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ALKALOIDS FROM *CRINUM AMABILE*

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Key Word Index—*Crinum amabile*; Amaryllidaceae; bulbs; alkaloids; crinamabine; 4a-dehydroxycrinamabine.

Abstract—From the bulbs of Vietnamese *Crinum amabile*, besides lycorine, buphanisine and augustine, for the first time, ambelline, flexinine, and two new alkaloids crinamabine and 4a-dehydroxycrinamabine were isolated. Their structures were established from spectroscopic evidence. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Amaryllidaceae alkaloids are known for their pharmacological and microbiological activities, among them, antiviral, antitumor, and anticholinergic effects. More recently, pharmacological activities against HIV were also reported [1].

Continuing our investigations of the constituents of the Amaryllidaceae, we examined *Crinum amabile* of Vietnamese origin. This widely grown species is not only a decorative plant, but also it has been used for a long time in Vietnamese folk medicine as an emetic and as a remedy for rheumatism and earache [2]. In the present paper, we report the isolation of seven alkaloids from dried bulbs of *C. amabile*. Besides the known alkaloids, lycorine (**1**), buphanisine (**4**) and augustine (**7**) [3, 4], for the first time, ambelline (**5**) and flexinine (**6**) were isolated (Fig. 1). In addition, two new alkaloids with a crinan-triol and -diol structure, designated as crinamabine (**2**) and 4a-dehydroxycrinamabine (**3**), respectively, were found. Their structures were established by spectroscopic methods, especially one- and two-dimensional NMR and circular dichroism (CD). The new alkaloid crinamabine is the only triol alkaloid with the OH group at C-4a among about 70 crinane alkaloids.

RESULTS AND DISCUSSION

Multiple column chromatography of the alkaloid extract on silica gel afforded alkaloids **1**–**7**. The major alkaloid lycorine (**1**) was identified on the basis of melting point, mass spectroscopic data and optical rotation characteristics. The structures of **2**–**7** were established on the basis of mass spectrometry, one- and two-dimensional ^{1}H and ^{13}C NMR and CD spectroscopy.

Alkaloids **2**–**7** contained the 5,10b-ethanophenanthridine system. They exhibit very similar UV spectra, showing maxima at *ca* 240 and 290 nm, corresponding to the aromatic methylendioxyphenylene chromopore. The presence of the methylendioxy group is also indicated by IR bands at 1615, 1480 and 940 cm^{-1}. All three alkaloids show in their mass spectra typical fragmentation of the crinine-type with a characteristic fragment at *m/z* 115 (C_9H_9) [5–7]. In the low mass region, alkaloids **2**–**4**, **6** and **7** show peaks at *m/z* 187, 185, 172, 157. The mass spectra of **4** and **5** are identical to those of buphanisine and ambelline, respectively. Those of **6** and **7** to flexinine and augustine, respectively, showing typical fragmentation patterns of compounds with an epoxide ring at the 1,2 position [7].

The EI mass spectrum of the new alkaloid **2** ($C_{16}H_{19}NO_5$) shows a $[M]^+$ peak at *m/z* 305. The spectrum showed a close structural relation to the other new alkaloid **3**, $C_{16}H_{19}NO_4$, which shows in its EI mass spectrum $[M]^+$ at *m/z* 289 as well as a base peak at *m/z* 202. It differs from **2** only by the loss of one hydroxyl group. Both spectra exhibit the base peak at *m/z* 202 arising from α-cleavage at the nitrogen and then from the elimination of the $C_4H_5O_2$ fragment, which is usually found for 1,2-diol crinane alkaloids [5]; they showed coincidence of all similar peaks in the low mass region. Moreover, the spectrum of **2** shows the loss of an OH group occurring before the elimination of the $C_4H_5O_2$ fragment.

The correspondence of relevant ^{1}H NMR signals led to the initial structural elucidation of alkaloids **2** and **3**. Their ^{1}H NMR spectra exhibit two singlets (**2**: at δ 7.64 and 6.63; **3**: at δ 7.58 and 6.54) and an AB-

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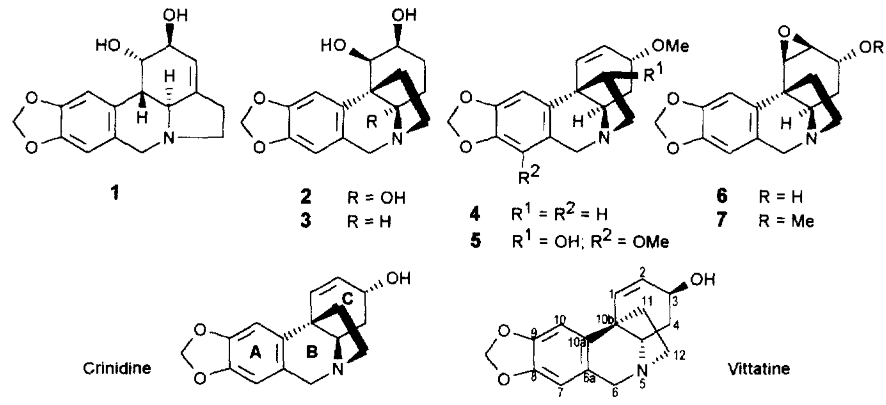

Fig. 1. Structures of lycorine (**1**), crinamabine (**2**), 4a-dehydroxycrinamabine (**3**), buphanisine (**4**), ambelline (**5**), flexinine (**6**) and augustine (**7**).

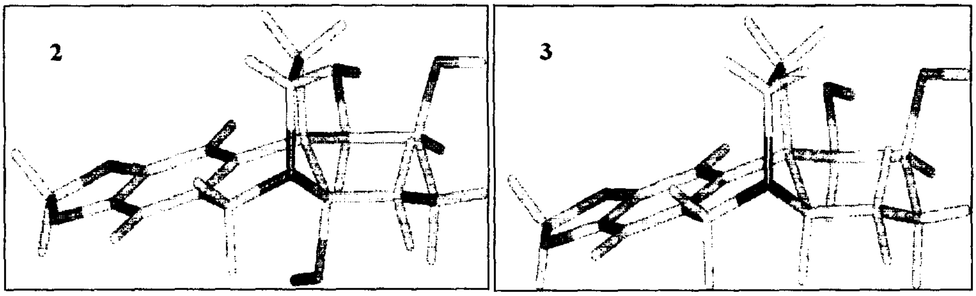

Fig. 2. Energy-minimized 3D structures of crinamabine (**2**) and 4*a*-dehydroxy-crinamabine (**3**).

system (**2**: at δ 5.93 and 5.92; **3** at δ 5.90 and 5.89) assignable to two *para*-aromatic protons H-10 and H-7, and the two protons of the methylenedioxy group, respectively (see Table 1). Additionally, an AB-system at δ 4.69 and 4.18 in **2** and at δ 4.53 and 4.05 in **3**, corresponds to the two benzylic methylene protons, H-6α and H-6β. Four multiplets (**2**: at δ 3.29, 2.05, 3.75 and 3.34; **3**: at δ 3.08, 2.06, 3.62 and 3.10) of four methylene protons at C-11 and C-12, as well as four multiplets (**2**: at δ 2.02, 2.01, 1.83 and 2.42; **3**: at δ 1.60, 2.00, 1.63 and 1.85) of four methylene protons at C-3 and C-4, are also observed.

The major differences between the two ^{1}H NMR spectra are associated with the signals resulting from the proton of C-4a, due to the substitution of the proton at C-4a of **3** by the hydroxyl group of **2**, which causes characteristic resonance shifts of the protons H-4α and 4β, H-6α and 6β, H-12α and 12β, and H-11α to lower field. This substitution has also been proved by the ^{13}C NMR of **2** and **3**. The ^{13}C NMR and DEPT spectra of **3** indicated the presence of five methylene carbons (δ 59.9, 52.6, 35.5, 28.8 and 19.7), three methine carbons (δ 72.7, 70.0 and 69.8) and quarternary carbon (δ 50.5, C-10b) in the aliphatic region. The spectra of **2** also show the presence of five methylene carbons (δ 54.8, 49.7, 34.5, 28.0 and 25.9) but also two methine carbons (δ 71.8 and 70.2) and two quarternary carbons (δ 96.8 for C-4a and 51.7 for C-10b). In the DEPT spectrum of **2**, the methine carbon resonance of C-4a of **3** (δ 69.76) disappeared and instead of this a quarternary carbon resonance (δ 96.8) occurred. The chemical shifts indicated that the two methine carbons (**2**: at δ 71.8 and 70.2; **3**: at δ 72.7 and 70.0) were hydroxylated.

The assignments of ^{1}H, as well as ^{13}C shifts, of **2** and **3** (Tables 1 and 2) were confirmed by two-dimensional ^{1}H and ^{13}C NMR (HMQC, HMBC, COSY, TOCSY and NOESY) spectra. The HMQC of **3** showed correlation of the methine carbon C-4a with the proton H-4a at δ 3.37, which has not been found in the corresponding spectrum of **2**. These spectra also verified the correlation of protons H-1 and H-2 (**2**: at δ 3.98 and 4.08; **3**: at δ 3.99 and 4.03) with the hydroxylated methine carbons at δ 71.8 and 70.2 of **2**, as well as at δ 72.7 and 70.0 of **3**. This fact and the vicinal coupling between these protons, which was observed in the COSY spectra, proved the glycol partial structure of **2** and **3**. The corresponding NOESY spectra show the NOE of the methine proton H-1 with H-2 and H-10 (**2**: at δ 7.64; **3**: at δ 7.58) as well as with H-3α axial (**2**: at δ 2.02; **3** at δ 1.60) and with H-4a in the axial α-position of **3** (δ 3.37). Therefore, H-1 possesses the α-position (axial) and the OH group at C-1 must have an β-equatorial orientation. The

Table 1. Proton shifts of alkaloids **2**–**7**; chemical shifts are in δ from TMS, coupling constants in Hz

H-Atom	Crinamabine (**2**) (CD_3OD)	4a-Dehydroxycrinamabine (**3**) (CD_3OD)	Buphanisine (**4**) ($CDCl_3$)	Ambelline (**5**) ($CDCl_3$)	Flexinine (**6**) ($CDCl_3$)	Augustine (**7**) ($CDCl_3$)
H-1	3.98 *d* (4.2)	3.99 *d* (4.3)	6.61 *d* (10.0)	6.54 *d* (10.1)	3.76 *d* (3.4)	3.77 *d* (3.5)
H-2	4.08 *ddd* (4.2, 3.2, 2.7)	4.03 *ddd* (4.3, 3.4, 2.3)	5.96 *dd* (10.0, 5.2)	6.03 *ddd* (10.1, 5.2, 0.9)	3.32 *dd* (3.4, 2.1)	3.32 *dd* (3.5, 2.5)
H-3α	2.02 *dddd* (−10.1, 10.7, 3.6, 2.7)	1.60 *dddd* (−14.4, 13.8, 3.5, 2.3)				
H-3β	2.01 *dddd* (−10.1, 6.9, 3.2, 3.0)	2.0 *dddd* (−14.4, 3.4, 3.4, 3.2)	3.82 *ddd* (5.2, 4.1, 1.8)	3.82*ddd* (5.2, 4.1, 1.9)	4.55 *ddd* (3.1, 2.4, 2.1)	3.97 *ddd* (3.0, 2.5, 2.4)
H-4α	1.83 *ddd* (−13.4, 3.6, 3.0)	1.63 *dddd* (−12.8, 5.1, 3.5, 3.4)	2.08 *ddd* (−13.8, 3.9, 1.8)	2.11 *ddd* (−13.8, 3.9, 1.9)	1.89 *ddd* (−13.8, 3.4, 2.4)	1.70 *ddd* (−13.9, 3.6, 2.4)
H-4β	2.42 *ddd* (−13.4, 10.7, 6.9)	1.85 *dddd* (−12.8, 13.8, 12.5, 3.2)	1.59 *ddd* (−13.8, 13.4, 4.1)	1.67 *ddd* (−13.8, 13.6, 4.1)	1.61 *ddd* (−13.8, 13.3, 3.1)	1.40 *ddd* (−13.9, 13.3, 3.0)
H-4a		3.37 *dd* (12.5, 5.1)	3.34 *dd* (13.4, 3.9)	3.40 *dd* (13.6, 3.9)	3.41 *dd* (13.3, 3.4)	3.09 *dd* (13.3, 3.6)
H-6α	4.69 *d* (−15.2)	4.53 *d* (−16.0)	4.40 *d* (−16.7)	4.28 *d* (−17.4)	4.48 *d* (−16.5)	4.37 *d* (−16.8)
H-6β	4.18 *d* (−15.2)	4.05 *d* (−16.0)	3.8 *d* (−16.7)	3.85 *d* (−17.4)	3.82 *d* (−16.5)	3.69 *d* (−16.8)
H-7	6.63 *s*	6.54 *s*	6.47 *s*		6.49 *s*	6.47 *s*
H-10	7.64 *s*	7.58 *s*	6.83 *s*	6.60 *s*	6.92 *s*	6.88 *s*
H-11α	3.29 *ddd*(−13.5, 11.5, 6.6)	3.08 *ddd* (−12.7, 11.2, 6.8)	1.91 *ddd* (−12.8, 11.2, 5.9)	4.36 *dd* (8.2, 4.3)	2.49 *ddd* (−12.5, 11.0, 6.0)	2.38 *ddd* (−13.0, 10.8, 5.7)
H-11β	2.05 *ddd* (−13.5, 9.5, 4.0)	2.06 *ddd* (−12.7, 9.2, 4.0)	2.16 *ddd* (−12.8, 9.1, 4.3)		2.09 *ddd* (−12.5, 9.1, 4.5)	2.0 *ddd* (−13.0, 9.2, 4.6)
H-12α	3.75 *ddd* (−12.5, 11.5, 4.0)	3.62 *ddd* (−12.8, 11.2, 4.0)	3.38 *ddd* (−13.2, 11.2, 4.3)	3.71 *dd* (−14.0, 8.2)	3.39 *ddd* (−13.0, 11.0, 4.5)	3.18 *ddd* (−12.9, 10.8, 4.6)
H-12β	3.34 *ddd* (−12.5, 9.5, 6.6)	3.10 *ddd* (−12.8, 9.2, 6.8)	2.89 *ddd* (−13.2, 9.1, 5.9)	2.48 *ddd* (−14.0, 4.3, 1.6)	2.92 *ddd* (−13.0, 9.1, 6.0)	2.80 *ddd* (−12.9, 9.2, 5.7)
OCH_2O	5.93, 5.92 *AB* (−1.4)	5.90, 5.89 *AB* (−1.4)	5.87, 5.86 *AB* (−1.4)	5.90, 5.89 *AB* (−1.4)	5.93, 5.92 *AB* (−1.4)	5.90, 5.89 *AB* (−1.4)
3-OMe			3.35 *s*	3.45 *s*		3.47 *s*
7-OMe				3.99 *s*		

Table 2. Carbon shifts of alkaloids **2**–**7**; chemical shifts are in δ from TMS

C-Atom	Crinamabine (**2**) (CD_3OD)	CH_n	4a-Dehydroxycrinamabine (**3**) (CD_3OD)	CH_n	Buphanisine (**4**) ($CDCl_3$)	CH_n	Ambelline (**5**) ($CDCl_3$)	CH_n	Flexinine (**6**) ($CDCl_3$)	CH_n	Augustine (**7**) ($CDCl_3$)	CH_n
C-1	71.8	CH	72.7	CH	132.9	CH	131.9	CH	53.1	CH	53.9	CH
C-2	70.2	CH	70.0	CH	125.3	CH	126.2	CH	56.2	CH	55.1	CH
C-3	28.0	CH_2	28.8	CH_2	72.7	CH	72.3	CH	64.7	CH	74.9	CH
C-4	25.9	CH_2	19.7	CH_2	28.9	CH_2	28.6	CH_2	28.9	CH_2	25.4	CH_2
C-4a	96.8	C	68.8	CH	63.1	CH	62.9	CH	61.8	CH	61.6	CH
C-6	54.8	CH_2	59.9	CH_2	62.4	CH_2	59.1	CH_2	61.3	CH_2	62.5	CH_2
C-6a	120.9	C	120.0	C	126.4	C	131.7	C	124.2	C	126.9	C
C-7	106.9	CH	107.2	CH	106.8	CH	118.2	C	107.2	CH	107.1	CH
C-8	147.9	C	148.3	C	145.6	C	148.2	C	146.3	C	145.7	C
C-9	149.1	C	149.1	C	146.0	C	141.0	C	146.8	C	146.1	C
C-10	108.4	CH	107.1	CH	102.9	CH	100.3	CH	102.7	CH	102.5	CH
C-10a	136.3	C	139.9	C	138.5	C	134.4	C	136.6	C	137.9	C
C-10b	51.7	C	50.5	C	44.32	C	48.1	C	42.0	C	41.6	C
C-11	34.5	CH_2	35.5	CH_2	44.28	CH_2	86.4	CH	38.4	CH_2	39.3	CH_2
C-12	49.7	CH_2	52.6	CH_2	53.6	CH_2	62.5	CH_2	51.9	CH_2	52.4	CH_2
OCH_2O	102.6	CH_2	102.7	CH_2	100.7	CH_2	100.8	CH_2	101.2	CH_2	100.8	CH_2
3-OMe					56.4	CH_3	56.5	CH_3			57.6	CH_3
7-OMe							59.2	CH_3				

small vicinal coupling constants between H-1 and H-2 (4.2 Hz), between H-2 and two protons H-3, also led us to assign the equatorial α-disposition for H-2. Additionally, the NOE between H-6β and H-12β, H-4β and H-12α, H-11α of **2** and **3**, as well as the NOE between H-4a and H-6α of **3** also support the assignments of the proton shifts of **2** and **3** in Table 1.

Important differences in the ^1H NMR spectrum (in DMSO) of the new alkaloid, 4a-dehydroxycrinamabine (**3**) compared with its isomer, amabiline of *Crinum amabile* of Thailand origin, are the shifts towards the lower field of the protons H-10 (ca 0.8 ppm), H-11α (ca 1 ppm) and H-11β (ca 0.3 ppm). For crinamabine (**2**) and 4a-dehyrdoxycrinamabine (**3**) this signal shift can be caused by the shorter relative spatial distances of the OH-group at C-1 and C-2 (equatorial β-position) to H-10 and H-11α, as well as to H-11β, as compared with those in the case of amabiline.

The energy-minimized three-dimensional structures of the two new alkaloids crinamabine (**2**) and 4a-dehydroxycrinamabine (**3**) were established by computer simulation with the SPARTAN program incorporating NMR, especially NOE data, and analysis of CD data (Table 3), respectively.

Buphanisine (**4**), ambelline (**5**) and augustine (**7**) have been the subject of various NMR studies [4, 8, 9, 10]. However, to the best of our knowledge, complete and reliable ^1H and ^{13}C NMR assignments have not been reported, especially in the case of flexinine (**6**). Therefore, a combination of several NMR techniques including COSY, TOCSY, NOESY, DEPT, HMQC, and HMBC was applied in the present study and the results obtained are summarized in Tables 1 and 2. Moreover, as the discrimination between C-8 and C-9, C-6a and C-10a, H-4α and 4β, H-6α and 6β, H-11α and 11β, H-12α and 12β has been insufficiently investigated up to now, it was also thoroughly examined in this study.

The stereochemistry of alkaloids **1**–**7** was also deduced by CD spectral analysis, using crinidine and vittatine as reference compounds. CD spectroscopy is a powerful tool in stereochemical analysis of Amaryllidaceae alkaloids [11, 12]. Recently, we examined the CD of a series of phenanthridine and benzopyranoindole amaryllidaceae alkaloids [13]. Our results indicate that the shape of the CD spectrum is determined by the stereochemistry of the appropriate heterocyclic ring system in conjunction with the type of dominant chromophores. Therefore, within given structural types and chromophores, the CD technique may be used as a rapid and reliable method for stereochemical analysis of new alkaloids, such as the stereochemistry of dominant ring junction.

Table 3 shows the CD spectral data of alkaloids **2**–**7** from *C. amabile* in comparison with data of crinidine and vittatine. With the exception of ambelline (**5**), the UV and CD transitions are dominated by the methylenedioxyphenyl chromophore. The spectra are characterized by two antipodal CD bands at ca 295 nm and 245 nm, which corresponds to the maxima observed in the UV. All alkaloids are related to the 5,10b-ethanophenanthridine system and possess a B : C *trans-diaxial* configuration, which corresponds to crinidine, and, therefore, exhibits a crinidine-type CD [∓(294 nm/245 nm) sequence of the sign of cor-

Table 3. CD spectral data on alkaloids **1**–**7** methanol

Alkaloid	Type of ring fusion*	CD maxima : λ (nm), [θ]
Lycorine (**1**)	B : C *trans*-1	293.0 (−6995) ; 245.2 (+5080)
Crinamabine (**2**)	B : C *trans*-1	292.4 (−916) ; 242.8 (+2912)
4a-Dehydroxycrinamabine (**3**)	B : C *trans*-1	298.0 (−1367) ; 246.0 (+4270)
Buphanisine (**4**)	B : C *trans*-1	294.0 (−10,330) ; 244.4 (+11,800)
Ambelline (**5**)	B : C *trans*-1	283.6 (−255) ; 254.4 (+94)
Flexinine (**6**)	B : C *trans*-1	295.4 (−4000) ; 244.4 (+7250)
Augustine (**7**)	B : C *trans*-1	295.0 (−5945) ; 244.4 (+9840)
Vittatine	B : C *trans*-2	294.2 (+9440) ; 244.2 (−11,790)
Crinidine	B : C *trans*-1	293.2 (−10,480) ; 244.4 (+13,140)

* Type of ring fusion refers to Fig. 2 in ref. [13].

responding Cotton effects] [13]. Substituents on the C-ring are not likely to have any substantial influence on the general shape of the CD, although significant differences of magnitude are obtained. On the contrary, ambelline (**4**), which has a methoxyl substituent in the aromatic A-ring, shows an unusual CD, exhibiting very small Cotton effects at 283.6 nm and 254.4 nm. Such unusual CD behaviour was also found for powellane in contrast to crinane [11] and this might also be caused by the methoxyl substituent in the aromatic A-ring of powellane.

EXPERIMENTAL

General

CD: $d = 0.5$ mm, $c = 0.5$ mg/ml. HRMS and EIMS: 70 eV. NMR spectra: 300/75.5 MHz (Bruker AM 300) and 600/150.9 MHz (Bruker AMX 600), $CDCl_3$ and CD_3OD. CC and FCC: silica gel 60 (Merck, 0.015–0.040 nm). TLC: silica gel 60 F_{254} (Merck), spots visualised UV (254 nm) or by spraying with Dragendorff's reagent.

Extracation and isolation of alkaloids

Bulbs of *C. amabile* Donn. were collected in May 1990 in Hanoi (Vietnam) and identified by Prof. Phan Tong Son at the University of Hanoi. A voucher specimen (named "Nang Hoa Do") is deposited in his herbarium. Bulbs (1.6 kg) were air-dried, powdered and macerated with MeOH (25 l) for one month. Extracts were concd in vacuum and acidified with HOAc to pH 4. After removing neutral components with petrol ether, the acidic soln was extracted with $CHCl_3$ to give extract A (1.31 g). Then, the acidic aq. phase was made alkaline with NH_4OH and again extracted with Et_2O and $CHCl_3$ (extract B). Extract B was dried (Na_2SO_4) and the solvent evapd, yielding crude bases (extract B : 4.77 g). Solvation ($CHCl_3$) and filtration yielded 0.7 g of the alkaloid **1** (lycorine). The $CHCl_3$ solns were combined and evapd to dryness to yield crude alkaloids (4.07 g).

Extract A (1.31 g) was subjected to CC on silica gel (35 cm × 3.2 cm), using toluene, EtOAc and MeOH mixts of increasing polarity until pure MeOH was used. Frs (50 ml, 80 frs) were examined by TLC (silica gel). Frs of similar composition were combined. Frs 30–60 (EtOAc, EtOAc–MeOH, 9 : 1, 4 : 1, 7 : 3, 914 mg) were separated by CC on silica gel (30 cm × 3 cm) eluting with $CHCl_3$, $CHCl_3$–MeOH, 99 : 1, 49 : 1, 97 : 3, 28 : 1, 9 : 1, 4 : 1, 7 : 3 to give 75 mg of alkaloid **7** (frs 22–24, $CHCl_3$–MeOH, 99 : 1), 78 mg of alkaloid **4** (frs 26–30, $CHCl_3$–MeOH, 49 : 1), and 28 mg of alkaloid **5** (frs 32–36, $CHCl_3$–MeOH, 97 : 3).

Extract B (2.64 g) was subjected to CC on silica gel (35 cm × 3.2 cm), using *n*-hexane, EtOAc and MeOH gradients. Frs 41–50 (EtOAc–MeOH, 24 : 1, 312 mg), frs 51–60 (EtOAc–MeOH, 19 : 1, 290 mg), frs 61–80 (EtOAc–MeOH, 9 : 1, 234 mg) and frs 81–100 (EtOAc–MeOH, 4 : 1, 200 mg) were separated using different CC and FCC on silica gel eluting with $CHCl_3$ and $CHCl_3$–MeOH in different proportions to give 195 mg of alkaloid **1**, 45 mg of **7**, 45 mg of **4**, 54 mg of **5**, 42 mg of **6** ($CHCl_3$–MeOH, 97 : 3), 26 mg of **2** ($CHCl_3$–MeOH, 24 : 1) and 30 mg of **3** ($CHCl_3$–MeOH, 9 : 1).

Lycorine (**1**)

Mp 277–279°. $[\alpha]_D^{23}$ −71.2° (*c* 0.125, MeOH). $C_{16}H_{17}NO_4$. MS [70 eV, *m/z* (rel. int.)]: 287 $[M^+]$ (41), 286 (18), 268 (25), 250 (16), 227 (84), 226 (100). UV and CD : see [13].

Crinamabine (**2**)

Mp 235–238°, 250° (dec.). $[\alpha]_D^{25}$ 35° (*c* 0.09, MeOH). HRMS (for $[M+H]^+$, $C_{16}H_{20}NO_5$): found 306.1343, requires: 306.1341. EIMS, *m/z* (rel. int.): 305 $[M]^+$ (60), 287 (11), 261 (30), 243 (87), 202 (100), 201 (53), 190 (44), 174 (62), 161 (37), 131 (49), 115 (59), 85 (63), 83 (60). UV [λ_{max}^{MeOH} nm (log ε)]: 205.6 (4.08), sh 238 (3.21), 292.5 (3.25). CD (MeOH, $[\theta]_\lambda$) : $[\theta]_{223.5}$ 0, $[\theta]_{242.8}$ +2912, $[\theta]_{259.2}$ 0, $[\theta]_{292.4}$ −916.

4a-Dehydroxycrinamabine (**3**)

Mp 208–210° (dec.). $[\alpha]_D^{29}$ 28° (*c* 0.125, MeOH). HRMS (for $[M]^+$, $C_{16}H_{19}NO_4$): found 289.1305, requires: 289.1314. EIMS, *m*/*z* (rel. int.): 289 $[M]^+$ (100), 272 (12), 245 (37), 216 (26), 202 (72), 201 (23), 131 (29), 115 (17), 103 (15). UV [λ_{max}^{MeOH} nm (log ε)]: 205.0 (4.07), sh 237.2 (3.40), 288.6 (3.24). CD (MeOH, $[\theta]_\lambda$): $[\theta]_{219.8}$ 0, $[\theta]_{227.0}$ -2210, $[\theta]_{234.5}$ 0, $[\theta]_{246/0}$ $+4270$, $[\theta]_{261.0}$ 0, $[\theta]_{298.0}$ -1367.

Buphanisine (**4**)

Mp 122–124°. $[\alpha]_D^{24}$ −20.0° (*c* 0.09, MeOH). HRMS (for $[M+H]^+$, $C_{17}H_{20}NO_3$): found: 286.1422, requires: 286.1443. EIMS, *m*/*z* (rel. int.): 285 (50), 270 (17), 254 (23), 253 (4), 230 (16), 216 (25), 215 (100), 201 (32), 198 (18), 187 (15), 185 (23), 172 (20), 157 (29), 128 (23), 115 (27). UV [λ_{max}^{MeOH}*nm* (log ε)]: 205.0 (4.39), sh 240 (3.55), 294.4 (3.73). CD (MeOH, $[\theta]_\lambda$): $[\theta]_{223.4}$ -3510. $[\theta]_{230.4}$ 0, $[\theta]_{244.4}$ $+11{,}800$, $[\theta]_{261.2}$ 0, $[\theta]_{294.0}$ $-10{,}330$.

Ambelline (**5**)

Mp 260–261°. $[\alpha]_D^{25}$ −13.6° (*c* 0.11, MeOH); HRMS (for $[M+H]^+$, $C_{18}H_{22}NO_5$): found: 332.1493, requires: 332.1498. EIMS, *m*/*z* (rel. int.): 331 (79), 316 (7), 302 (31), 300 (29), 299 (38), 298 (26), 287 (100), 270 (36), 260 (94), 257 (68), 256 (26), 255 (79), 254 (50), 241 (64), 239 (56), 211 (84), 190 (54), 115 (63). UV [λ_{max}^{MeOH} nm (log ε)]: 212.7 (4.60), sh 244 (3.64), 286.4 (3.24). CD (MeOH, $[\theta]_\lambda$): $[\theta]_{217.4}$ $-16{,}010$, $[\theta]_{251.7}$ 0, $[\theta]_{254.4}$ $+95$, $[\theta]_{259.4}$ 0, $[\theta]_{283.6}$ -255.

Flexinine (**6**)

Mp 232–234°. $[\alpha]_D^{25}$ −12.7° (*c* 0.11, MeOH); HRMS (for $[M+H]^+$, $C_{16}H_{18}NO_4$): found: 288.1236, requires: 288.1219. EIMS, *m*/*z* (rel. int.): 287 (42), 258 (76), 228 (17), 187 (31), 175 (52), 173 (29), 159 (28), 143 (75), 128 (27), 115 (100). UV [λ_{max}^{MeOH} nm (log ε)]: 205.0 (4.27), sh 240 (3.49), 294.5 (3.64). CD (MeOH, $[\theta]_\lambda$): $[\theta]_{215.8}$ $+8480$, $[\theta]_{230.4}$ $+2000$ (valley), $[\theta]_{244.4}$ $+7250$, $[\theta]_{262.4}$ 0, $[\theta]_{295.4}$ -4000.

Augustine (**7**)

Mp 174–176°. $[\alpha]_D^{24}$ −44.8° (*c* 0.105, MeOH); HRMS (for $[M+H]^+$, $C_{17}H_{20}NO_4$): found: 302.1387, requires: 302.1392. EIMS, *m*/*z* (rel. int.) 301 (60), 286 (6), 272 (7), 270 (5), 268 (2), 256 (9), 228 (27), 187 (24), 175 (100), 143 (57), 115 (71). UV [λ_{max}^{MeOH} nm (log ε)]: 205.0 (4.34), 238.9 (3.56), 294.7 (3.74). CD (MeOH, $[\theta]_\lambda$): $[\theta]_{215.8}$ $+11{,}945$, $[\theta]_{229.4}$ $+2315$ (valley), $[\theta]_{244.4}$ $+9840$, $[\theta]_{262.2}$ 0, $[\theta]_{295.0}$ -5945.

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