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Alkaloidal Constituents of *Crinum latifolium* and *Crinum bulbispermum* (Amaryllidaceae)[1)]

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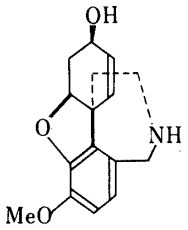
A new base, 3-*O*-acetylhamayne (**11**), was isolated from *Crinum latifolium* L. (Amaryllidaceae) along with crinamine (**3**), powelline (**4**), crinine (**5**), 1-*O*-acetyllycorine (**6**), hamayne (**8**), undulatine (**13**), and cherylline (**14**). The bases **3**, **4**, **5**, and **14**, as well as diacetyllycorine (**7**), crinamidine (**16**), *O*-acetylcrinine (**17**), deacetylbowdensine (**18**), and bowdensine (**19**), were also isolated from *Crinum bulbispermum* MILNE-REDHEAD *et* SCHWEICKERDT (Amaryllidaceae).

Keywords——*Crinum latifolium*; *Crinum bulbispermum*; *O*-acetylcrinine; powelline; hamayne; 3-*O*-acetylhamayne; cherylline; undulatine; crinamidine; bowdensine

We have previously reported[2)] the isolation of *N*-demethylgalanthamine (**1**), lycorine (**2**), and crinamine (**3**) from *Crinum asiaticum* L. var *japonicum* BAKER (Amaryllidaceae). This paper deals with the isolation and structural elucidation of the alkaloids from two *Crinum* species of Amaryllidaceae, *C. latifolium* L. (Japanese name, Indohamayu), and *C. bulbispermum* MILNE-REDHEAD *et* SCHWEICKERDT (Japanese name, Afurikahamayu). Various minor alkaloids, crinamine (**3**), powelline (**4**), *etc.*, have been isolated from *C. bulbispermum* L., along with lycorine (**2**) and crinine (**5**) as major alkaloids.[3)]



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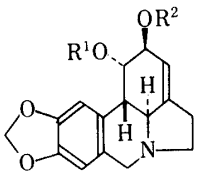
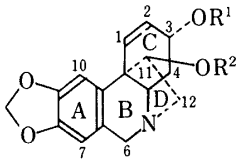
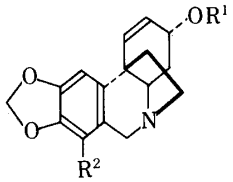


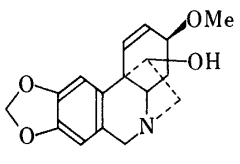
2 : $R^1=R^2=H$
6 : $R^1=Ac$, $R^2=H$
7 : $R^1=R^2=Ac$



3 : $R^1=Me$, $R^2=H$
8 : $R^1=R^2=H$
9 : $R^1=R^2=Ac$
10 : $R^1=R^2=Me$
11 : $R^1=Ac$, $R^2=H$



4 : $R^1=H$, $R^2=OMe$
5 : $R^1=R^2=H$
17 : $R^1=Ac$, $R^2=H$



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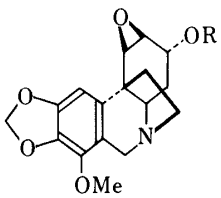
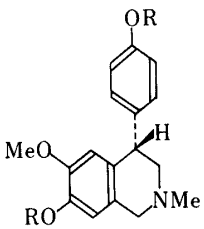
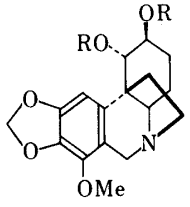


13 : R=Me
16 : R=H



14 : R=H
15 : R=Me



18 : R=H
19 : R=Ac

Chart 1

Isolation of Alkaloids from *C. latifolium* L.

Crude basic material was extracted from fresh bulbs of *C. latifolium* L. by the method of Wildman and Bailey.[4] Lycorine (**2**)[2,5] was isolated from a chloroform solution of the crude basic material, utilizing its low solubility in this solvent, and was identified by direct comparison with an authentic sample of **2**. The chloroform solution was subjected to preparative thin-layer chromatography (PLC) using silica gel–methanol–chloroform, as described in Experimental, to separate seven alkaloids, bases A, B, C, D, E, F, and H. Similarly, three alkaloids, lycorine (**2**) and bases G and H, were obtained from fresh leaves of the plant.

Base A (**6**) was recrystallized from acetone as colorless needles, $C_{18}H_{19}NO_5 \cdot 1/2H_2O$, mp 217—219 °C. From spectral and physical data (see Experimental), base A was assigned as 1-*O*-acetyllycorine (**6**). This assignment was confirmed by direct comparison of base A with authentic **6** prepared[6] from diacetyllycorine (**7**).

Similarly, base B (mp 204—205 °C, $C_{16}H_{17}NO_3$), base C (mp 200—202 °C, $C_{17}H_{19}NO_4$), and base D (mp 190—191 °C, $C_{17}H_{19}NO_4$) were confirmed to be crinine (**5**),[7,8] powelline (**4**),[3,9] and crinamine (**3**),[2] respectively.

Base E (**8**) was isolated as colorless needles, mp 83—84 °C, $C_{16}H_{17}NO_4$, $[\alpha]_D^{18}$ +78.2° (c=1.1, EtOH), and as its picrate, mp 205—207 °C. Treatment of base E with acetic anhydride and pyridine gave a diacetate (**9**), mp 113—114 °C, $C_{20}H_{21}NO_6$. The proton nuclear magnetic resonance (^{1}H-NMR) data (see Table I) for the diacetate were very similar to those for an acetylated product (**9**)[10a] of hamayne (**8**),[10a] which was isolated from *C. asiaticum* L. var *japonicum* BAKER. In addition, the molecular formulas of base E and its diacetate were identical with those of **8** and **9**, respectively, and the melting point of the former was similar to the reported value. These findings suggested that base E is hamayne (**8**). However, the optical rotation of base E and the melting point of its diacetate were different from the reported values for **8** and **9**.[10a] Base E was established as **8** by its chemical transformation to 11-*O*-methylcrinamine (**10**) by the method of Fales and Wildman[10b] as follows: the potassium salt of base E was treated with methyl *p*-toluenesulfonate to give *O,O*-dimethylated base E, mp 170—172 °C, $C_{18}H_{21}NO_4$, which was shown to be identical with authentic **10** (prepared by similar treatment of **3**) by direct comparison of spectral [^{1}H-NMR, infrared (IR), mass spectrum (MS), and optical rotatory dispersion (ORD)] data and by the mixed melting point test.

Base F (**11**), a new alkaloid, showed a melting point of 112—114 °C, formula of $C_{18}H_{19}NO_5$, and $[\alpha]_D^{21}$ +123.5° (c=0.3, $CHCl_3$). Its IR spectrum (KBr) showed absorptions due to a hydroxyl group at 3350 cm^{-1}, a carbonyl group at 1730 cm^{-1}, and a methylenedioxy group at 930 cm^{-1}. The ^{1}H-NMR spectrum showed the presence of two olefinic protons and one *para*-oriented aromatic proton, a methylenedioxy group, an acetyl group, and a benzylamino group, but no signal due to an *N*-methyl group (see Table I). These findings suggest that base F has a crinine-type skeleton (with undefined stereochemistry). The position and configuration of the above functional groups were proven by NMDR studies: monitoring the line of 1-H (δ 6.32) gave internuclear double resonance (INDOR) peaks at δ 6.06 (2-H) and 5.44 (3-H) and a nuclear Overhauser effect (NOE) peak at δ 6.78; irradiation at δ 6.78 (10-H) resulted in a 16% NOE increment in the signal of 1-H. Minitoring the line of 3-H gave INDOR peaks at δ 6.06, 6.32, and 2.22 (m, 4-H_2). These facts suggest the presence of the partial formula –CH=CH–CH(OAc)–CH_2– and an equatorial (α-oriented) acetoxy group at C-3, especially on the basis of the allylic coupling constant ($J_{1,3}$=2.0 Hz).[11] Monitoring the line of 11-H (δ 3.98) led us to find an INDOR peak at δ 3.38 (m, 12-H_2). Monitoring the signal at δ 3.23 (4a-H) gave an INDOR peak at δ 2.22 (4-H_2), and NOE and decoupling peaks (long-range coupling) at δ 3.98 (11-H). This long-range coupling (W rule) between 4a-H and 11-H indicates that base F has the C/D *cis* configuration (α-ethylene bridge) and that a hydroxyl

group is located as shown for **11**. Hence, base F was assigned as 3-*O*-acetylhamayne (**11**).

This assignment was supported by the MS and ORD results: in the MS of base F, the characteristic fragmentation pattern[8] of crinine-type alkaloids appeared as peaks (a)—(g), as shown in Table II. Comparison of the ORD curves of base F with those of crinamine (**3**) and haemanthamine[12] (**12**) indicated the same *cis* relationship between the acetoxy group at C-3 and the ethylene bridge in base F as in **3**.

The final evidence for the stereochemistry of base F was obtained by conversion of **11** to its acetate (**9**) by treatment with acetic anhydride and pyridine. The resulting acetate was found to be identical with diacetylhamayne (**9**) by direct comparison of spectral data and by the mixed melting point test. Consequently, the structure of base F was established as **11**.

Base G (**13**) was crystallized from acetone as pale yellow needles, mp 143—144 °C, $C_{18}H_{21}NO_5$. The ^{1}H-NMR spectrum (see Table I) exhibited four singlets assignable to an aromatic proton, two protons of the methylenedioxy group, and three protons each of aliphatic and aromatic *O*-methyl groups. In addition, two oxiran protons could be identified at δ 3.80 (d, 1-H) and 3.35 (m, 2-H). Furthermore, in the MS of base G, the presence of the oxiran ring was supported by the elimination of a CHO fragment[13] from the molecular ion

TABLE I. ^{1}H-NMR Data for Crinamine (**3**) and Related Compounds (δ)[a]

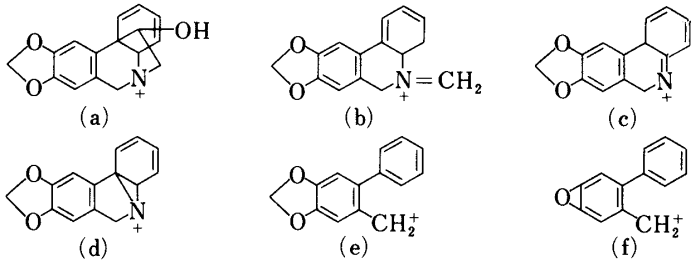
	1-H	2-H	3-H	4-H_2	4a-H	6-H_2	7-H	10-H	11-H or 11-H_2	12-H_2	OCH_2O	OMe or OAc
3	6.22		3.98 (m)	2.08 (m)	b)	3.66, 4.28 (d, 17)	6.47	6.79	3.92 (t-like)	b)	5.86	3.40
4	6.50 (d, 10)	5.90 (dd, 10, 4)	4.30 (m)	1.85 (m)	2.82 (m)	3.96, 4.18 (d, 17)		6.75	1.85 (m)	3.30 (m)	5.82	3.90
5	6.53 (d, 10)	5.91 (dd, 10, 6)	4.28 (m)	1.99 (m)	2.82 (m)	3.65, 4.28 (d, 17)	6.39	6.81	1.99 (m)	3.30 (m)	5.84	
8	6.58 (d, 11)	6.38 (d, 11)	b)	b)	b)	4.51, 5.02 (d, 16)	6.74	7.16	b)	b)	6.03	
9	6.22 (dd, 10, 2)	5.85 (dd, 10, 1)	5.42 (m)	2.07 (m)	3.24 (m)	3.66, 4.30 (d, 18)	6.46	6.86	4.94 (t-like)	3.37 (d-like)	5.89	2.02, 2.07
11	6.32 (dd, 10, 2)	6.06 (dd, 10, 1)	5.44 (m)	2.22 (m)	3.23 (m)	3.66, 4.30 (d, 17)	6.46	6.78	3.98 (t-like)	3.38 (m)	5.88	2.06
13	3.80 (d, 3, 5)	3.35 (m)	4.00 (m)	1.61 (m)	3.10 (m)	3.72, 4.20 (d, 18)		6.61	b)	b)	5.86	3.42, 3.99
16	3.76 (d, 3, 5)	3.27 (m)	4.46 (m)	1.59 (m)	3.24 (m)	3.71, 4.24 (d, 16)		6.62	b)	b)	5.87	3.97
17	6.66 (d, 10)	5.90 (dd, 10, 6)	5.31 (m)	1.99 (m)	2.92 (m)	3.80, 4.42 (d, 17)	6.48	6.82	1.99 (m)	3.40 (m)	5.87	2.00
19	5.30 (d, 4)	5.54 (br s)	b)	b)	3.40 (m)	3.74, 4.18 (d, 17)		6.16	b)	b)	5.82	2.08 (6H) 3.94

a) Measured in $CDCl_3$ as free bases except that **8** was measured in pyridine-d_5 as its picrate. All signals are singlets unless otherwise indicated in parentheses.
b) Obscured signals.

TABLE II. Mass Data for 3-*O*-Acetylhamayne (**11**) and Related Compounds

	3	**8**	**9**	**11**	**12**[a]
m/z (rel. int.)	301 (M^+, 0.5)	287 (M^+, 0.4)	371 (M^+, 34)	329 (M^+, 1.1)	301 (M^+, 100)
			311 (27)	300 (5)	
	(a) 269 (100)	(a) 269 (100)	(a) 269 (31)	(a) 269 (100)	(a) 269 (30)
	251 (17)		251 (41)	251 (9)	257 (50)
	(b) 240 (42)	(b) 240 (31)	(b) 240 (29)	(b) 240 (37)	227 (90)
	(c) 225 (25)	(c) 225 (16)	(c) 225 (40)	(c) 225 (22)	(c) 225 (65)
	(d) 224 (42)	(d) 224 (14)	(d) 224 (63)	(d) 224 (24)	(d) 224 (30)
	223 (73)	(e) 211 (21)	(e) 211 (33)	(e) 211 (26)	
	(f) 181 (26)	(f) 181 (36)	(f) 181 (68)	(f) 181 (73)	(f) 181 (50)

a) From ref. 8.



(a) (b) (c) (d) (e) (f)

(see Experimental). Based on these findings and on spectral and physical data, base G was identified as undulatine (**13**).[14]

Base H (**14**), a phenolic base, mp 210—213 °C, $C_{17}H_{19}NO_3$, gave a blue-violet color with ferric chloride reagent. Treatment of the base with diazomethane gave an *O,O*-dimethylated product (**15**), mp 82—83 °C, $C_{19}H_{23}NO_3$. The ^{1}H-NMR spectra of base H (a diphenolic base) and its methylated product (**15**) both showed signals characteristic of a 1,4-disubstituted aromatic ring [δ 6.74 and 7.01, and 6.82 and 7.10 (both 2H, A_2B_2-patterns)] and of *para*-oriented aromatic protons [δ 6.32 and 6.56, and 6.34 and 6.55 (both 1H, s)] on a second aromatic ring. From these findings and by comparison of the physical and spectral data (see Experimental) with those reported for cherylline (**14**) and its dimethylated derivative (**15**),[15] base H was assigned as cherylline (**14**). This assignment was consistent with the carbon 13 nuclear magnetic resonance (^{13}C-NMR) data and was confirmed by direct X-ray analysis of the base (**14**).

Isolation of Alkaloids from *C. bulbispermum* MILNE-REDHEAD *et* SCHWEICKERDT

As described in Experimental, fresh bulbs of this plant treated in the same way as described for *C. lactifolium* L. gave nine bases, bases B (**5**), C (**4**), D (**3**), H (**14**), I, J, K, L, and M.

Base I (**16**) was crystallized from acetone as colorless needles, mp 214—215 °C, $C_{17}H_{19}NO_5$. Its ^{1}H-NMR spectrum and MS showed the presence of an oxiran ring (δ 3.27 and 3.67, and *m/z* 288 $[M-CHO]^+$) and were similar to those of undulatine (**13**),[14] except for a signal and fragments due to the aliphatic *O*-methyl group. Thus, base I was assigned as crinamidine (**16**).[15a,16] This assignment was confirmed by the identity of physical data for

base I with those for **16** in the literature.[14a,15a,16]

Similarly, base J (mp 138—139 °C, $C_{18}H_{19}NO_4$) and base K (mp 208—210 °C, $C_{20}H_{21}NO_6$) were confirmed to be *O*-acetylcrinine (**17**)[15a,17] and diacetyllycorine (**7**),[5b] respectively.

Base L (**18**), $C_{17}H_{21}NO_5$, was isolated as an amorphous powder. Its ^{1}H-NMR spectrum showed the presence of an aromatic ring having an aromatic proton (δ 7.54, s), an *O*-methyl group and a methylenedioxy group, and of two methine protons (δ 4.10 and 4.20) attached to oxygenated carbon atoms. The methine proton signals are deshielded at δ 5.32 and 5.58 in the ^{1}H-NMR spectrum of its diacetylated product (bowdensine) (**19**), for which monitoring of the line of 1-H (δ 5.32) gave an INDOR peak at δ 5.58 (2-H) and an NOE peak at δ 6.18; irradiation at δ 6.18 (10-H) gave a 17% NOE increment in the signal of 1-H. In the MS of base L (see Experimental), the fragmentation pattern is very similar to that of deacetylbowdensine (**18**).[8] From these findings and the identity of the diacetylated product of base L with natural bowdensine (**19**) (see below), base L was established as deacetylbowdensine (**18**), although it was an amorphous powder [lit.[16] deacetylbowdensine, mp 277—278 °C (dec.)].

Base M (**19**), amorphous powder, $C_{21}H_{25}NO_7$, $[\alpha]_D^{20}$ +25.9° ($CHCl_3$), was established to be bowdensine (**19**)[16,18] on the basis of its NMDR data and the fact that physical data for base M were in good agreement with those for the diacetylated derivative of **18** (prepared by treatment of **18** with acetic anhydride and pyridine) and those in the literature.[16,18]

Experimental

All melting points are uncorrected. IR, MS, and ORD spectra were measured with Hitachi IR-215, JEOL JKS-D-300, and JASCO ORD/UV-5 spectrometers, respectively. ^{1}H-NMR spectra were recorded with a JEOL JNM-PS-100 or Hitachi R-22 spectrometer and ^{13}C-NMR spectra with a JEOL JNM-PX-200 spectrometer (50.10 MHz). Chemical shifts are measured on the δ (ppm) scale with tetramethylsilane as an internal standard. The plates used for PLC were coated with silica gel (Kieselgel, PF_{254} Merck) and aluminum oxide (GF_{254} Merck).

Isolation of Alkaloids from *C. latifolium* L.——Following the method of Wildman and Bailey,[4] fresh bulbs (3.8 kg) of this plant collected on the campus of Tokushima University were ground in 99% EtOH in a mixer. The insoluble material was extracted three times with 6 l of 99% EtOH. The ethanolic extract was evaporated to approximately 3 l *in vacuo*, made acidic (pH 4) with tartaric acid, and washed with ether to remove the neutral and acidic material. The aqueous acidic solution was made basic (pH 7.3) with conc. NH_4OH and extracted three times with 600 ml of $CHCl_3$. The extract was evaporated *in vacuo* to give crude alkaloids (8.5 g). The crude alkaloids gave 2.5 g of $CHCl_3$-insoluble material and 4.5 g of $CHCl_3$-soluble material when mixed with $CHCl_3$ (30 ml). The above aqueous solution (pH 7.3) was made more basic (pH 8.0) and similar treatment gave $CHCl_3$-insoluble material (2.2 g, total 4.7 g 0.0012% yield) and $CHCl_3$-soluble material (2.4 g, total 6.9 g, 0.0018% yield). The $CHCl_3$-soluble material (3.3 g) (from pH 7.3) was subjected to PLC using SiO_2–[$CHCl_3$–MeOH (10 : 1)] to give four fractions: I, *Rf* 0.59—0.52 (110 mg); II, *Rf* 0.41—0.34 [133 mg, crinamine (**3**)]; III, *Rf* 0.28—0.23 (383 mg), and IV, *Rf* 0.23—0.10 [659 mg, crinine (**5**)]. Fraction I was further subjected to PLC using SiO_2–ether to give two fractions: I-A, *Rf* 0.23—0.12 [38 mg, 1-*O*-acetyllycorine (**6**) and I-B, *Rf* 0.11—0.09 [42 mg, 3-*O*-acetylhamayne (**11**)]. Fraction III was further subjected to PLC using SiO_2–[acetone–MeOH (5 : 1)] to give two fractions: III-A, *Rf* 0.62—0.54 [40 mg, cherylline (**14**)] and III-B, *Rf* 0.29—0.18 [106 mg, powelline (**4**)]. The $CHCl_3$-soluble material (2.4 g) (from pH 8.0) was subjected to PLC using SiO_2–[$CHCl_3$–MeOH (10 : 1)] to give a fraction of *Rf* 0.15—0.09 (567 mg), which was further purified by PLC using SiO_2–[$CHCl_3$–MeOH–Et_2NH (92 : 3 : 5)] to give crude hamayne (**8**) (250 mg).

Similar treatment of the fresh leaves (1.9 kg) of this plant gave $CHCl_3$-insoluble material [51 mg, crude lycorine (**2**)] and $CHCl_3$-soluble material (551 mg, 0.0003% yield) from a basic solution of pH 7.3. The latter material was subjected to PLC using SiO_2–[$CHCl_3$–MeOH (10 : 1)] to give three fractions: I, *Rf* 0.70—0.62 [21 mg, undulatine (**13**)]; II, *Rf* 0.41—0.31 (31 mg), which was subjected to PLC using SiO_2–[$CHCl_3$–MeOH–Et_2NH (92 : 3 : 5)] to give base N (*Rf* 0.44—0.34, 15 mg), which was not examined further, and III, *Rf* 0.26—0.19 [35 mg, cherylline (**14**)].

Lycorine (2)——The mp of this base, 256—261 °C (dec.), was not depressed by admixture with an authentic sample of **2** and its IR spectrum was identical with that of authentic **2**.[2]

1-*O*-Acetyllycorine (6) (Base A)——The crude base (**6**) (38 mg) was recrystallized from acetone to give **6** (20 mg), mp 217—219 °C (lit.[16] mp 220—221 °C). $[\alpha]_D^{23}$ −106.0° (*c* = 0.5, $CHCl_3$) (lit.[16] $[\alpha]_D^{24}$ −96° (*c* = 1.1, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.88 (3H, s, $OCOCH_3$), 3.25 (1H, m, 11c-H), 3.48 and 4.14 (each 1H, d, *J* = 13 Hz, 7-H_2), 4.10 (1H, m, 2-H), 5.50 (1H, brs, 3-H), 5.54 (1H, brs, 1-H), 5.86 (2H, s, OCH_2O), 6.50 (1H, s, 8-H), 6.54 (1H, m, 11-H). IR ν_{max}^{KBr} cm^{-1}: 3200 (OH), 1730 (C=O). *Anal.* Calcd for $C_{18}H_{19}NO_5 \cdot 1/2H_2O$: C, 63.89; H, 5.96; N, 4.14. Found: C, 64.23; H, 5.81; N, 3.82.

1-*O*-Acetyllycorine (6) from Diacetyllycorine (7)——According to Nakagawa *et al.*,[6] a mixture of **7** (117 mg), MeOH (30 ml), and 36% HCl (5 ml) was refluxed for 10 min. The product (**6**, 58 mg) was isolated in the usual manner and was shown to be identical with base A by direct comparison of spectral data and by the mixed melting point test.

Crinine (5) (Base B)——The crude base (**5**, 659 mg) was recrystallized from acetone to give **5** (146 mg), mp 204—205 °C (lit.[7] mp 209—210 °C). $[\alpha]_D^{23}$ −17.5° (c=1.0, $CHCl_3$) (lit.[7] $[\alpha]_D^{28}$ −11.1° (c=1.9, $CHCl_3$)). IR ν_{max}^{KBr} cm^{-1}: 3150 (OH), 930 (OCH_2O). ORD (c=0.0049, MeOH) $[M]^{22}$ (nm): −110° (320), −2870° (310), −4390° (307) (trough), 0° (296), +7700° (270), +10500° (254) (peak), 0° (244), −3850° (240). MS m/z (%) (lit.):[8] 271 (M^+, 100) (100), 252 (50) (5), 242 (8) (10), 228 (30) (21), 199 (70) (48), 187 (75) (41). *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.76; H, 6.65; N, 5.07. For ^{1}H-NMR, see Table I.

Powelline (4) (Base C)——The crude base (**4**) (106 mg) was recrystallized from acetone to give **4** (77 mg), mp 200—202 °C (lit.[9b] mp 200—201 °C). $[\alpha]_D^{23}$ +3.9° (c=1.0, $CHCl_3$) (lit.[9b] $[\alpha]_D$ 0° ($CHCl_3$)). IR ν_{max}^{KBr} cm^{-1}: 3170 (OH), 940 (OCH_2O). ORD (c=0.0199, MeOH) $[M]^{22}$ (nm): −30° (340), −301° (320), −1060° (300), −1210° (296) (trough), 0° (285), +1210° (260) (peak), 0° (254), −4700° (250). MS m/z (%): 301 (M^+, 100), 258 (20), 246 (20), 229 (61), 217 (39). High MS: Calcd for $C_{17}H_{19}NO_4$: 301.1315. Found: 301.1315. For ^{1}H-NMR, see Table I.

Crinamine (3) (Base D)——The crude base (**3**) (83 mg) was recrystallized from acetone to give **3** (28 mg), mp 190—191 °C (lit.[2] mp 192—193 °C). IR ν_{max}^{KBr} cm^{-1}: 3200 (OH), 930 (OCH_2O). ORD (c=0.0051, MeOH) $[M]^{21}$ (nm): +1880° (340), +2350° (330), +7650° (310) (peak), +7050° (305), 0° (297), −1180° (290), −2350° (280) (trough), −1770° (270), −2940° (255) (trough), 0° (250), +11800° (240). Base D was identical with authentic **3** on the basis of the IR and ^{1}H-NMR (see Table I) spectra and the mixed melting point test.

Hamayne (8) (Base E)——The base (**8**, 100 mg), mp 83—84 °C, was obtained by recrystallization of the crude base (250 mg) from acetone (lit.[10a] mp 79—80 °C). $[\alpha]_D^{18}$ +78.2° (c=1.1, EtOH) (lit.[10a] $[\alpha]_D^{12}$ +43° (c=0.1, EtOH). IR ν_{max}^{KBr} cm^{-1}: 3380 (OH). ORD (c=0.0052, MeOH) $[M]^{21}$ (nm): +1110° (400), +2760° (330), +7730° (306) (peak), +4970° (300), 0° (290), −1110° (280), −2180° (260) (trough), 0° (254), +13300° (240). High MS. Found: 287.1142, 269.1078, 240.0981, 225.0730, 224.0717, 211.0734, 181.0645. Calcd for $C_{16}H_{17}NO_4$ (M^+): 287.1158, $C_{16}H_{15}NO_3$ (a): 269.1053, $C_{15}H_{14}NO_2$ (b): 240.1025, $C_{14}H_{11}NO_2$ (c): 225.0790, $C_{14}H_{10}NO_2$ (d): 224.0712, $C_{14}H_{11}O_2$ (e): 211.0759, $C_{13}H_9O$ (f): 181.0654 (see Table II). For ^{1}H-NMR, see Table I. Hamayne picrate: mp 205—208 °C (from acetone). ^{1}H-NMR (pyridine-d_5) δ: 8.99 (2H, s, aromatic H of picrate), 7.16 (1H, s, 10-H), 6.74 (1H, s, 7-H), 6.58 (1H, d, J=11 Hz, 1-H), 6.38 (1H, d, J=11 Hz, 2-H). 6.03 (2H, s, OCH_2O), 4.51 and 5.02 (each 1H, d, J=16 Hz, 6-H_2).

11-*O*-Methylcrininamine (10)——(a) From Hamayne (**8**): A solution of **8** (30 mg) in dry benzene (10 ml) was added to a suspension of potassium (150 mg) in dry benzene (30 ml) at 60 °C over a period of 20 min, and the mixture was stirred at 60 °C for 30 min. Then a solution of methyl *p*-toluenesulfonate (55 mg) in dry benzene (0.5 ml) was added at 40 °C and the whole was stirred at 40 °C for 3.5 h. EtOH (1.5 ml) was added to the mixture, and the crude product (**10**) was isolated in the usual manner and recrystallized from ether–petr. ether to give **10** (14 mg), mp 170—172 °C. ORD (c=0.0051, MeOH) $[M]^{25}$ (nm): +3090° (330), +3720° (320), +7400° (310) (peak), +7400° (302) (peak), 0° (292), −2470° (280) (trough), −1850° (262), 0° (252), +142000° (242). High MS: Calcd for $C_{18}H_{21}NO_4$: 315.1471. Found: 315.1449. ^{1}H-NMR ($CDCl_3$) δ: 3.24 (3H, s, 11-OCH_3), 3.38 (3H, s, 3-OCH_3), 3.65 and 4.30 (each 1H, d, J=16 Hz, 6-H_2), 3.98 (1H, t-like, 3-H), 5.87 (2H, s, OCH_2O), 6.02 (1H, dd, J=10 and 1.5 Hz, 2-H), 6.29 (1H, dd, J=10 and 2 Hz, 1-H), 6.44 (1H, s, 7-H), 6.82 (1H, s, 10-H).

(b) From Crinamine (**3**)——Compound **10** (4 mg) was prepared from **3** (15 mg), potassium (45 mg), and methyl *p*-toluenesulfonate (30 mg) by the same procedure as described in (2). It melted at 175—176 °C. High MS: Found: 315.1487. $[\alpha]_D^{25}$ +156.4° (c=0.11, EtOH), +120.0° (c=0.17, $CHCl_3$). ORD (c=0.0059, MeOH) $[M]^{25}$ (nm): +3210° (330), +4280° (320), +8000° (310 and 302) (peak), 0° (290), −2140° (280) (trough), −1600° (262), 0° (252), +128000° (242). The samples of *O*-methylated product (**10**) prepared by procedures (a) and (b) were shown to be identical by the mixed melting test and comparison of spectral data (IR, ^{1}H-NMR and ORD).

3-*O*-Acetylhamayne (11) (Base F)——Colorless prisms, mp 112—114 °C (from benzene), $[\alpha]_D^{21}$ +123.5° (c=0.3, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1730 (C=O), 930 (OCH_2O). ORD (c=0.0116, MeOH) $[M]^{21}$ (nm): +849° (380), +1130° (370), +1700° (350), +2550° (330), +6510° (310) (peak), +3680° (300), 0° (292), −283° (290), −1130° (280) (trough), −849° (270), −566° (256), +2830° (250). High MS: Found: 329.1248, 300.1207, 269.1050, 240.0983, 224.0678, 211.0752, 181.0707. Calcd for $C_{18}H_{19}NO_5$ (M^+): 329.1261, $C_{17}H_{18}NO_4$: 300.1236, $C_{16}H_{15}NO_3$ (a): 269.1053, $C_{15}H_{14}NO_2$ (b): 240.1025, $C_{14}H_{10}NO_2$ (d): 224.0711, $C_{14}H_{11}O_2$ (e): 211.0759, $C_{13}H_9O$ (f): 181.0654 (see Table II). For ^{1}H-NMR, see Table I.

Diacetylhamayne (9)——(a) From Hamayne (**8**): A mixture of **8** (21 mg), Ac_2O (2 ml), and pyridine (3 ml) was heated at 130 °C for 3 h. The crude product (43 mg) was isolated in the usual manner and subjected to PLC using SiO_2–[$CHCl_3$–MeOH–H_2O (50 : 15 : 2)] to give **9** (12 mg), mp 113—114 °C (from ether–pet.ether) (lit.[10] mp 77.5—78 °C). $[\alpha]_D^{20}$ +42.1° (c=0.12, MeOH). High MS: Found: 371.1348, 311.1144, 269.1043, 251.0941, 240.0961, 225.0754, 224.0732, 211.0774. Calcd for $C_{20}H_{21}NO_6$ (M^+): 371.1369, $C_{18}H_{17}NO_4$: 311.1158, $C_{16}H_{15}NO_3$ (a): 269.1053, $C_{16}H_{13}NO_2$: 251.0947, $C_{15}H_{14}NO_2$ (b): 240.1025, $C_{14}H_{11}NO_2$ (c): 225.0790, $C_{14}H_{10}NO_2$ (d): 224.0711, $C_{14}H_{11}O_2$ (e): 211.0759 (see Table II). For ^{1}H-NMR see Table I.

(b) From 3-*O*-Acetylhamayne (**11**)——Similar treatment of **11** (14 mg), Ac_2O (2 ml), and pyridine (3 ml) gave

crude **9** (6 mg), which was recrystallized from ether to give **9**, mp 107—108 °C. $[\alpha]_D^{20}$ +45.7° (c=0.15, MeOH). The samples of **9** prepared by procedures (a) and (b) were shown to be identical by the mixed melting point test and comparison of spectral data (IR, ^{1}H-NMR, and ORD).

Undulatine (13) (Base G)——The crude base (13.21 mg) was recrystallized from acetone as needles (12 mg), mp 143—144 °C (lit. mp 148—149 °C,[14a] 151—152 °C[14b]). High MS: Found: 331.1399, 302.1300. Calcd for $C_{18}H_{21}NO_5$ (M^+): 331.1419, $C_{17}H_{20}NO_4$: 302.1392. MS m/z (%): 331 (base peak), 302 (14), 300 (18), 286 (24), 270 (42), 258 (28). ORD (c=0.0103, MeOH) $[M]^{20}$ (nm): −332° (310), −2580° (295) (trough), 0° (280), +1290° (270), +1930° (256) (peak), 0° (251), −3220° (245) (trough), −2580° (240). For ^{1}H-NMR, see Table I.

Cherylline (14) (Base H)——The crude base (40 mg) was recrysatllized from EtOH to give **14** (21 mg), mp 210—213 °C (lit. mp 217—218 °C, [15b] 213—214 °C[15a]). $[\alpha]_D^{20}$ −70.6° (c=0.24, MeOH) (lit.[15b] $[\alpha]_D^{26}$ −69° (c=0.2, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3330 (OH). High MS: Found: 285.1373. Calcd for $C_{17}H_{19}NO_3$: 285.1365. MS m/z (%): 285 (M^+, 32), 242 (100), 241 (77), 227 (21), 225 (64), 211 (49), 181 (19). ^{1}H-NMR (CD_3OD) δ: 2.40 (3H, s, NCH_3), 2.40 and 3.04 (each 1H, m, 3-H_2), 3.42 and 3.68 (each 1H, d, J=14 Hz, 1-H_2), 3.58 (3H, s, OCH_3) 4.12 (1H, m, 4-H), 6.32 (1H, s, 5-H), 6.56 (1H, s, 8-H), 6.74 and 7.01 (each 2H, A_2B_2-pattern, aromatic H). ^{13}C-NMR (CD_3OD): 45.5 (d, C-4), 45.6 (q, N$\underline{C}H_3$), 56.4 (q, O$\underline{C}H_3$), 58.6 (t, C-3), 63.0 (t, C-1), 113.4 (d, C-5), 113.6 (d, C-8), 116.4 (d, C-3′ and C-5′), 127.8 (s, C-4a), 129.5 (s, C-8a), 131.0 (d, C-2′ and C-6′), 136.1 (s, C-1′), 146.4 (s, C-4′), 148.2 (s, C-7), 157.3 (s, C-6).

Crystal Data: Crystals of $C_{17}N_{19}NO_3$ (**14**) are orthorhombic, space group $P2_12_12_1$, with a=9.838 (5), b=16.676 (3), c=8.742 (2) Å; V=1434.0 (8) A^3; Z=4 and D_x=1.32 g/cm^3. A computer-controlled Rigaku four-circle diffractometer with graphite-monochromated Mo-$K\alpha$ radiation was used for all measurements. Within the range $2\theta \leqq 50°$, 1609 independent reflections with $|F| \leqq 3\sigma(F)$ were observed. The structure was solved by the direct method using MULTAN[19] and refined by the block-diagonal least-squares method to an R value of 0.058.

All hydrogen atoms were located on a difference map and they were included only in the calculations of the structure factors with an isotropic temperature factor.[20]

***O,O*-Dimethylcherylline (15)**——A mixture of ethereal diazomethane [prepared from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (4.3 g), KOH (1.5 g), H_2O (2 ml), carbitol (7 ml), and ether (27 ml)] and **14** (50 mg) was allowed to stand overnight at 0 °C. The crude product (30 mg) was isolated in the usual manner and recrystallized from acetone–petr. ether to give **15** (16 mg), mp 82—83 °C (lit.[15b] mp 87—89 °C). MS m/z (%): 313 (M^+, 14), 270 (51), 239 (100), 224 (7), 195 (6). ^{1}H-NMR ($CDCl_3$) δ: 2.41 (3H, s, NCH_3), 2.48 and 2.98 (each 1H, d, J=11 Hz, 1-H_2), 3.64, 3.78, and 3.84 (each 3H, s, 6-, 7-, and 4′-OCH_3, respectively), 4.14 (1H, m, 4-H), 6.34 and 6.55 (each 1H, s, 5- and 8-H), 6.82 and 7.10 (each 2H, A_2B_2-pattern, aromatic H). The mass and ^{1}H-NMR spectra of this compound were identical with those of the antipode of **14** given in the literature.[15b]

Isolation of Alkaloids from *C. bulbispermum* Milne-Redhead *et* Schweickerdt——Fresh bulbs (9 kg) of this plant were treated in the same way as those of *C. latifolium* L. to give $CHCl_3$-insoluble basic material (540 mg, 0.00006% yield) and $CHCl_3$-soluble basic material [13.0 g (from pH 8.0), 0.00144% yield, and 4.4 g (from pH 10.0), 0.00049% yield]. The $CHCl_3$-soluble material (900 mg of 13.0 g) was subjected to PLC using SiO_2–[$CHCl_3$–MeOH (10 : 1)] to give seven fractions: I, *Rf* 0.84—0.79 [2.5 mg, diacetyllycorine (**7**)]; II, *Rf* 0.62—0.58 [38 mg, bowdensine (**19**)]; III, *Rf* 0.57—0.51 (31 mg); IV, *Rf* 0.36—0.28 [81 mg, crinamine (**3**)]; V, *Rf* 0.28—0.22 (105 mg); VI, *Rf* 0.21—0.15 [217 mg, powelline (**4**)]; VII, *Rf* 0.15—0.05 (279 mg). Fraction III was further subjected to PLC using SiO_2–[$CHCl_3$–MeOH–Et_2NH (92 : 3 : 5)] to give *O*-acetylcrinine (**17**) (18 mg, *Rf* 0.94—0.86). Fractions V and VII were further subjected to PLC using SiO_2–[$CHCl_3$–MeOH–H_2O (70 : 15 : 2)] to give crinamidine (**16**) (43 mg, *Rf* 0.72—0.57) and cherylline (**14**) (29 mg, *Rf* 0.55—0.43), and crinine (**5**) (200 mg, *Rf* 0.49—0.23), respectively. The $CHCl_3$-soluble material (280 mg of 4.4 g) was subjected to PLC using Al_2O_3–[$CHCl_3$–MeOH (20 : 1)] to give two fractions: I, *Rf* 0.74—0.59 [198 mg, crinine (**5**)], and II, *Rf* 0.58—0.45 (57 mg), which was further subjected to PLC using SiO_2–

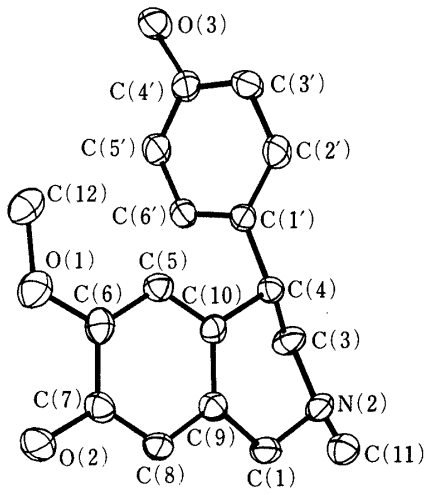


Fig. 1. Molecular Structure of Cherylline (**14**)

[$CHCl_3$–MeOH–Et_2NH (92 : 3 : 5)] to give deacetylbowdensine (**18**) (36 mg, *Rf* 0.74—0.62).

Crinamidine (16) (Base I)——Colorless needles, mp 214—215 °C (lit.[16] mp 232—233 °C). $[\alpha]_D^{21}$ −9.3° (*c* = 0.11, $CHCl_3$) (lit.[16] $[\alpha]_D^{27}$ −7° (*c* = 0.6, $CHCl_3$)). High MS: Found: 317.1263, 288.1238. Calcd for $C_{17}H_{19}NO_5$: 317.1264, $C_{16}H_{18}NO_4$: 288.1236. MS *m/z* (%): 317 (M^+, 78), 299 (17), 288 (100), 270 (34), 258 (26), 245 (31), 217 (35), 205 (42), 189 (24), 173 (42). For ^{1}H-NMR, see Table I.

***O*-Acetylcrinine (17) (Base J)**——Colorless prisms, mp 138—139 °C (lit. mp 140—141 °C,[15a] 142—143 °C,[17] 145—146 °C[21]). $[\alpha]_D^{17}$ +69.4° (*c* = 0.23, EtOH) (lit.[20] $[\alpha]_D^{20}$ +68° ± 2° (*c* = 1.1, EtOH). High MS: Found: 313.1318. Calcd for $C_{18}H_{19}NO_4$: 313.1315. IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O), 940 (OCH_2O). For ^{1}H-NMR, see Table I.

Diacetyllycorine (7) (Base K)——Pale yellow needles, mp 208—210 °C (lit.[5b] mp 215—216 °C (dec.)). IR ν_{max}^{KBr} cm^{-1}: 1730 and 1720 (C=O), 930 (OCH_2O). High MS: Found: 371.1381. Calcd for $C_{20}H_{21}NO_6$: 371.1369. ^{1}H-NMR ($CDCl_3$) δ: 1.92 and 2.06 (each 3H, s, $OCOCH_3$), 3.50 and 4.14 (each 1H, d, *J* = 14 Hz, 6-H_2), 5.24 (1H, br s, 2-H), 5.52 (1H, br s, 3-H), 5.72 (1H, br s, 1-H), 5.90 (2H, s, OCH_2O), 6.57 (1H, s, 8-H), 6.76 (1H, s, 11-H).

Deacetylbowdensine (18) (Base L)——Amorphous powder (lit.[16] mp 277—278 °C (dec.)). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). High MS: Found: 319.1418. Calcd for $C_{17}H_{21}NO_5$: 319.1420. MS *m/z* (%) (lit.[8] %): 319 (M^+, 100) (100), 302 (11) (16), 290 (8) (18), 275 (32) (13), 232 (46) (20). ^{1}H-NMR ($CDCl_3$–pyridine-d_5) δ: 3.86 and 4.34 (each 1H, d, *J* = 17 Hz, 6-H_2), 3.94 (3H, s, OCH_3), 4.10 (1H, d, *J* = 4 Hz, 1-H), 4.20 (1H, m, 2-H), 5.80 (1H, s, OCH_2O), 7.54 (1H, s, 10-H).

Acetylation of Deacetylbowdensine (18)——A mixture of **18** (36 mg), Ac_2O (1 ml), and pyridine (0.7 ml) was stirred at 100 °C for 45 min. The product was isolated in the usual manner to give bowdensine (**19**) (36 mg, 79% yield) as an amorphous powder. ^{1}H-NMR ($CDCl_3$) δ: 2.09 (6H, s, $OCOCH_3 \times 2$), 3.41 (1H, m, 4a-H), 3.78 and 4.22 (each 1H, d, *J* = 17 Hz, 6-H_2), 3.97 (3H, s, OCH_3), 5.32 (1H, d, *J* = 4 Hz, 1-H), 5.58 (1H, m, 2-H), 5.83 (2H, s, OCH_2O), 6.18 (1H, s, 10-H). This sample appeared to be identical with natural **19** (see below) by direct comparison of IR and ^{1}H-NMR spectra.

Bowdensine (19) (Base M)——Amorphous powder, $[\alpha]_D^{20}$ +25.9° (*c* = 1.0, $CHCl_3$) (lit.[16] $[\alpha]_D^{24}$ +17.3° (*c* = 1.06, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 940 (OCH_2O). High MS: Found: 403.1651. Calcd for $C_{21}H_{25}NO_7$: 403.1632. For ^{1}H-NMR, see Table I.

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