Alkaloidal Constituents of the Tubers of *Stephania cepharantha* Cultivated in Japan: Structure of 3,4-Dehydrocycleanine, a New Bisbenzylisoquinoline Alkaloid

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Full details of the isolation and characterization of 52 alkaloids obtained from the tubers of *Stephania cepharantha* HAYATA (Menispermaceae) cultivated in Japan are presented, along with the structural determination of a new bisbenzylisoquinoline alkaloid, 3,4-dehydrocycleanine (8).

Key words 3,4-dehydrocycleanine; *Stephania cepharantha*; tuber; bisbenzylisoquinoline alkaloid; cycleanine

In previous papers,[1] we have reported the isolation and structural determination of four new morphinane alkaloids, cephamonine (**1**),[1a] cephamuline (**2**),[1a] cephasamine (**3**),[1b] cephakicine (**4**),[1b] one new hasubanane alkaloid, cephatonine (**5**),[1b] and two new stephaoxocane[2] alkaloids, stephaoxocanine (**6**),[1c] stephaoxocanidine (**7**),[1d] from the tubers of *Stephania cepharantha* HAYATA (Menispermaceae) cultivated in Japan. In our continuing investigations of the alkaloidal constituents of the tubers of this plant, we have obtained a new bisbenzylisoquinoline alkaloid, 3,4-dehydrocycleanine (**8**), together with 51 known alkaloids as shown in Table 1. This paper describes the isolation and structural determination of **8** and full details of the isolation and characterization of all the alkaloids.

The methanol extract of the tubers of *S. cepharantha* was fractionated, and the alkaloid-containing fractions were repeatedly subjected to crystallization, column chromatography, and preparative TLC, to give 3,4-dehydrocycleanine (**8**) as colorless needles, together with 51 known alkaloids.

The molecular formula of 3,4-dehydrocycleanine (**8**)

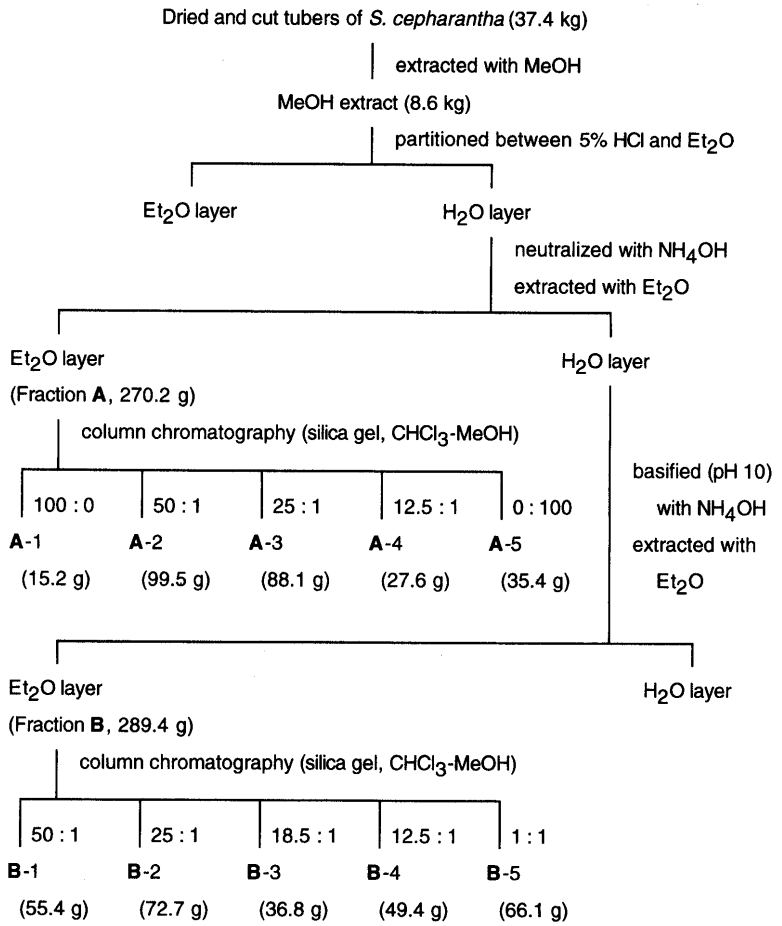

Chart 1. Fractionation of *Stephania cepharantha* HAYATA

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Table 1. Alkaloids from *Stephania cepharantha*

Fraction	Compound[a]	mp (°C)[b]	$[\alpha]_D$[c] (°)
A-1	Cepharanthine (**11**, BBI)	142—143	+350
	Cepharamine (**33**, Has)	187—188	−243
A-2	Cephasamine[d] (**3**, Mor)	142—144	+105
	Cephakicine[d] (**4**, Mor)	Amor. powder	−161
	Cephatonine[d] (**5**, Has)	Amor. powder	−264
	Stephaoxocanidine[d] (**7**, Steph)	188—191	+30
	(−)-Cycleanine (**9**, BBI)	277—280 (d)	−13
	Cepharanthine (**11**, BBI)	142—143	+350
	Isotetrandrine (**20**, BBI)	185—187	+146
	14-Episinomenine (**30**, Mor)	101—103	−55
	Sinoacutine (**32**, Mor)	190—192	−76
	Cepharamine (**33**, Has)	187—188	−243
	Aknadinine (**34**, Has)	Amor. powder	−290
	Aknadicine (**35**, Has)	153—155	−231
	Aknadilactam (**36**, Has)	Amor. powder	−152
	Corydine (**37**, Apo)	145—147	+208
	Isocorydine (**38**, Apo)	184—185	+197
	Isocorytuberine (**39**, Apo)	Amor. powder	+203
	N-Methyllaurotetanine (**40**, Apo)	Amor. powder	+121
	(−)-Anonaine (**42**, Apo)	Gum	−60
	(−)-Scoulerine (**51**, Pro-ber)	193—194	−269
A-3	Stephaoxocanine[d] (**6**, Steph)	160—162	+60
	(−)-Cycleanine (**9**, BBI)	277—280 (d)	−13
	Cepharanoline (**13**, BBI)	272—273 (d)	+273[e]
	Homoaromoline (**18**, BBI)	241—243 (d)	+268[e]
	Isotetrandrine (**20**, BBI)	185—187	+146
	trans-*N*-Feruloyltyramine (**52**, Tyr)	Amor. powder	—
A-4	Cepharanoline (**13**, BBI)	272—273 (d)	+273[e]
	Homoaromoline (**18**, BBI)	241—243 (d)	+268[e]
	Berbamine (**21**, BBI)	148—150	+297
	Juziphine (**47**, BI)	Amor. powder	+5
A-5	Berbamine (**21**, BBI)	148—150	+124
B-1	(−)-Cycleanine (**9**, BBI)	277—280 (d)	−13
	Cepharanthine (**11**, BBI)	142—143	+350
	Obaberine (**15**, BBI)	Amor. powder	+308
	Isotetrandrine (**20**, BBI)	185—187	+146
	Secocepharanthine (**26**, BBI)	Amor. powder	−14
	(+)-Reticuline (**46**, BI)	Amor. powder	+45
B-2	Cephamonine[d] (**1**, Mor)	Amor. powder[f]	−36
	Cephamuline[d] (**2**, Mor)	Amor. powder	−63
	3,4-Dehydrocycleanine[d] (**8**, BBI)	259—261 (d)	+79
	(−)-Cycleanine (**9**, BBI)	277—280 (d)	−13
	2-Norcepharanthine (**12**, BBI)	Amor. powder	+345
	Isotetrandrine (**20**, BBI)	185—187	+146
	Tannagine (**29**, Mor)	Amor. powder	+23
	FK-3000 (**31**, Mor)	160—161	−142
	(+)-Isoboldine (**41**, Apo)	122—123	+39
	(+)-Laudanidine (**48**, BI)	184—186	+265
	Stepharine (**49**, Proapo)	181—184	+142
	N-Methylcrotsparine (**50**, Proapo)	219—221	−32
B-3	Cepharanoline (**13**, BBI)	272—273 (d)	+273[e]
	Oxyacanthine (**16**, BBI)	Amor. powder	+297
	Stephibaberine (**17**, BBI)	Amor. powder	+254
	Homoaromoline (**18**, BBI)	241—243 (d)	+268[e]
	Thalrugosine (**22**, BBI)	Amor. powder	+297
	2-Norisotetrandrine (**24**, BBI)	Amor. powder	+136
	Sinomenine (**28**, Mor)	164—166	−54
	14-Episinomenine (**30**, Mor)	101—103	−55
B-4	(−)-Norcycleanine (**10**, BBI)	251—252 (d)	−27
	Cepharanoline (**13**, BBI)	272—273 (d)	+273[e]
	Homoaromoline (**18**, BBI)	241—243 (d)	+268[e]
	Berbamine (**21**, BBI)	148—150	+124
	Sinomenine (**28**, Mor)	164—166	−54
	Protosinomenine (**43**, BI)	Amor. powder	+53
	(+)-*N*-Methylcoclaurine (**44**, BI)	Amor. powder	±0[g]
B-5	2-Norcepharanoline (**14**, BBI)	280—282 (d)	+283
	Aromoline (**19**, BBI)	217—220 (d)	+343
	Berbamine (**21**, BBI)	148—150	+124
	Obamegine (**23**, BBI)	Amor. powder	+297
	2-Norberbamine (**25**, BBI)	184—187	+77
	3′,4′-Dihydrostephasubine (**27**, BBI)	Amor. powder	+171
	(+)-Coclaurine (**45**, BI)	210—212	+23

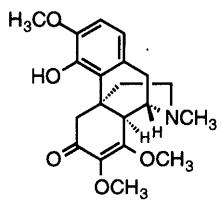
a) BBI: bisbenzylisoquinoline, Has: hasubanane, Mor: morphinane, Steph: stephaoxocane, Apo: aporphine, Pro-ber: protoberberine, Tyr:tyramine derivative, BI: benzylisoquinoline, Proapo: proaporphine. *b*) Amor. powder: amorphous powder, (d): decomposition. *c*) Measured in $CHCl_3$, except for **13** and **18**. *d*) New alkaloid. *e*) Measured in 0.1 N HCl. *f*) HCl salt; mp 185—187 °C. *g*) CD (MeOH) $\Delta\varepsilon$ (nm): +0.3 (290), ±0 (271), +1.5 (232), −0.5 (216).

Table 2. ^{1}H- and ^{13}C-NMR Data for **8** and **9**

Position	^{1}H		^{13}C	
	8	**9**	**8**	**9**
1	4.70 d (10.4)	4.26 d (10.4)	58.04	59.48
3	6.15 d (7.0)	2.90 m	136.87	44.62
		3.25 m		
4	5.44 d (7.0)	2.91 m	98.20	24.79
		3.02 m		
4a			129.81	129.73
5	6.45 s	6.57 s	103.10	109.18
6			152.19	151.80
7			138.95	138.87
8			142.34	143.64
8a			114.98	125.59
α	2.81 d (13.1)	2.52 dd (12.8, 10.4)	33.67	37.72
	2.96 dd (13.1, 10.4)	3.22 d (12.8)		
9			129.35	130.43
10	6.26 dd (8.5, 2.1)	6.28 dd (8.2, 2.1)	128.97	128.68
11	5.89 dd (8.5, 2.8)	5.83 dd (8.2, 2.8)	114.23	113.98
12			154.02	154.10
13	6.57 dd (8.2, 2.8)	6.60 dd (8.5, 2.8)	117.26	117.36
14	6.95 dd (8.2, 2.1)	7.04 dd (8.5, 2.1)	128.46	128.10
N-CH_3	3.12 s	2.53 s	40.10	42.37
6-OCH_3	3.82 s	3.81 s	56.04	55.99
7-OCH_3	3.39 s	3.40 s	60.33	60.01
1′	4.23 d (10.1)	4.26 d (10.4)	59.59	59.48
3′	2.92 m	2.90 m	44.67	44.62
	3.26 m	3.25 m		
4′	2.90 m	2.91 m	24.81	24.79
	3.02 m	3.02 m		
4a′			129.78	129.73
5′	6.58 s	6.57 s	109.24	109.18
6′			151.84	151.80
7′			138.97	138.87
8′			143.55	143.64
8a′			125.51	125.59
α′	2.52 dd (12.8, 10.1)	2.52 dd (12.8, 10.4)	37.73	37.72
	3.19 dd (12.8)	3.22 d (12.8)		
9′			130.57	130.43
10′	6.25 dd (8.2, 2.1)	6.28 dd (8.2, 2.1)	128.95	128.10
11′	5.81 dd (8.2, 2.8)	5.83 dd (8.2, 2.8)	114.23	113.98
12′			153.84	154.10
13′	6.62 dd (8.5, 2.8)	6.60 dd (8.5, 2.8)	117.03	117.36
14′	7.02 dd (8.5, 2.1)	7.04 dd (8.5, 2.1)	128.09	128.10
N′-CH_3	2.52 s	2.53 s	42.44	42.37
6′-OCH_3	3.82 s	3.81 s	55.98	55.99
7′-OCH_3	3.41 s	3.40 s	60.05	60.01

Values in parentheses are coupling constants (Hz).

was established by the high-resolution mass spectrum (HR-MS) as $C_{38}H_{40}N_2O_6$, and the electron impact mass spectrum (EI-MS) showed the molecular ion peak at *m/z* 620 (100%) and strong peaks at *m/z* 312 (29%), 311 (26%), 310 (54%), and 309 (79%), indicating that **8** is a bisbenzylisoquinoline alkaloid having two "head-to-tail" diphenyl ether linkages.[3] The IR spectrum suggested the absence of hydroxy and primary and secondary amino groups (no absorption from 3500 to 3200 cm^{-1}). The UV spectrum showed the presence of an olefin conjugated to an aromatic ring (absorption maximum at 340 nm). The ^{1}H- and ^{13}C-NMR spectra were similar to those of (−)-cycleanine (**9**), which is an alkaloid possessing two "head-to-tail" diphenyl ether linkages, and the molecular formula has 2H more than that of **8**. The ^{1}H-NMR spectrum of **8** showed two coupled olefinic proton signals at δ_H 5.44 and 6.15, and the ^{13}C-NMR spectrum



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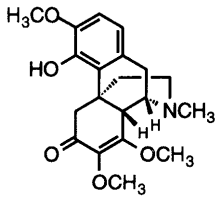

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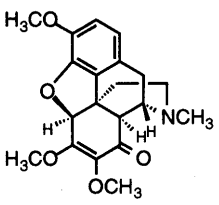

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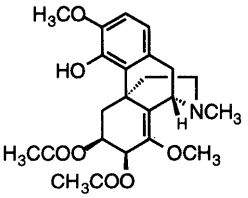

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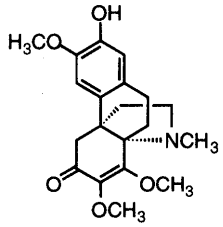

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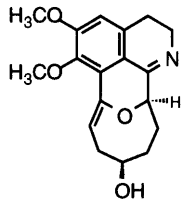

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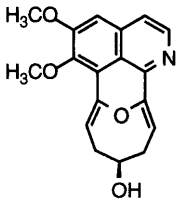

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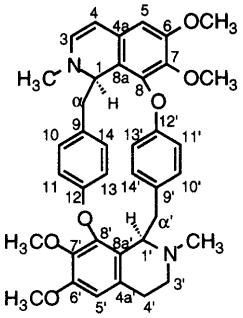

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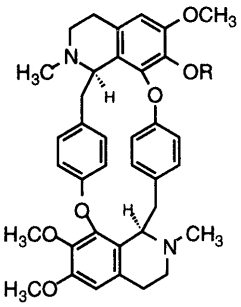
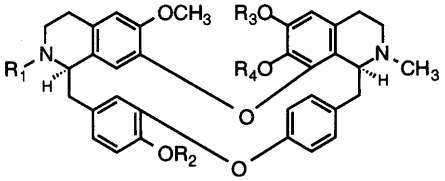
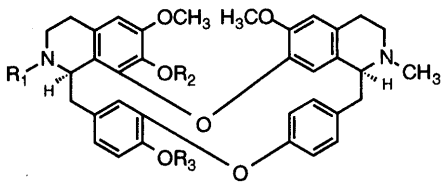


	R
9	CH_3
10	H



	R_1	R_2	R_3	R_4
11	CH_3	CH_3	$-CH_2-$	
12	H	CH_3	$-CH_2-$	
13	CH_3	H	$-CH_2-$	
14	CH_3	H	$-CH_2-$	
15	CH_3	CH_3	CH_3	CH_3
16	CH_3	H	CH_3	CH_3
17	CH_3	CH_3	H	CH_3
18	CH_3	CH_3	CH_3	H
19	CH_3	H	CH_3	H



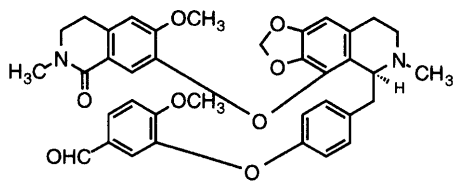
	R_1	R_2	R_3
20	CH_3	CH_3	CH_3
21	CH_3	CH_3	H
22	CH_3	H	CH_3
23	CH_3	H	H
24	H	CH_3	CH_3
25	H	CH_3	H

Chart 2

exhibited two sp^2-tertiary carbon signals at δ_C 98.20 and 136.87 instead of the two signals due to C-3 (δ_C 44.62) and C-4 (δ_C 24.79) of **9** (Table 2). These data indicated that **8** should be the 3,4-dehydro derivative of **9**. The heteronuclear multiple-bond connectivity (HMBC) spectrum also supported the 3,4-dehydro structure of **9**, showing correlations between the *N*-CH_3 (δ_H 3.12) and C-3 (δ_C 136.87) signals and between the H-5 (δ_H 6.45) and C-4 (δ_C 98.20) signals.

Hydrogenation of **8** in the presence of 10% palladium–carbon in ethanol gave a saturated compound that was identified by direct comparison with an authentic sample of **9**. Thus, the structure of **8** was determined as 1*R*,1′*R*-3,4-dehydrocycleanine.

Finally, from the tubers of *Stephania cepharantha* HAYATA (Menispermaceae) cultivated in Japan, the following 52 alkaloids were isolated: 20 bisbenzylisoquinoline alkaloids, 3,4-dehydrocycleanine (**8**), (−)-cycleanine (**9**),[4,5] (−)-norcycleanine (**10**),[5] cepharanthine (**11**),[6] 2-norcepharanthine (**12**),[6] cepharanoline (**13**),[7] 2-norceph-



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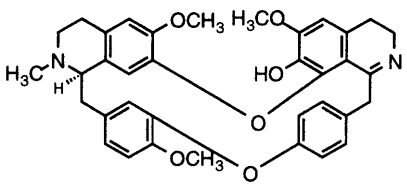

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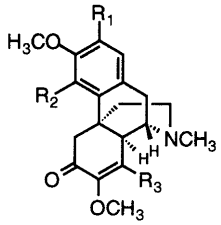
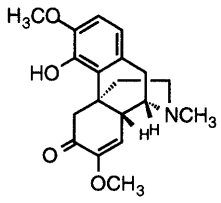


	R_1	R_2	R_3
28	H	OH	H
29	OCH_3	H	OCH_3



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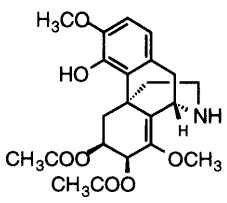

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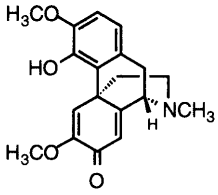

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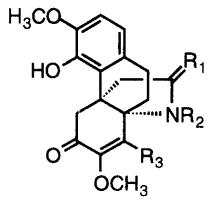
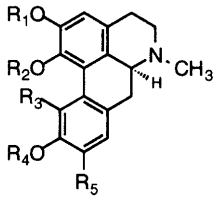
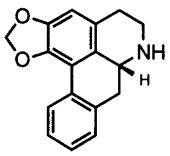


	R_1	R_2	R_3
33	H_2	CH_3	H
34	H_2	CH_3	OCH_3
35	H_2	H	OCH_3
36	O	CH_3	OCH_3





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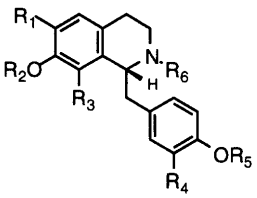

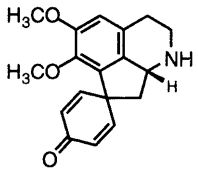

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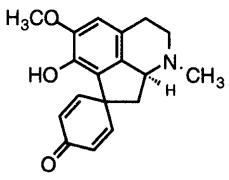
	R_1	R_2	R_3	R_4
37	H	OCH_3	CH_3	H
38	CH_3	OH	CH_3	H
39	H	OCH_3	H	H
40	CH_3	H	CH_3	OH
41	H	H	CH_3	OH

	R_1	R_2	R_3	R_4	R_5	R_6
43	OH	CH_3	H	OH	CH_3	CH_3
44	OCH_3	H	H	H	H	CH_3
45	OCH_3	H	H	H	H	H
46	OCH_3	H	H	OH	CH_3	CH_3
47	H	CH_3	OH	H	H	CH_3
48	OCH_3	CH_3	H	OH	CH_3	CH_3



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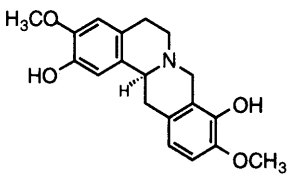

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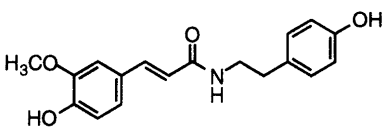

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Chart 2

aranoline (**14**),[8] obaberine (**15**),[9] oxyacanthine (**16**),[10] stephibaberine (**17**),[8] homoaromoline (**18**),[9,11] aromoline (**19**),[9] isotetrandrine (**20**),[12] berbamine (**21**),[13] thalrugosine (**22**),[11,14] obamegine (**23**),[15] 2-norisotetrandrine (**24**),[8] 2-norberbamine (**25**),[16] secocepharanthine (**26**),[17] and 3′,4′-dihydrostephasubine (**27**)[18]; nine morphinane alkaloids, cephamonine (**1**), cephamuline (**2**), cephasamine (**3**), cephakicine (**4**), sinomenine (**28**),[19] tannagine (**29**),[20]

14-episinomenine (**30**),[21] FK-3000 (**31**),[22] and sinoacutine (**32**)[23]; five hasubanane alkaloids, cephatonine (**5**), cepharamine (**33**),[24] aknadinine (**34**),[25,26] aknadicine (**35**),[26] and aknadilactam (**36**)[26,27]; two stephaoxocane alkaloids, stephaoxocanine (**6**) and stephaoxocanidine (**7**); six aporphine alkaloids, corydine (**37**),[28] isocorydine (**38**),[29] isocorytuberine (**39**),[30] *N*-methyllaurotetanine (**40**),[31] (+)-isoboldine (**41**),[32] and (−)-anonaine (**42**)[33]; six benzylisoquinoline alkaloids, protosinomenine (**43**),[34] (+)-*N*-methylcoclaurine (**44**),[31] (+)-coclaurine (**45**),[35] (+)-reticuline (**46**),[36] juziphine (**47**),[37] and (+)-laudanidine (**48**)[31]; two proaporphine alkaloids, stepharine (**49**)[38] and *N*-methylcrotsparine (**50**)[39]; one protoberberine alkaloid, (−)-scoulerine (**51**),[23] and one tyramine derivative, *trans*-*N*-feruloyltyramine (**52**).[40]

The structures of the known alkaloids were identified by direct comparison with authentic samples or by comparison of the spectroscopic data with the literature values.

Experimental

Melting points were measured on a Yanagimoto hot-stage melting point apparatus without correction. IR spectra were recorded on an FT/IR-5000 (JASCO) spectrometer as KBr pellets. UV spectra were measured on a Ubest-35 (JASCO) spectrometer in MeOH. CD spectra were measured on a J-600 (JASCO) spectrometer in dioxane. NMR spectra were taken on a JNM-α500 (JEOL) (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Optical rotations were determined on a DIP-140 (JASCO) instrument in $CHCl_3$. MS were taken on a JMS-D300 (JEOL) spectrometer at 30 eV. Column chromatography was performed on Wakogel C-200 (Wako Pure Chemical Industries, Ltd.). Preparative TLC was done on precoated Silica gel 60 F_{254} (0.25 mm thick) plates (Merck).

Plant Material *Stephania cepharantha* HAYATA was cultivated at Yasato-machi, Ibaraki prefecture, Japan and collected in October 1987. The plants were kept at the Yasato factory of Kaken Shoyaku Co., Ltd.

Extraction and Isolation Dried and cut tubers of *S. cepharantha* (37.4 kg) were extracted twice with hot MeOH. The extract (8.6 kg) was evaporated *in vacuo*, and the residue was treated with 5% HCl. The mixture was filtered, and the filtrate was extracted with Et_2O. The aqueous layer was adjusted to pH 7 with NH_4OH and extracted with Et_2O to yield fraction A (270.2 g). Then, the aqueous layer was basified with NH_4OH to pH 10 and extracted with Et_2O to yield fraction B (289.4 g). Fraction A was subjected to silica gel column chromatography using $CHCl_3$, 2%, 4%, and 8% MeOH–$CHCl_3$, and MeOH as eluents to afford fractions A-1 (15.2 g), A-2 (99.5 g), A-3 (88.1 g), A-4 (27.6 g), and A-5 (35.4 g). Fraction B was also chromatographed on silica gel using 2%, 4%, 6%, 8%, and 50% MeOH–$CHCl_3$ as eluents to give fractions B-1 (55.4 g), B-2 (72.7 g), B-3 (36.8 g), B-4 (49.4 g), and B-5 (66.1 g). Each fraction (A-1-5 and B-1-5) was further subjected to a combination of crystallization, column chromatography, and preparative TLC, to afford 52 alkaloids.

From fraction A-1; cepharanthine (**11**, 8.36 g), cepharamine (**33**, 0.110 g). From fraction A-2; cephasamine (**3**, 0.034 g), cephakicine (**4**, 0.217 g), cephatonine (**5**, 0.015 g), stephaoxocanidine (**7**, 0.022 g), (−)-cycleanine (**9**, 1.25 g), cepharanthine (**11**, 68.20 g), isotetrandrine (**20**, 12.37 g), 14-episinomenine (**30**, 0.015 g), sinoacutine (**32**, 0.22 g), cepharamine (**33**, 0.192 g), aknadinine (**34**, 0.478 g), aknadicine (**35**, 0.057 g), aknadilactam (**36**, 0.032 g), corydine (**37**, 0.098 g), isocorydine (**38**, 0.275 g), isocorytuberine (**39**, 0.178 g), *N*-methyllaurotetanine (**40**, 0.009 g), (−)-anonaine (**42**, 0.016 g), (−)-scoulerine (**51**, 0.101 g). From fraction A-3; stephaoxocanine (**6**, 0.058 g), (−)-cycleanine (**9**, 5.03 g), cepharanoline (**13**, 7.72 g), homoaromoline (**18**, 1.29 g), isotetrandrine (**20**, 54.66 g), *trans*-*N*-feruloyltyramine (**52**, 0.048 g). From fraction A-4; cepharanoline (**13**, 4.49 g), homoaromoline (**18**, 0.970 g), berbamine (**21**, 11.24 g), juziphine (**47**, 0.128 g). From fraction A-5; berbamine (**21**, 27.03 g). From fraction B-1; (−)-cycleanine (**9**, 4.22 g), cepharanthine (**11**, 3.96 g), obaberine (**15**, 0.072 g), isotetrandrine (**20**, 20.31 g), secocepharanthine (**26**, 0.050 g), (+)-reticuline (**46**, 0.359 g). From fraction B-2; cephamonine (**1**, 2.65 g), cephamuline (**2**, 0.047 g), 3,4-dehydrocycleanine (**8**, 0.034 g), (−)-cycleanine (**9**, 12.38 g), 2-norcepharanthine (**12**, 0.102 g), isotetrandrine (**20**, 37.33 g), tannagine (**29**, 0.038 g), FK-3000 (**31**, 11.17 g), (+)-isoboldine (**41**, 0.153 g), (+)-laudanidine (**48**, 0.125 g), stepharine (**49**, 0.398 g), *N*-methylcrotsparine (**50**, 0.083 g). From fraction B-3; cepharanoline (**13**, 0.880 g), oxyacanthine (**16**, 0.041 g), stephibaberine (**17**, 0.102 g), homoaromoline (**18**, 6.32 g), thalrugosine (**22**, 0.099 g), 2-norisotetrandrine (**24**, 0.030 g), sinomenine (**28**, 1.06 g), 14-episinomenine (**30**, 0.065 g). From fraction B-4; (−)-norcycleanine (**10**, 5.53 g), cepharanoline (**13**, 0.325 g), homoaromoline (**18**, 3.36 g), berbamine (**21**, 20.35 g), sinomenine (**28**, 0.580 g), protosinomenine (**43**, 0.150 g), (+)-*N*-methylcoclaurine (**44**, 0.072 g). From fraction B-5; 2-norcepharanoline (**14**, 0.152 g), aromoline (**19**, 14.73 g), berbamine (**21**, 33.96 g), obamegine (**23**, 3.82 g), 2-norberbamine (**25**, 0.077 g), 3′,4′-dihydrostephasubine (**27**, 0.022 g), (+)-coclaurine (**45**, 2.43 g).

3,4-Dehydrocycleanine (8) mp 259—261 °C (dec.) (acetone). $[\alpha]_D^{24}$ +79° (c=0.65). IR: 1609, 1508, 1491, 1421, 1342, 1321, 1220, 1172, 1118 cm^{-1}. UV λ_{max} nm (log ε): 340 (3.97). CDΔε (nm): +15.1 (339), +2.4 (306), +7.2 (290), +7.1 (287), +8.7 (279), −9.2 (257). EI-MS *m/z* (%): 620 (M^+, 100), 312 (29), 311 (26), 310 (54), 309 (79), 204 (15), 202 (27), 174 (15), 157 (16). HR-MS *m/z*: 620.2908 ($C_{38}H_{40}N_2O_6$ requires 620.2887).

Hydrogenation of 8 A mixture of **8** (10 mg) and 10% Pd–C (5 mg) in EtOH (20 ml) was stirred for 4 h at room temperature under an H_2 atmosphere. Work-up of the product was done in a usual manner and was followed by preparative TLC [with EtOAc–Et_2NH (9 : 1)] to afford **9** (2 mg) and **8** (4 mg). The identification of **9** was accomplished by comparison of its TLC behavior and CD, IR, and ^{1}H-NMR spectra with those of an authentic sample of **9**.

(−)-Cycleanine (9) mp 277—280 °C (dec.) (MeOH) [mp 268—271 °C[4]]. $[\alpha]_D^{25}$ −13° (c=1.00) [$[\alpha]_D$ −20° (c=1.00, $CHCl_3$)[4]]. IR: 1607, 1580, 1508, 1454, 1417, 1344, 1296, 1220, 1118 cm^{-1}. UV λ_{max} nm (log ε): 277 (3.68). CD Δε (nm): +14.7 (276), +9.4 (265), +25.3 (255), −1.2 (246). EI-MS *m/z* (%): 622 (M^+, 88), 621 (36), 313 (22), 312 (100), 311 (32), 309 (8), 204 (6), 190 (6). HR-MS *m/z*: 622.3005 ($C_{38}H_{42}N_2O_6$ requires 622.3040).

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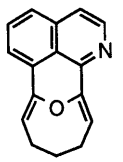
References and Notes

1) *a*) Kashiwaba N., Morooka S., Kimura M., Murakoshi Y., Toda J., Sano T., *Chem. Pharm. Bull.*, **42**, 2452—2454 (1994); *b*) Kashiwaba N., Morooka S., Kimura M., Ono M., Toda J., Suzuki H., Sano T., *J. Nat. Prod.*, **59**, 476—480 (1996); *c*) *Idem*, *ibid.*, **59**, 803—805 (1996); *d*) *Idem*, *Nat. Prod. Lett.*, in press.

2) We have proposed the name "stephaoxocane" for skeleton A.[1d]



A

3) Tomita M., Kikuchi T., Fujitani K., Kato A., Furukawa H., Aoyagi Y., Kitano M., Ibuka T., *Tetrahedron Lett.*, **1966**, 857—864.

4) Scheinmann F., Scriven E. F. V., Ogbeide O. N., *Phytochemistry*, **19**, 1837—1840 (1980).

5) Ohiri F. C., Verpoorte R., Svendsen A. B., *Planta Med.*, **47**, 87—89 (1983).

6) Patra A., Freyer A. J., Guinaudeau H., Shamma M., Tantisewie B., Pharadai K., *J. Nat. Prod.*, **49**, 424—427 (1986).

7) Tomita M., Sawada T., Kozuka M., Takeuchi M., Akasu M., *Yakugaku Zasshi*, **89**, 1678—1681 (1969).

8) Tantisewie B., Amurrio S., Guinaudeau H., Shamma M., *J. Nat. Prod.*, **52**, 846—851 (1989).

9) Siwon J., Verpoorte R., van Beek T., Meerburg H., Svendsen A. B., *Phytochemistry*, **20**, 323—325 (1981).

10) Knapp J. E., Hussein F. T., Beal J. L., Doskotch R. W., Tomimatsu T., *J. Pharm. Sci.*, **56**, 139—141 (1967).
11) Lin L.-Z., Shieh H.-L., Angerhofer C. K., Pezzuto J. M., Cordell G. A., Xue L., Johnson M. E., Ruangrungsi N., *J. Nat. Prod.*, **56**, 22—29 (1993).
12) Mouris C., *J. Nat. Prod.*, **44**, 101—103 (1981).
13) Koike L., Marsaioli A. J., Rúveda E. A., de A. M. Reis F., Bick I. R. C., *Tetrahedron Lett.*, **1979**, 3765—3768.
14) Mitscher L. A., Wu W.-N., Doskotch R. W., Beal J. L., *Lloydia*, **35**, 167—176 (1972).
15) Suess T. R., Stermitz F. R., *J. Nat. Prod.*, **44**, 680—687 (1981).
16) Hussain S. F., Khan L., Guinaudeau H., Leet J. E., Freyer A. J., Shamma M., *Tetrahedron*, **40**, 2513—2517 (1984).
17) Kunitomo J., Murakami Y., Oshikata M., Akasu M., Kodama K., Takeda N., Harada K., Suzuki M., Tatematsu A., Kawanabe E., Ishii H., *Chem. Pharm. Bull.*, **33**, 135—143 (1985).
18) Patra A., Mandal T. K., Mukhopadhyay P. K., Ranu B. C., *Phytochemistry*, **27**, 653—655 (1988).
19) Terui Y., Tori K., Maeda S., Sawa Y. K., *Tetrahedron Lett.*, **1975**, 2853—2856.
20) Charles B., Guinaudeau H., Bruneton J., *Can. J. Chem.*, **67**, 1257—1260 (1989).
21) Vecchietti V., Casagrande C., Ferrari G., *Tetrahedron Lett.*, **1976**, 1631—1634.
22) Deng J.-Z., Zhao S.-X., Miao Z.-C., *Phytochemistry*, **31**, 1448—1450 (1992).
23) Hussain S. F., Siddiqui M. T., *Planta Med.*, **58**, 108 (1992).
24) Tomita M., Kozuka M., *Yakugaku Zasshi*, **87**, 1203—1208 (1967).
25) Wang X.-K., Zhao Y.-R., Zhao T.-F., Lai S., Che C.-T., *Phytochemistry*, **35**, 263—265 (1994).
26) Moza B. K., Bhaduri B., Basu D. K., Kunitomo J., Okamoto Y., Yuge E., Nagai Y., Ibuka T., *Tetrahedron*, **26**, 427—433 (1970).
27) Kunitomo J., Okamoto Y., Yuge E., Nagai Y., *Tetrahedron Lett.*, **1969**, 3287—3289.
28) Desai H. K., Joshi B. S., Pelletier S. W., Sener B., Bingöl F., Baykal T., *Heterocycles*, **36**, 1081—1089 (1993).
29) Yang M.-H., Patel A. V., Blunden G., Turner C. H., O'Neill M. J., Lewis J. A., *Phytochemistry*, **33**, 943—945 (1993).
30) Cortes D., Davoust D., Hadi A. H. A., Myint S. H., Hocquemiller R., Cavé A., *J. Nat. Prod.*, **53**, 862—866 (1990).
31) Wu J., Beal J. L., Wu W.-N., Doskotch R. W., *Lloydia*, **40**, 593—601 (1977).
32) Bhakuni D. S., Gupta S., *Planta Med.*, **48**, 52—54 (1983).
33) Bhakuni D. S., Tewari S., Dhar M. M., *Phytochemistry*, **11**, 1819—1822 (1972).
34) Jossang A., Lebœuf M., Cabalion P., Cavé, A., *Planta Med.*, **49**, 20—24 (1983).
35) Johns S. R., Lamberton J. A., Sioumis A. A., *Aust. J. Chem.*, **20**, 1729—1735 (1967).
36) Chou C.-J., Lin L.-C., Chen K.-T., Chen C.-F., *J. Nat. Prod.*, **57**, 689—694 (1994).
37) Ziyaev R., Irgashev T., Israilov I. A., Abdullaev N. D., Yunusov M. S., Yunusov S. Y., *Khim. Prir. Soedin.*, **1977**, 239—243.
38) Bartley J. P., Baker L.T., Carvalho C. F., *Phytochemistry*, **36**, 1327—1331 (1994).
39) Dasgupta S., Ray A. B., Bhattacharya S. K., Bose R., *J. Nat. Prod.*, **42**, 399—406 (1979).
40) Fukuda N., Yonemitsu M., Kimura T., *Chem. Pharm. Bull.*, **31**, 156—161 (1983).