *J* = 7.7)			5.02 (*d*, *J* = 7.7)	5.10 (*d*, *J* = 7.7)		4.98 (*d*, *J* = 7.3)
H–C(2‴)	4.03[a])			4.01[a])	4.01[a])		4.02[a])
H–C(3‴)	4.25[a])			4.23[a])	4.21[a])		4.20[a])
H–C(4‴)	4.22[a])			4.21[a])	4.30[a])		4.28[a])
H–C(5‴)	3.91[a])			3.90[a])	3.91[a])		3.91[a])
H_α–C(6‴)	4.33			4.32	4.32 (*dd*, *J* = 11.8, 5)		4.29
H_β–C(6‴)	4.52 (*dd*, *J* = 12.0, 2)			4.81 (*dd*, *J* = 11.2, 2)	4.47 (*dd*, *J* = 11.8, 2)		4.73[a])
H–C(1⁗)				5.07 (*d*, *J* = 7.9)			4.99 (*d*, *J* = 7.0)
H–C(2⁗)				4.02[a])			4.03[a])
H–C(3⁗)				4.24[a])			4.21[a])
H–C(4⁗)				4.20a)			4.27[a])
H–C(5⁗)				3.90[a])			3.93[a])
H_α–C(6⁗)				4.34[a])			4.31[a])
H_β–C(6⁗)				4.46 (*dd*, *J* = 12.0, 2)			4.46 (*dd*, *J* = 11.5, 2)

[a]) Overlapping with other signals.

there occurred four olefinic C-atoms instead. In addition, **1a** exhibited an absorption band at 244 nm in the UV spectrum, representing the $\Delta^{8,14}$-diene compound. Since adynerin, one of the major cardenolides isolated from the leaves of *Nerium odorum*, is known to form this type of diene on acid hydrolysis [3], the aglycone of **1** was considered to experience the same chemical change during acid hydrolysis. The absolute configuration at the remaining chiral centers of **1a** was unaffected, including the ratio of the C(20)-epimers. Thus, **1a** was determined to be the new compound, (17*R*)-3β,4β-dihydroxy-5α-card-20(22)-dihydroenolide.

The two monosaccharides of **1** were found to be D-glucose and L-cymarose based on their optical rotations and TLC comparison with authentic samples. The ^{13}C-NMR spectral data and optical rotation value of L-cymarose were consistent with those reported [5]. The carbohydrate ^{1}H- and ^{13}C-NMR signals of **1** were assigned by ^{1}H,^{1}H-COSY, HMQC, and HMQC-TOCSY experiments. In the HMBC spectrum, long-range couplings were observed for H−C(1′) of the cymarosyl unit to C(3) of the aglycon, H−C(1″) of the glucosyl unit to C(4′) of the cymarosyl unit, and H−C(1‴) of the terminal glucosyl unit to C(6″) of the glucosyl unit. The anomeric configurations of the D-glucose and L-cymarose moieties were determined to be β and α, respectively, from the coupling constants of the anomeric H-atoms. On the basis of the above evidence, the structure of **1** was elucidated as (17*R*)-4β-acetoxy-8,14β-epoxy-3β-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-α-L-cymaropyranosyloxy]-5α-card-20(22)-dihydroenolide, which was named *funingenoside K*. This is the first report on the isolation of a 5α-adynerin-type dihydrocardenolide.

Funingenoside L (**2**) and M (**3**) were assigned the molecular formulae $C_{38}H_{58}O_{14}$ and $C_{50}H_{78}O_{24}$, respectively, by negative-ion HR-FAB-MS. Comparison of the ^{1}H- and ^{13}C-NMR spectral data of **2** and **3** with those of **1** showed that the three structures were very similar, except that there were only two sugar units in **2**, and there was an additional sugar unit in **3**. This was confirmed by the C(6″) signal of the glucosyl unit of **2**, which was shifted upfield to δ_C 63.0. The $[M-H]^-$ ion at 1061, *i.e.*, 162 mass units higher than that of **1**, and the sugar ^{1}H- and ^{13}C-NMR signals indicated that **3** had one additional glucose unit. In the HMBC spectrum of **3**, long-range couplings were observed between H−C(1⁗) of the terminal glucosyl unit to C(6‴) of the glucosyl unit, H−C(1‴) of the glucosyl unit to C(6″) of the glucosyl unit, and H−C(1″) of the glucosyl unit to C(4′) of the cymarosyl unit. The configurations at the chiral centers in both **2** and **3** were identical to those of **1**. The two compounds are also C(20)-epimeric mixtures according to the NMR spectra. Based on the above results, the structures of **2** and **3** could be deduced as (17*R*)-4β-acetoxy-8,14β-epoxy-3β-[β-D-glucopyranosyl-(1 → 4)-α-L-cymaropyranosyloxy]-5α-card-20(22)-dihydroenolide and (17*R*)-4β-acetoxy-8,14β-epoxy-3β-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-α-L-cymaropyranosyloxy]-5α-card-20(22)-dihydroenolide, respectively.

A molecular formula of $C_{44}H_{68}O_{19}$ was deduced for funingenoside N (**4**) by negative-ion HR-FAB-MS. The ^{1}H- and ^{13}C-NMR spectral data of **4** were almost identical to those of **1**, except that there was a different inner deoxysugar in compound **4**. Acid hydrolysis of **1** with 1N HCl furnished two monosaccharides. The different deoxycarbohydrate was determined to be D-oleandrose, identified by its optical rotation and TLC comparison with an authentic sample. Its ^{13}C-NMR spectral data and optical rotation value were consistent with those reported [6]. The configuration at the

anomeric center of D-oleandrose was determined to be α from the coupling constant of the corresponding H-atom. Hence, the structure of **4** was elucidated as (17*R*)-4β-acetoxy-3β-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-α-D-oleandropyranosyloxy]-8,14β-epoxy-5α-card-20(22)-dihydroenolide, which was named *funingenoside N*. It also exists in solution as the C(20) epimeric mixture.

Funingenoside O (**5**) and P (**6**) were assigned the molecular formulae $C_{38}H_{58}O_{14}$ and $C_{50}H_{78}O_{24}$, respectively, by negative-ion HR-FAB-MS. A careful comparison of the ^{1}H- and ^{13}C-NMR spectra of **4** and **5** with those of **2** and **3**, respectively, showed that the four compounds were very similar. The only difference between **5** and **2**, and between **6** and **3** was the inner deoxysugar, which, for **5** and **6**, was α-D-oleandrose. The sugar linkages of these compounds and the configurations at the chiral centers are identical. Similarly, both **5** and **6** are C(20)-epimeric mixtures. Thus, the structures of **5** and **6** were established as (17*R*)-4β-acetoxy-3β-[β-D-glucopyranosyl-(1 → 4)-α-D-oleandropyranosyloxy]-8,14β-epoxy-5α-card-20(22)-dihydroenolide and (17*R*)-4β-acetoxy-3β-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-α-D-oleandropyranosyloxy]-8,14β-epoxy-5α-card-20(22)-dihydroenolide, respectively.

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Experimental Part

General. Optical rotations: *Horiba SEAP-300* spectropolarimeter. UV Spectra: *UV-210A* spectrophotometer; λ_{max} in nm. IR Spectra: KBr pellets; *Bio-Rad FTS-135* infrared spectrophotometer; in cm^{-1}. NMR Spectra: 1D, *Bruker AM-400* spectrometer; 2D, *Bruker DRX*-500 spectrometer; δ in ppm rel. to $SiMe_4$ (=0 ppm), *J* in Hz. MS: *VG Autospec-3000* spectrometer.

Plant Material. The roots of *Parepigynum funingense* were collected from Jinchang, Malipo County, Yunnan Province, China, in April 2000. The plant was identified by Prof. *X. Gong*, Kunming Insitiute of Botany, Chinese Academy of Sciences, Kunming, Yunnan, China, where a voucher specimen (No. 0774313) is deposited.

Extraction and Isolation. The dried roots (15 kg) of *P. funingense* were extracted with 75% aq. EtOH under reflux (3 × 3 l). After removal of the solvent *in vacuo*, the aq. soln. was passed through a *HPD-100* column, and the absorbed materials were successively eluted with 65% aq. MeOH and pure MeOH. The aq.-MeOH eluate was concentrated *in vacuo* to give a residue (138 g), which was chromatographed on a silica-gel (200–300 mesh) column with mixtures of $CHCl_3$/MeOH 9:1 → 2:1 to afford eight fractions (Fr.). Each fraction was further subjected to repeated silica-gel column chromatography (CC) with mixtures of Et_2O/MeOH/H_2O 8:1:0.1 → 4:1:0.1 as eluents, and passed finally over an *RP-18* column with MeOH/H_2O 4:6. *Fr. 5* (12.1 g) yielded pure **1** (526 mg) and **4** (439 mg); *Fr. 2* (9.0 g) gave pure **2** (45 mg) and **5** (120 mg); *Fr. 8* (8.2 g) afforded pure **3** (40 mg) and **6** (35 mg).

Acid Hydrolysis. Compound **1** (100 mg) was hydrolyzed with 40 ml 2N HCl/1,4-dioxane 1:1 for 2 h. The mixture was extracted with AcOEt (3 × 50 ml) to afford **1a** (18 mg). Evaporation of the aq. layer of the hydrolysate gave a residue (49 mg) of monosaccharides, which were separated by CC (SiO_2; 200–300 mesh, acetone/petroleum ether 2:3 → 3:1) to afford D-glucose (14.5 mg; $[\alpha]_D^{25} = +52.9$ ($c = 0.40$, H_2O)) and L-cymarose (7.5 mg; $[\alpha]_D^{25} = -50.6$ ($c = 0.28$, H_2O)). Compound **4** (100 mg) was subjected to acid hydrolysis as described for **1**, and afford **1a**, D-glucose (16.0 mg), and D-oleandrose (5.8 mg, $[\alpha]_D^{25} = -11.2$ ($c = 0.22$, H_2O)).

Funingenoside K (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-α-L-cymaropyranosyloxy]-5α-card-20(22)-dihydroenolide*; **1**). White powder. $[\alpha]_D^{26} = -72.34$ ($c = 0.65$, MeOH). IR (KBr): 3441, 2940, 1783, 1737, 1454, 1371, 1246, 1053. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 899 (100), 737 (7), 575 (3), 431, (1), 159 (16), 119 (20). HR-FAB-MS (neg.): 899.4261 ([*M* − H]$^-$, $C_{44}H_{67}O_{19}$; calc.: 899.4276).

8,9,14,15-Didehydro-5α-cardenolide (**1a**). Yellow solid. M.p. 230–234°. $[\alpha]_D^{23} = -44.6$ ($c = 0.36$, MeOH). UV (MeOH): 244. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. EI-MS: 372 (100), 354 (20), 264 (35), 145 (42), 105 (15).

Funingenoside L (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β*-D*-glucopyranosyl-(1 → 4)-α*-L*-cymaropyranosyl-oxy]-5α-card-20(22)-dihydroenolide*; **2**). White powder. $[\alpha]_D^{25} = -56.4$ ($c = 0.55$, MeOH). IR (KBr): 3441, 2941, 1783, 1739, 1455, 1371, 1246, 1054. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 737 (100), 575 (3), 431 (1), 159 (12), 119 (16). HR-FAB-MS (neg.): 737.3705 ($[M-H]^-$, $C_{38}H_{57}O_{14}$; calc.: 737.3748).

Funingenoside M (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β*-D*-glucopyranosyl-(1 → 6)-β*-D*-glucopyranosyl-(1 → 6)-β*-D*-glucopyranosyl-(1 → 4)-α*-L*-cymaropyranosyloxy]-5α-card-20(22)-dihydroenolide*; **3**). White powder. $[\alpha]_D^{27} = -58.0$ ($c = 0.43$, MeOH). IR (KBr): 3440, 2940, 1783, 1737, 1454, 1370, 1245, 1052. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 1061 (100), 899 (5) 737 (3), 575 (1). HR-FAB-MS (neg.): 1061.3276 ($[M-H]^-$, $C_{50}H_{77}O_{24}$; calc.: 1061.3239).

Funingenoside N (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β*-D*-glucopyranosyl-(1 → 6)-β*-D*-glucopyranosyl-(1 → 4)-α*-D*-oleandropyranosyloxy]-5α-card-20(22)-dihydroenolide*; **4**): White powder. $[\alpha]_D^{27} = -52.3$ ($c = 0.34$, MeOH). IR (KBr): 3442, 2944, 1785, 1737, 1454, 1370, 1246, 1054. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 899 (100), 737 (5), 575 (3), 431, (1), 159 (16), 101 (45). HR-FAB-MS (neg.): 899.4235 ($[M-H]^-$, $C_{44}H_{67}O_{19}$; calc.: 899.4276).

Funingenoside O (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β*-D*-glucopyranosyl-(1 → 4)-α*-D*-oleandropyrano-syloxy]-5α-card-20(22)-dihydroenolide*; **5**). White powder. $[\alpha]_D^{25} = -76.7$ ($c = 0.55$, MeOH). IR (KBr): 3441, 2941, 1782, 1737, 1454, 1370, 1246, 1052. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 737 (100), 575 (4), 431 (1), 159 (12), 101 (16). HR-FAB-MS (neg.): 737.3779 ($[M-H]^-$, $C_{38}H_{57}O_{14}$; calc.: 737.3749).

Funingenoside P (=*(17*R*)-4β-Acetoxy-8,14β-epoxy-3β-[β*-D*-glucopyranosyl-(1 → 6)-β*-D*-glucopyranosyl-(1 → 6)-β*-D*-glucopyranosyl-(1 → 4)-α*-D*-oleandropyranosyloxy]-5α-card-20(22)-dihydroenolide*; **6**). White powder. $[\alpha]_D^{25} = -55.9$ ($c = 0.38$, MeOH). IR (KBr): 3442, 2940, 1784, 1737, 1455, 1371, 1246, 1054. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (neg.): 1061 (100), 899 (4) 737 (3), 575 (1). HR-FAB-MS (neg.): 1061.3654 ($[M-H]^-$, $C_{50}H_{77}O_{24}$; calc.: 1061.3639).

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