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FURTHER ALKALOIDS FROM *BRUNSVIGIA JOSEPHINAE*

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Key Word Index—*Brunsvigia josephinae*; Amaryllidaceae; alkaloids; crinine; buphanisine; buphanidrine; undulatine; 11-*O*-acetylambelline; brunsbelline; hippadine.

Abstract—From the bulbs of *Brunsvigia josephinae* (Amaryllidaceae), crinine, buphanisine, buphanidrine, undulatine, 11-*O*-acetylambelline, brunsbelline and hippadine have been isolated and identified. 11-*O*-Acetylambelline and brunsbelline are reported here for the first time. The structure and stereochemistry of the new alkaloids have been determined by spectroscopic analyses and by the application of 2D NMR techniques. ^{1}H and ^{13}C NMR spectra of crinine, buphanisine, buphanidrine and undulatine have now been completely characterized.

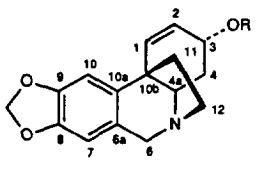
INTRODUCTION

In a previous paper on the alkaloid composition of *Brunsvigia josephinae* (Red.) Ker-Gall., and endemic Amaryllidaceae species from southern Africa, we reported on the isolation and characterization of the known alkaloids: 3-*O*-acetylhamayne, hamayne, crinamine, ambelline (**5**) and sternbergine, together with the novel structure, josephinine [1]. In the present study, we describe the characterization from the same extract of a further two new alkaloids — 11-*O*-acetylambelline (**6**) and brunsbelline (**7**) — as well as the previously known crinine (**1**), buphanisine (**2**), buphanidrine (**3**), undulatine (**4**) and hippadine (**8**).

RESULTS AND DISCUSSION

Extensive column and prep. TLC of an EtOH extract of the bulbs of *B. josephinae* afforded a further seven alkaloids. The EIMS of **1**–**4** gave the molecular ion as the base peak and the fragmentations of **1**–**3** were consistent with compounds of the crinine series with no bridge substituent, and having a double bond in the 1,2-position [2]. Compound **4** exhibited the typical fragmentation pattern for structures with an epoxide group at the 1,2-position [3, 4]. In addition, the molecular ellipticities of **1**–**7** showed CD-curves which were qualitatively similar to those of related β-5,10b-ethanophenanthridine alkaloids [5, 6].

Crinine (**1**). The ^{1}H and ^{13}C resonances were in agreement with previously published data [7–9], but we report here for the first time the unequivocal assignment of both ^{1}H and ^{13}C spectra using multipulse and 2D NMR techniques. In the ^{1}H spectrum the two doublets at δ4.41 and 3.78 were assigned to the 6α and 6β protons, respectively (ROESY). The large coupling (J = 13.5 Hz), which is due to their *trans* diaxial config-



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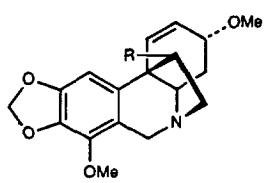
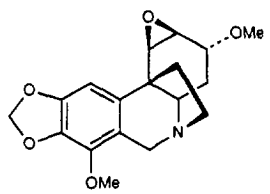


3: R= H
5: R= OH
6: R=OAc



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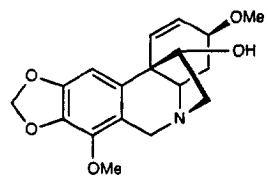

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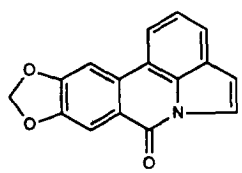

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uration allowed the *dd* at δ3.42 and the *ddd* at δ1.74 to be assigned to H-4a and H-4β, respectively. The H-12 protons were observed as a broad doublet at δ3.36 and a *ddd* at δ2.91, and the low field signal was attributed to H-12*exo* because of its co-planarity with the nitrogen lone pair and the NOE contour correlation with H-4β. The H-11*endo* was found to resonate as a *ddd* at δ2.19 and the H-11*exo* as a *ddd* at δ1.94, the latter being confirmed by the NOE contour between H-4β and H-11*exo*. For the ^{13}C spectrum, the resonances at δ62.9 (*d*) and 61.5 (*t*) could be correctly assigned to C-4a and C-6, respectively, and it was possible to distinguish between C-10b (δ44.3) and C-11 (δ43.6).

Buphanisine (**2**). The ^{1}H and ^{13}C spectra correlated broadly with those in the literature [10, 11]. However, as with **1** the proton signals at high field were not completely assigned and application of techniques similar to those for **1** allowed correct assignments to be made. The XCOR and HMBC techniques were used to confirm the ^{13}C resonances and also to make correct assignments for the C-1 (δ131.9), C-2 (δ125.8) and C-6a (δ124.3) signals which had previously been incompletely assigned [11].

Buphanidrine (**3**). The ^{1}H NMR spectrum was completely assigned, providing additional information with respect to previously published data [12]. The spectrum was similar to that of **2**, aside from the presence of a singlet at δ3.92, attributable to a methoxyl group, and the absence of an aromatic proton. The methoxyl group was assigned to the C-7 position because of the three bond HMBC correlations between H-10 and C-6a as well as with C-10b, and between H-6 protons and C-7, and because of the observed NOE between H-10 and H-1. Shielding effects were also observed on H-10 and H-6α. The ^{13}C spectrum is reported for the first time, all resonances having been unambiguously confirmed by means of the XCOR and HMBC experiments. The methoxyl group at δ59.1 induced a pronounced deshielding effect on C-7 and a shielding effect on C-8, C-6a and C-10 with respect to the buphanisine data.

Undulatine (**4**). The analysis of the ^{1}H and ^{13}C NMR spectra as reported in the literature was incomplete [8, 13, 14]. All ^{1}H and ^{13}C resonances were, therefore unambiguously assigned. The shielding effect of the epoxide on H-1 and H-2 was pronounced and the small coupling constant between H-1 and H-2 (J = 3.5 Hz) and between H-2 and H-3 (J = 2.5 Hz), allowed us to assign the configuration of the epoxide ring. The assignment of the methoxyl group at δ3.97 was made in the same way as for **3**. In the ^{13}C NMR spectrum, the highfield shift of the C-4 signal (δ24.9) with respect to the corresponding signal in the 1,2-unsaturated alkaloids in this series, which are present at a lower field between δ28 and 32.5, was an indicator for the 1,2-oxiran ring [4]. Moreover, HMBC correlations led us to assign the resonances at δ141.1 and 138.5 to C-7 and C-10a and by means of XCOR the signals at δ53.7 and 55.1 were assigned to C-1 and C-2, respectively.

Compound **6**. $C_{20}H_{23}NO_6$, was a new alkaloid which was identified as 11-*O*-acetylambelline. Its MS showed a molecular ion peak at *m/z* 373 and a base peak at *m/z* 254, which together with the fragment ions at *m/z* 270, 255, 241 and 211 are characteristic for the alkaloids of the ambelline series [15]. Moreover, the fragment ion at *m/z* 330 indicated the presence of an acetoxy group. The signals of the ^{1}H NMR spectrum were similar to those of **5** (Table 1) [1] and were assigned in the same way as those of the above alkaloids. However, due to the presence of the acetoxy group (δ1.81) at the 11*endo* position, confirmed by the NOE contour between H-11*exo* and H-4β, a pronounced deshielding effect on the H-11*exo*, with respect to the ambelline data was observed. A significant feature, confirmed by COSY experiment, was the long range W coupling between H-2 and H-4α and between H-4a and H-12*endo*, indicating that they were in the same plane. The ^{13}C NMR spectrum of **6**, with the exception of the acetoxy group, was very similar to that of **5** (Table 2) [1]. The assignment of the carbon signals were confirmed by XCOR and HMBC techniques.

The name brunsbelline was proposed for the second new alkaloid **7**. The IR spectrum exhibited the methylenedioxy group, as well as the hydroxyl band. Its MS showed a molecular peak at *m/z* 331 consistent with $C_{18}H_{21}NO_5$, and a base peak at *m/z* 287 $[M-C_2H_6N]^+$, which together with the fragment ions at *m/z* 299, 270, 260, 257, 255, 241, 239 and 211 is characteristic of 1,2-unsaturated alkaloids of the crinine series bearing a hydroxyl substituent at C-11 [15]. In the ^{1}H NMR spectrum, the small chemical shift difference between the olefinic protons and the small coupling constant between H-2 and H-3 (J = 1.8 Hz) were indicative of a *cis* relationship between the C-3 substituent and the 5,10b-ethano bridge. The deshielding effect on H-11, observed as a *dd* at δ4.02 and on the H-4β when compared with the data for **1**–**3** and **5**, as well as the close proximity of the H-12 signals were consistent with an hydroxyl substituent at C-11*exo* position [16]. This was substantiated by the NOE contour correlation between H-10 and H-11*endo*. The methoxyl group at δ3.95 was again assigned to the C-7 position, confirmed by the HMBC correlations and the ROESY experiments. The rest of the signals were consistent with the proposed structure and were assigned in the manner previously described. The ^{13}C NMR spectra of **7** was confirmed by means of XCOR and HMBC techniques. The skeleton contains 18 carbon atoms, nine of which showed resonance in the shift range of δ > 90 ppm. The low field signals were five singlets for the quaternary carbons C-9, C-7, C10a, C-8 and C-6a, three doublets (C-2, C-1 and C-10) and a quartet for the methylenedioxy group. The aliphatic shift range was characterized by one singlet (C-10b), three doublets (C-11, C-3 and C4a), three triplets (C-12, C-6 and C-4) and two quartets for the aliphatic and aromatic methoxy carbons. The pronounced deshielding effect on C-11, observed as a doublet, together with the less pronounced deshielding effect on C-12, C-10b and C-2 and, the shielding effect on C-1 and C-10a, compared with **3**, as well as the deshielding effect on C-2, C-10a and C10b and, the shielding effect on C-1 and C-11, compared with **5**, were also consistent with the 11*exo* position for the hydroxyl group.

Table 1. ^{1}H NMR data for compounds **5**–**7** (*J* values are given in Hz in parentheses)

H	5	6	7
1	6.57 *d* (10.0)	6.51 *d* (10.0)	6.35 *d* (10.0)
2	6.01 *dd* (5.0, 10.0)	6.02 *ddd* (1.0, 5.5, 10.0)	6.32 *dd* (1.8, 10.0)
3	3.84 *m*	3.83 *ddd* (2.0, 4.0, 5.5)	3.84 *m*
4α	2.11 *dd* (4.5, 14.0)	2.16 *br d* (13.5)	2.14 *m*
4β	1.67 *ddd* (4.0, 14.0, 14.0)	1.70 *ddd* (4.0, 13.5, 13.5)	2.14 *m*
4a	3.36 *dd* (4.5, 14.0)	3.43 *dd* (3.0, 13.5)	3.39 *m*
6α	4.27 *dd* (17.0)	4.33 *d* (17.5)	4.22 *d* (17.0)
6β	3.86 *d* (17.0)	3.86 *d* (17.5)	3.80 *d* (17.0)
10	6.59 *s*	6.43 *s*	6.54 *s*
11*endo*	—	—	4.02 *dd* (3.5, 7.0)
11*exo*	4.39 *dd* (4.5, 8.5)	5.11 *dd* (4.0, 8.0)	—
12*endo*	2.52 *ddd* (1.5, 4.5, 13.5)	2.72 *ddd* (1.5, 4.0, 14.0)	3.39 *m*
12*exo*	3.63 *dd* (8.5, 13.5)	3.78 *dd* (8.0, 14.0)	3.39 *m*
–O–CH_2–O–	5.87 *d*–5.88 *d* (1.5)	5.83 *d*–5.87 *d* (1.5)	5.84 *d*–5.85 *d* (1.5)
3-OMe	3.35 *s*	3.32 *s*	3.34 *s*
7-OMe	3.99 *s*	3.97 *s*	3.95 *s*
–O–CO–CH_3	—	1.81 *s*	—

Table 2. ^{13}C NMR chemical shifts assignments of **5**–**7**

C	5	6	7
1	131.7 *d*	132.3 *d*	127.0 *d*
2	126.4 *d*	126.7 *d*	132.0 *d*
3	72.1 *d*	72.7 *d*	72.5 *d*
4	28.2 *t*	29.3 *t*	27.7 *t*
4a	62.8 *d*	64.0 *d*	62.5 *d*
6	59.0 *t*	59.3 *t*	57.3 *t*
6a	117.8 *s*	117.9 *s*	116.7 *s*
7	141.0 *s*	141.0 *s*	140.8 *s*
8	134.3 *s*	134.3 *s*	133.4 *s*
9	148.5 *s*	148.2 *s*	148.6 *s*
10	100.3 *d*	99.7 *d*	97.3 *d*
10a	132.0 *s*	134.2 *s*	135.7 *s*
10b	48.0 *s*	48.0 *s*	50.1 *s*
11	86.0 *d*	87.9 *d*	79.6 *d*
12	62.2 *t*	60.0 *t*	63.3 *t*
–O–CH_2O–	100.9 *t*	101.0 *t*	100.7 *t*
3-OMe	56.5 *q*	57.0 *q*	56.7 *q*
7-OMe	59.0 *q*	59.6 *q*	59.2 *q*
–O–CO–Me	—	171.5 *s*	—
–O–CO–Me	—	21.4 *q*	—

EXPERIMENTAL

General. Mps were uncorr. IR spectra were measured in KBr discs or $CHCl_3$. EIMS at 70 eV. NMR spectra were recorded in the solvent specified and using TMS as int. stand. Chemical shifts were reported in δ (ppm) values and coupling constants (*J*) in Hz. Silica gel SDS chromagel 60 A CC (230–400 mesh) was used for flash CC and Sephadex LH-20 Pharmacia for gel filtration. Silica gel 60 F_{254} (Merck) was used for analyt. (0.25 mm) and prep. (1 mm) TLC. Spots on chromatograms were detected under UV light (254 nm) and by Dragendorff's reagent.

Plant material. The bulbs of *B. josephinae* were collected in the Karoo National Gardens (Worcester, Republic of South Africa) in December 1991. A voucher specimen is on deposit at the Compton Herbarium (No. 20484), National Botanical Gardens (Kirstenbosch, Cape Town, Republic of South Africa).

Extraction and isolation of alkaloids. Bulbs of *B. josephinae* were extracted as previously reported [1]. Flash CC on silica gel eluting with CH_2Cl_2–MeOH (19:1) and Me_2CO, followed by PTLC using MeOH and Me_2CO and final purification on Sephadex LH-20 gave **1** (35 mg), **2** (11 mg), **3** (58 mg), **4** (15 mg), **6** (135 mg), **7** (16 mg) and **8** (12 mg).

Crinine (**1**). Found: C, 70.80; H, 6.38; N, 5.10. Calc. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16%. Mp 208–210°. $[\alpha]_D^{22}$ − 9° (EtOH; *c* 0.6); CD $[\Theta]_{245}$ + 7743, $[\Theta]_{287}$ − 4920. IR ν_{max} cm^{-1}: 3400–3100 (–OH), 3025, 1640, 1602, 1483, 937 (–OCH_2O–). EIMS 70 eV, *m/z* (rel. int.): 271 $[M]^+$ (100), 270 (7), 254 (6), 242 (7), 228 (17), 216 (5), 200 (11), 199 (32), 187 (20), 173 (7), 172 (6), 129 (6), 115 (5), 57 (9), 56 (11). ^{1}H NMR (300 MHz, $CDCl_3$): δ1.74 (1H, *ddd*, *J* = 4.2, 13.5, 13.5 Hz, H-4β), 1.94 (1H, *ddd*, *J* = 6.3, 10.8, 12.5 Hz, H-11*exo*), 2.06 (1H, *brd*, *J* = 13.5 Hz, H-4α), 2.19 (1H *ddd*, *J* = 3.9, 8.7, 12.5 Hz, H-11*endo*), 2.91 (1H, *ddd*, *J* = 6.3, 8.7, 12.8 Hz, H-12*endo*), 3.36 (1H, *brd*, *J* = 12.8 Hz, H-12*exo*), 3.42 (1H, *dd*, *J* = 3.9, 13.5 Hz, H-4a), 3.78 (1H, *d*, *J* = 16.8 Hz, H-6β), 4.33 (1H, *m*, H-3), 4.41 (1H, *d*, *J* = 16.8 Hz, H-6α), 5.89-5.91 (2H, 2*d*, *J* = 1.2 Hz, OCH_2O), 5.96 (1H, *dd*, *J* = 5.4, 10.0 Hz, H-2), 6.48 (1H, *s*, H-7), 6.59 (1H, *d*, *J* = 10.0 Hz, H-1), 6.85 (1H, *s*, H-10). ^{13}C NMR (50 MHz, $CDCl_3$): δ32.3 (*t*, C-4), 43.6 (*t*, C-11), 44.3 (*s*, C-10b), 53.1 (*t*, C-12), 61.5 (*t*, C-6), 62.9 (*d*, C-4a), 63.3 (*d*, C-3), 100.8 (*t*, OCH_2O), 102.9 (*d*, C-10), 106.9 (*d*, C-7), 125.0 (*s*, C-6a), 128.0 (*d*, C-2), 131.0 (*d*, C-1), 137.8 (*s*, C-10a), 145.8 (*s*, C-8), 146.3 (*s*, C-9).

Buphanisine (**2**). Found: C, 71.64; H, 6.77; N, 4.85 Calc. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91%. Mp 123–125°. $[\alpha]_D^{22}$ − 28° (EtOH; *c* 0.6); CD $[\Theta]_{249}$ + 10623, $[\Theta]_{278}$ − 5453. IR ν_{max} cm^{-1}: 3032, 2950, 1640, 1615, 1480, 1070, 940 (–OCH_2O–). EIMS 70 eV, *m/z* (rel. int.): 285 $[M]^+$ (100), 270 (22), 254 (15), 253 (18), 230 (31), 215 (55), 201 (24), 187 (16), 185 (10), 172 (13), 157 (14), 115 (25). ^1H NMR (300 MHz, $CDCl_3$): δ1.64 (1H, *ddd*, *J* = 3.9, 13.5, 13.5 Hz, H-4β), 2.01 (1H, *ddd*, *J* = 6.0, 10.8, 12.3 Hz, H-11*exo*), 2.23 (1H, *ddd*, *J* = 4.0, 9.0, 12.3 Hz, H-11*endo*), 2.33 (1H, *brd*, *J* = 13.5 Hz, H-4α), 3.02 (1H, *ddd*, *J* = 6.0, 9.0, 13.0 Hz, H-12*endo*), 3.37 (3H, *s*, 3-OMe), 3.50 (1H, *dd*, *J* = 3.6, 13.5 Hz, H-4a), 3.56 (1H, *brd*, *J* = 13.0 Hz, H-12*exo*), 3.85 (1H, *m*, H-3), 3.90 (1H, *d*, *J* = 16.8 Hz, H-6β), 4.52 (1H, *d*, *J* = 16.8 Hz, H-6α), 5.91-5.92 (2H, 2*d*, *J* = 1.3 Hz, OCH_2O), 6.03 (1H, *dd*, *J* = 5.2, 10.0 Hz, H-2), 6.51 (1H, *s*, H-7), 6.57 (1H, *d*, *J* = 10.0 Hz, H-1), 6.86 (1H, *s*, H-10). ^{13}C NMR (50 MHz, $CDCl_3$): δ29.0 (*t*, C-4), 43.4 (*t*, C-11), 44.6 (*s*, C-10b), 53.2 (*t*, C-12), 56.7 (*q*, 3-OMe), 61.6 (*t*, C-6), 63.4 (*d*, C-4a), 72.2 (*d*, C-3), 101.0 (*t*, OCH_2O), 103.1 (*d*, C-10), 107.0 (*d*, C-7), 124.3 (*s*, C-6a), 125.8 (*d*, C-2), 131.9 (*d*, C-1), 137.5 (*s*, C-10a), 146.1 (*s*, C-8), 146.5 (*s*, C-9).

Buphanidrine (**3**). Found: C, 68.49; H, 6.65; N, 4.51. Calc. for $C_{18}H_{21}NO_4$: C, 68.57; H, 6.66; N, 4.44%. Mp 90–92°. $[\alpha]_D^{22}$ + 4.2° (EtOH; *c* 0.54); CD $[\Theta]_{250}$ + 3710, $[\Theta]_{289}$ − 1430. IR ν_{max} cm^{-1}: 3016, 2932, 2398, 1618, 1480, 1316, 1280, 1085, 1048, 939 (–OCH_2O–). EIMS 70 eV, *m/z* (rel. int.): 315 $[M]^+$ (100), 300 (21), 285 (9), 284 (27), 260 (18), 257 (11), 246 (8), 245 (30), 231 (13), 228 (13), 215 (10), 202 (7), 187 (7), 115 (7), 55 (7). ^1H NMR (500 MHz, $CDCl_3$): δ1.60 (1H, *ddd*, *J* = 4.0, 13.5, 13.5 Hz, H-4β), 1.99 (1H, *ddd*, *J* = 6.0, 10.5, 12.5 Hz, H-11*exo*), 2.20 (1H, *ddd*, *J* = 4.0, 9.0, 12.5 Hz, H-11*endo*), 2.46 (1H, *brd*, *J* = 13.5 Hz, H-4α), 2.99 (1H, *ddd*, *J* = 6.0, 9.0, 13.0 Hz, H-12*endo*), 3.29 (3H, *s*, 3-OMe), 3.50 (1H, *dd*, *J* = 3.5, 13.5 Hz, H-4a), 3.64 (1H, *m*, H-12*exo*), 3.77 (1H, *m*, H-3), 3.92 (3H, *s*, 7-OMe), 3.95 (1H, *d*, *J* = 17.0 Hz, H-6β), 4.35 (1H, *d*, *J* = 17.0 Hz, H-6α), 5.81-5.82 (2H, 2*d*, *J* = 1.5 Hz, OCH_2O), 5.95 (1H, *dd*, *J* = 5.0, 10.0 Hz, H-2), 6.42 (1H, *d*, *J* = 10.0 Hz, H-1), 6.50 (1H, *s*, H-10). ^{13}C NMR (50 MHz, $CDCl_3$): δ28.0 (*t*, C-4), 43.4 (*t*, C-11), 44.3 (*s*, C-10b), 53.3 (*t*, C-12), 56.5 (*q*, 3-OMe), 58.1 (*t*, C-6), 59.1 (*q*, 7-OMe), 62.8 (*d*, C-4a), 72.2 (*d*, C-3) 96.9 (*d*, C-10), 100.6 (*t*, OCH_2O), 115.8 (*s*, C-6a), 125.5 (*d*, C-2), 132.1 (*d*, C-1), 133.4 (*s*, C-8), 138.6 (*s*, C-10a), 140.8 (*s*, C-7), 148.2 (*s*, C-9).

Undulatine (**4**). Found: C, 65.32; H, 6.42; N, 4.22. Calc. for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23%. Mp 149–150°. $[\alpha]_D^{22}$ − 46.0° ($CHCl_3$; *c* 0.5); CD $[\Theta]_{250}$ + 2425, $[\Theta]_{287}$ − 215. IR ν_{max} cm^{-1}: 3428, 2924, 2369, 1734, 1617, 1482, 1397, 1279 (epox.), 1215, 1083, 1047, 924 (–OCH_2O–), 805 (epox.). EIMS 70 eV, *m/z* (rel. int.): 331 $[M]^+$ (100), 316 (7), 302 (8), 300 (7), 286 (9), 260 (11), 258 (15), 244 (8), 232 (10), 219 (9), 217 (11), 205 (21), 189 (12), 173 (9), 115 (5), 73 (5), 69 (5), 56 (7). ^1H NMR (500 MHz, $CDCl_3$): δ1.42 (1H, *ddd*, *J* = 3.0, 13.5, 13.5 Hz, H-4β), 2.10 (1H, *ddd*, *J* = 5.0, 9.0, 12.5 Hz, H-11*endo*), 2.11 (1H, *brd*, *J* = 13.5 Hz, H-4α), 2.49 (1H, *ddd*, *J* = 6.0, 11.0, 12.5 Hz, H-11*exo*), 2.92 (1H, *ddd*, *J* = 6.0, 9.0, 12.8 Hz, H-12*endo*), 3.25 (1H, *dd*, *J* = 3.4, 13.5 Hz, H-4a), 3.32 (1H, *dd*, *J* = 2.5, 3.5 Hz, H-2), 3.42 (3H, *s*, 3-OMe), 3.42 (1H, *m*, H-12*exo*), 3.71 (1H, *d*, *J* = 3.5 Hz, H-1), 3.88 (1H, *d*, *J* = 17.0 Hz, H-6β), 3.96 (1H, *m*, H-3), 3.97 (3H, *s*, 7-OMe), 4.35 (1H, *d*, *J* = 17.0 Hz, H-6α), 5.87-5.88 (2H, 2*d*, *J* = 1.5 Hz, OCH_2O), 6.60 (1H, *s*, H-10). ^{13}C NMR (50 MHz, $CDCl_3$): δ24.9 (*t*, C-4), 38.9 (*t*, C-11), 41.6 (*s*, C-10b), 52.4 (*t*, C-12), 53.7 (*d*, C-1), 55.1 (*d*, C-2), 57.6 (*q*, 3-OMe), 58.4 (*t*, C-6), 59.1 (*q*, 7-OMe), 61.3 (*d*, C-4a), 74.7 (*d*, C-3), 96.4 (*d*, C-10), 100.7 (*t*, OCH_2O), 117.1 (*s*, C-6a), 133.4 (*s* C-8), 138.5 (*s*, C-10a), 141.1 (*s*, C-7), 148.1 (*s*, C-9).

11-O-*acetylambelline* (**6**). Found: C, 64.05; H, 6.24; N, 3.73. $C_{20}H_{23}NO_6$ requires: C, 64.32; H, 6.21; N, 3.75%. Mp 80–82°. $[\alpha]_D^{22}$ − 23.5° ($CHCl_3$; *c* 0.59); CD $[\Theta]_{252}$ + 1830, $[\Theta]_{287}$ − 1490. IR ν_{max} cm^{-1}: 3010, 2942, 1735 (> C=O), 1618, 1476, 1376, 1248, 1084, 1048, 938 (–OCH_2O–). EIMS 70 eV, *m/z* (rel. int.): 373 $[M]^+$ (94), 358 (11), 342 (10), 330 (9), 314 (78), 313 (86), 298 (42), 282 (70), 270 (37), 258 (70), 255 (62), 254 (100), 241 (70), 227 (38), 218 (69), 211 (73), 190 (58), 183 (44), 168 (32), 153 (28), 139 (30), 128 (41), 115 (65), 87 (49), 77 (55), 55 (57). ^1H NMR (500 MHz, $CDCl_3$), see Table 1. ^{13}C NMR (50 MHz, $CDCl_3$), see Table 2.

Brunsbelline (**7**). Found: C, 65.18; H, 6.12; N, 4.16. $C_{18}H_{21}NO_5$ requires: C, 65.24; H, 6.39; N, 4.23%. Mp 226–228°. $[\alpha]_D^{22}$ − 97.8° (EtOH; *c* 0.1); CD $[\Theta]_{250}$ + 4365, $[\Theta]_{288}$ − 3324. IR ν_{max} cm^{-1}: 3400–3100 (–OH), 2924, 1732, 1619, 1481, 1282, 1230, 1072, 1036, 970, 933 (–OCH_2O–), 856, 822, 780. EIMS 70 eV, *m/z* (rel. int.): 331 $[M]^+$ (54), 302 (29), 300 (32), 299 (44), 298 (26), 288 (27), 287 (100), 270 (40), 260 (69), 257 (64), 256 (27), 255 (65), 254 (40), 242 (30), 241 (58), 240 (28), 239 (64), 227 (45), 226 (50), 211 (74), 190 (41), 115 (45), 77 (49), 55 (46). ^1H NMR (500 MHz, $CDCl_3$), see Table 1. ^{13}C NMR (50 MHz, $CDCl_3$). see Table 2.

Hippadine (**8**). Found: C, 72.81; H, 3.41; N, 5.20. Calc. for $C_{16}H_9NO_3$: C, 73.00; H, 3.45; N, 5.32%. Mp 212–214°. $[\alpha]_D^{22}$ + 27.5° ($CHCl_3$: *c* 0.58). IR, EIMS, ^1H and ^{13}C NMR were in agreement with Refs [17] and [18].

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REFERENCES

1. Viladomat, F., Bastida, J., Codina, C., Campbell, W. E. and Mathee, S. (1994) *Phytochemistry* **35**, 809.
2. Longevialle, P., Smith, D. H., Burlingame, A. L., Fales, H. M. and Highet, R. J. (1973) *Org. Mass Spectrom.* **7**, 401.
3. Samuel, E. H. C. (1975) *Org. Mass Spectrom.* **10**, 427.
4. Frahm, A. W., Ali, A. A. and Kating, H. (1981) *Phytochemistry* **20**, 1735
5. Ali, A. A., Ramadan, M. A. and Frahm, A. W. (1984) *Planta Med.* **50**, 424.

6. De Angelis, G. G. and Wildman, W. C. (1969) *Tetrahedron* **25**, 5099.
7. Martin, S. F. and Campbell, C. L. (1988) *J. Org. Chem.* **53**, 3184.
8. Kobayashi, S., Tokumoto, T., Kihara, M., Imakura, Y., Shingu, T. and Taira, Z. (1984) *Chem. Pharmacol. Bull.* **32**, 3015.
9. Frahm, A. W., Ali, A. A. and Ramadan, M. A. (1985) *Magnet. Res. Chem.* **23**, 804.
10. Ali, A. A., Kating, H., Frahm, A. W., El-Moghazi, A. M. and Ramadan, M. A. (1981) *Phytochemistry* **20**, 1121.
11. Likhitwitayawuid, K., Angerhofer, C. K., Chai, H., Pezzuto, J. M. and Cordell, G. A. (1993) *J. Nat. Prod.* **56**, 1331.
12. Haugwitz, R. D., Jeffs, P. W. and Wenkert, E. (1965) *J. Chem. Soc. B* 2001.
13. Pettit, G. R., Gaddamidi, V., Goswami, A. and Cragg, G. M. (1984) *J. Nat. Prod.* **47**, 796.
14. Zetta, L. and Gatti, G. (1973) *J. Chem. Soc., Perkin II*, 1180.
15. Longevialle, P., Fales, H. M., Highet, R. J. and Burlingame, A. L. (1973) *Org. Mass Spectrom.* **7**, 417.
16. Pabuççuoğlu, V., Richomme, P., Gözler, T., Kivçak, B., Freyer, A. J. and Shamma, M. (1989) *J. Nat. Prod.* **52**, 785.
17. Ghosal, S., Rao, P. H., Jaiswal, D. K., Kumar, Y. and Frahm, A. W. (1981) *Phytochemistry* **20**, 2003.
18. Ali, A. A., Mesbah, M. K. and Frahm, A. W. (1981) *Planta Med.* **43**, 407.