Hydrolytic analyses. Acid and alkaline hydrolyses, and H_2O_2 oxidation were performed by the usual methods [11].

Cy 3-Lat·TFA (**1**). IR ν_{max}^{KBr} cm^{-1}: 3372 (O–H), 1680, 1644, 1498, 1336, 1196, 1074, 724; UV-VIS $\lambda_{max}^{0.01\%\,HCl-MeOH}$ nm: 530 (shifted bathochromically with $AlCl_3$), 282, $E_{282}/E_{530}=0.57$, $E_{440}/E_{530}=0.16$; FAB-MS positive mode (in *m*-nitrobenzyl alcohol): *m/z* 581 $[M]^+$; ^1H NMR δ ppm (400 MHz; solvent DMSO-d_6: CF_3CO_2D, 9:1; standard TMS) 8.81 (1H, *s*, H-4 of Cy), 8.29 (1H, *dd*, $J=1.8$, 8.8 Hz, H-6′ of Cy), 7.99 (1H, *d*, $J=1.8$ Hz, H-2′ of Cy), 7.00 (1H, *d*, $J=8.8$ Hz, H-5′ of Cy), 6.89 (1H, *m*, H-8 of Cy), 6.69 (1H, *d*, $J=1.8$ Hz, H-6 of Cy), 5.50 (1H, *d*, $J=7.7$ Hz, H-1″ of Gal), 4.60 (1H, *d*, $J=7.7$ Hz, H-1‴ of Xyl), 4.12 (1H, *t*, $J=8.4$ Hz, H-2″ of Gal), 3.79–3.82 (2H, *m*, H-4″ and H-6″a of Gal), 3.76 (1H, *dd*, $J=2.9$, 9.5 Hz, H-3″ of Gal), 3.58 (1H, *dd*, $J=5.9$, 11.0 Hz, H-6″b of Gal), 3.47–3.52 (1H, *m*, H-5″ of Gal), 3.43 (1H, *dd*, $J=5.1$, 11.4 Hz, H-5‴a of Xyl), 3.16–3.22 (1H, *m*, H-4‴ of Xyl), 3.08 (1H, *t*, $J=9.0$ Hz, H-3‴ of Xyl), 2.94 (1H, *t*, $J=8.4$ Hz, H-2‴ of Xyl), 2.89 (1H, *t*, $J=10.8$ Hz, H-5‴b of Xyl).

Cy 3-Gal·TFA (**2**). Crude **1** (300 mg) was dissolved in 100 ml 2 M HCl and the soln heated at 80° for 10 min, diluted to 1 l with H_2O, and applied on Amberlite XAD-2000 column (2 ϕ × 20 cm). The column was washed with 1.5 l of H_2O and eluted with EAW. The pigment eluate was sepd by a prep. PC in 10% HCO_2H and the middle pigment band cut out and eluted with EAW and further purified by prep. ODS-HPLC using SS2 (A:B = 19:1) at 520 nm with flow rate 9 ml min^{-1}. From the main pigment fraction, TFA salts of **2** were obtained as red powders (7 mg): IR ν_{max}^{KBr} cm^{-1}: 3356 (O–H), 1680, 1646, 1494, 1336, 1198, 1068, 724; UV-VIS $\lambda_{max}^{0.01\%\,HCl-MeOH}$ nm: 530 (shifted bathochromically with $AlCl_3$), 282, $E_{282}/E_{530}=0.57$, $E_{440}/E_{530}=0.21$.

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A MORPHINANE ALKALOID FROM ROOTS OF *STEPHANIA CEPHARANTHA*

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Key Word Index—*Stephania cepharantha*; Menispermaceae; roots; morphinane promorphinane alkaloids; cephamorphinanine.

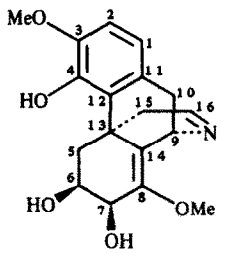
Abstract—From the roots of *Stephania cepharantha*, a new morphinane alkaloid, named cephamorphinanine, was isolated along with seven known alkaloids including one aporphine, two morphinanes, one promorphinane and three bisbenzylisoquinolines. The structure of cephamorphinanine was established from spectral analysis and chemical correlation.

INTRODUCTION

In previous papers [1, 2], it was reported that six bisbenzylisoquinoline and one hasubanane alkaloids were obtained from the root of *Stephania cepharantha* (Menispermaceae), native to Taiwan and cultivated in Japan. Our phytochemical investigation of the root of *S. cepharantha*, native to mainland China, under the Chinese name 'bei-yan-zi' commonly used as a folk medicinal herb, afforded a new morphinane alkaloid, named cephamorphinanine (**1**), and seven known alkaloids: isocorydine, sinococuline (**2**), FK-3000 (**3**), sinomenine, cycleanine, cepharanthine and berbamine.

RESULTS AND DISCUSSION

The alkaloidal fraction of the roots of *S. cepharantha* was subjected to column chromatography on silica gel to give isocorydine, FK-3000 (**3**), cycleanine, cepharanthine,



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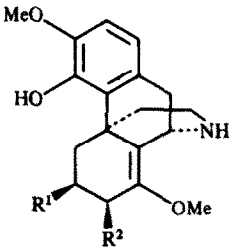

2 $R^1 = R^2 = OH$
3 $R^1 = R^2 = OAc$

berbamine, sinomenine, cephamorphinanine (**1**) and sinococuline (**2**). All these alkaloids, except **3** and **1**, were identified by the comparison of their mp, $[\alpha]_D$ (and CD), IR, UV, ^1H NMR (and ^{13}C NMR) with literature data [2–5].

The novel morphinane alkaloid, cephamorphinanine (**1**), was isolated as needles. The molecular formula $C_{18}H_{21}O_5N$ was determined by HR mass spectrometry. Its IR spectrum showed a middle strong absorption at 1625 cm^{-1}, and its mass spectrum exhibited an intense peak at *m/z* 289 $[M-(CH_2C{\equiv}N+H)]^+$ (58%), suggesting the presence of a $\succ C{=}N-$ group. The ^1H NMR spectrum was similar to that of sinococuline (**2**) (Table 1), except for the presence of a downfield olefinic proton signal at δ7.14 (1H, *dd*, J = 5.1, 2.2 Hz), instead of two methylene proton signals in **2**. The ^1H–^1H COSY spectrum of **1** revealed the olefinic proton correlative with the methylene protons (δ2.77 and 3.06) at C-15. Furthermore, the ^{13}C NMR (DEPT) (Table 2) spectrum of **1** displayed an additional downfield olefinic carbon signal at δ144.7 (*d*) as compared with **2**, and the ^1H–^{13}C COSY showed the olefinic carbon adjacent to the proton at δ7.14. On the basis of this evidence, there is a –CH=N– group in **1**, and the olefinic carbon of the group was assigned to C-16. The C-9 configuration was determined to be *S* from the positive effect at 234 nm ($\Delta\varepsilon$ + 2.5) in its CD spectrum [3]. The coupling constants (J = 13.4, 3.6, 3.6 Hz and J = 3.6 Hz) of the two hydroxymethine protons on C-6 and C-7 indicated that the hydroxyl groups on C-6 and C-7 both had β-configurations. Reduction of **1** with $NaBH_4$ gave a product which was identical ($[\alpha]_D$, IR, CD and ^1H NMR) to sinococuline (**2**). Another morphinane alkaloid isolated was subsequently found to be FK-3000 (**3**) [6]. We report here for the first time its detailed NMR (Tables 1 and 2) analysis and configuration. Its ^1H NMR spectrum displayed two acetomethine protons on C-6 and C-7 at δ5.18 (1H, *ddd*, J = 13.4, 3.8, 3.8 Hz) and δ5.87 (1H, *d*, J = 3.8 Hz), showing that the acetyl groups both also have β-configurations. All assignments of the substituents were confirmed by ^1H–^1H COSY and ^1H–^{13}C COSY spectra. Deacetylation of **3** with K_2CO_3 yielded a compound which was identical ($[\alpha]_D$, IR, UV, ^1H NMR and ^{13}C NMR) to **2**.

Table 2. ^{13}C NMR spectral data of compounds **1–3** (100 MHz, TMS)

C	**1** (CD_3OD)	**2** (CD_3OD)	**3** ($CDCl_3$)
1	121.33 *d*	119.73 *d*	118.53 *d*
2	112.30 *d*	111.11 *d*	109.27 *d*
3	149.42 *s*	147.92 *s*	145.51 *s*
4	148.73 *s*	146.08 *s*	143.89 *s*
5	36.51 *t*	37.51 *t*	37.00 *t*
6	68.68 *d*	69.12 *d*	68.53 *d*
7	66.07 *d*	67.23 *d*	65.28 *d*
8	146.52 *s*	146.80 *s*	140.01 *s*
9	65.19 *d*	47.33 *d*	45.89 *d*
10	34.81 *t*	37.33 *t*	33.48 *t*
11	130.68 *s*	131.90 *s*	130.89 *s*
12	126.71 *s*	124.57 *s*	128.50 *s*
13	37.76 *s*	40.34 *s*	39.01 *s*
14	115.28 *s*	130.69 *s*	129.26 *s*
15	39.60 *t*	38.65 *t*	39.11 *t*
16	144.66 *d*	41.59 *t*	40.58 *t*
MeO-3	57.50 *q*	57.81 *q*	57.59 *q*
MeO-8	56.50 *q*	57.24 *q*	56.34 *q*
			20.91 *q* (2 × AcO)

Table 1. ^1H NMR spectral data of compounds **1–3** (400 MHz, TMS)

H	**1** (CD_3OD)	**2** (CD_3OD)	**3** ($CDCl_3$)
1	6.55 (*d*, J = 8.3 Hz)	6.54 (*d*, J = 8.3 Hz)	6.61 (*d*, J = 8.3 Hz)
2	6.80 (*d*, J = 8.3 Hz)	6.75 (*d*, J = 8.3 Hz)	6.72 (*d*, J = 8.3 Hz)
5	3.16 (*dd*, J = 13.4, 3.6 Hz)	2.98 (*dd*, J = 13.3, 3.7 Hz)	2.84 (*dd*, J = 13.4, 3.8 Hz)
	2.01 (*dd*, J = 13.4, 13.4 Hz)	2.19 (*dd*, J = 13.3, 13.3 Hz)	2.34 (*dd*, J = 13.4, 13.4 Hz)
6	3.84 (*ddd*, J = 13.4, 3.6, 3.6 Hz)	3.84 (*ddd*, J = 13.3, 3.7, 3.5 Hz)	5.18 (*ddd*, J = 13.4, 3.8, 3.8 Hz)
7	4.36 (*d*, J = 3.6 Hz)	4.30 (*d*, J = 3.5 Hz)	5.87 (*d*, J = 3.8 Hz)
9	5.09 (*br s*)	4.36 (*d*, J = 6.0 Hz)	4.47 (*d*, J = 6.0 Hz)
10	3.40 (*dd*, J = 17.3, 2.1 Hz)	3.20 (*dd*, J = 17.8, 6.0 Hz)	3.22 (*dd*, J = 17.8, 6.0 Hz)
	3.17 (*dd*, J = 17.3, 2.1 Hz)	2.91 (*d*, J = 17.8 Hz)	3.03 (*d*, J = 17.8 Hz)
15	3.06 (*dd*, J = 19.3, 5.1 Hz)	2.04 (*dd*, J = 12.7, 3.4 Hz)	1.98 (*dd*, J = 12.8, 3.8 Hz)
	2.77 (*br d*, J = 19.3 Hz)	1.88 (*ddd*, J = 12.7, 12.5, 4.7 Hz)	1.90 (*ddd*, J = 13.4, 12.8, 4.8 Hz)
16	7.14 (*dd*, J = 5.1, 2.2 Hz)	2.73 (*dd*, J = 13.1, 4.7 Hz)	2.84 (*dd*, J = 13.1, 4.8 Hz)
		2.63 (*ddd*, J = 13.1, 12.5, 3.4 Hz)	2.71 (*ddd*, J = 13.4, 13.1, 3.8 Hz)
MeO-3	3.81	3.82	3.85 —
MeO-8	3.75	3.70	3.55 —
AcO-6	—	—	2.00 —
AcO-7	—	—	2.02 —

EXPERIMENTAL

Mps uncorr. ^{1}H NMR were recorded at 400 MHz, ^{13}C NMR at 100 MHz. CD were measured in MeOH soln.

Isolation. Dried roots of *S. cepharantha* Hayata were collected in the south west of Jiangxi province, China and kindly identified by Prof. Xian-Rui Lo, South China Institute of Botany, Academia Sinica, where a voucher specimen is deposited. Root powder (8 kg) was extracted with EtOH at room temp. The solvent was evapd under red. pres. and the residue treated with 2.5% HCl. The mixt. was filtered and the filtrate extracted with $CHCl_3$ to give part A. The filtrate was then basified with NH_4OH and extracted with $CHCl_3$ to yield part B. Part A (40 g) was chromatographed by silica gel CC and eluted with petrol–EtOAc (2:1, 1:1 and 1:2) to provide isocorydine and FK-3000 (**3**) (700 mg). Part B (102 g) was placed on silica gel columns. Elution with petrol–EtOAc (2:1, 1:1 and 1:4) afforded cycleanine, cepharanthine, berbamine and sinomenine (80 mg) and then gave part C with MeOH. Part C was rechromatographed on a silica gel column and eluted with $CHCl_3$ gradually enriched with MeOH to furnish cephamorphinanine (**1**) (45 mg) and sinococuline (**2**) (60 mg). Compounds **1** and **2** were purified by prep. TLC on silica gel using $CHCl_3$–MeOH–NH_4OH (9:1:tr).

Cephamorphinanine (**1**). Needles from Me_2CO–MeOH, mp 284–285°. $[\alpha]_D^{22}$ −118° (MeOH; *c* 0.07). UV λ_{max} nm: 215, 235sh, 270 (log ε 4.23, 4.00. 3.25); IR ν_{max} cm^{-1}: 3400, 1625, 1605, 1490. MS *m/z* (%): 331.1375 $[M]^+$($C_{18}H_{21}O_5N$, 19), 289 (58), 271 (21), 256 (36), 229 (100), 197 (85), 169 (27). CD $\Delta\varepsilon$ (nm): −24 (210), +2.5 (234), +2.4 (240), +5.5 (262). NOEDS: MeO-3→H-2 (11%), MeO-8→H-7 (11%).

Reduction of compound **1**. Cephamorphinanine (15 mg) in MeOH (5 ml) was treated with $NaBH_4$ (50 mg). The mixt. was stirred for 8 hr and then worked-up to afford sinococuline (**2**) (10 mg) (TLC, $[\alpha]_D$, IR, CD and ^{1}H NMR).

FK-3000 (**3**). Needles from EtOAc; mp 185–186°. $[\alpha]_D^{22}$ −163° (MeOH; *c* 0.73). UV λ_{max} nm: 217, 286 (log ε 4.28, 3.40). IR ν_{max} cm^{-1}: 3450, 1735, 1605, 1480. MS *m/z* (%): 417.1694 ($C_{22}H_{27}O_7N$, 4), 372 (2), 358 (100), 316 (5), 299 (2), 258 (40), 244 (13), 216 (13), 43 (43). CD $\Delta\varepsilon$ (nm): −32 (217), +8.3 (242). NOEDS: MeO-3→H-2 (12%), MeO-8→H-7 (10%).

Deacetylation of compound **3**. FK-3000 (45 mg) in MeOH (10 ml) was stirred with 5% aq. K_2CO_3 soln at pH 11 for 4 hr. The solvent was removed under red. pres. at room temp. Purification of the residue by prep. TLC gave sinococuline (**2**) ($[\alpha]_D$, IR, CD, ^{1}H and ^{13}C NMR).

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