FULL PAPER

New Alkaloids from *Hippeastrum papilio* (Ravenna) Van Scheepen

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A new phytochemical study of the indigenous Brazilian species *Hippeastrum papilio* is reported herein. Three novel Amaryllidaceae alkaloids were isolated, including hippapiline (**1**), papiline (**2**), and 3-*O*-demethyl-3-*O*-(3-hydroxybutanoyl)-haemanthamine (**3**). Their structures were determined by physical and spectroscopic methods. In addition, the known alkaloids, haemanthamine (**4**), galanthamine (**5**), narwedine (**6**), 11β-hydroxygalanthamine (**7**), apogalanthamine (**8**), and 9-*O*-demethyllycosinine B (**9**) were identified. The unusual *cis-B*/*C*-ring fusion for the new homolycorine representative hippapiline was ratified by NMR and CD spectroscopy.

Introduction. – The plant family Amaryllidaceae comprises *ca.* 1600 species in 73 genera which are distributed through the tropics and warm, temperate regions of the globe [1][2]. These perennial, bulbous geophytes belong to one of the 20 most significant alkaloid-producing plant families [1][2]. A striking feature of the Amaryllidaceae is the presence of an exclusive group of isoquinoline alkaloids, which are responsible for a wide-range of biological activities [3].

Structurally, these alkaloids have been grouped into nine skeletal types formed *via* specific oxidative phenolic couplings from the common amino acid-derived biogenetic precursor norbelladine [3]. The homolycorine-type skeleton is characterized by a *cis-B*/*C*-ring fusion, in which H–C(1) and H–C(10b) are both α-oriented. The correct configurational characterization of Amaryllidaceae alkaloids thus allows for a better understanding of the biosynthetic pathway diagnostic for a particular skeleton.

Over the past two decades, gas chromatography/mass spectrometry (GC/MS) has been applied successfully in the analysis of Amaryllidaceae alkaloids [4]. A preliminary study of *H. papilio via* GC/MS indicated the presence of several unknown structures with MS fragmentation patterns diagnostic of Amaryllidaceae alkaloids [5]. A larger collection of *H. papilio* bulbs was here subjected to a comprehensive phytochemical investigation leading to the identification of hippapiline (**1**), papiline (**2**), and 3-*O*-demethyl-3-*O*-(3-hydroxybutanoyl)haemanthamine (**3**) as the novel constituents, in addition to six other known Amaryllidaceae alkaloids. The β-orientation for both H–C(1) and H–C(10b) in **1**, uncovered by rigorous spectroscopic analysis, is indicative of an unsual *cis-B*/*C*-ring fusion previously not seen for homolycorine-type alkaloids.

Results and Discussion. – GC/MS Analysis (*Table 1*) revealed that galanthamine (**5**) was the main constituent in the hexane extract (86.3%), also featuring as one of the major components in the AcOEt extract (39.0%) together with haemanthamine (**4**; 26.9%). These results are in agreement with a previous study of *H. papilio*, in which these alkaloids were isolated and identified by NMR and CD spectroscopic techniques [5]. However, apogalanthamine (**8**) and 9-*O*-demethyllycosinine B (**9**) are now reported in this species for the first time (*Fig.*), whilst narwedine (**6**) as in the previous instance [5] was here also detectable only in minimal quantity.

Compound **1** had a HR-ESI-MS signal at *m*/*z* 318.1706 ($[M+H]^+$, $C_{18}H_{24}NO_4^+$; calc. 318.1700) and a base peak at *m*/*z* 109 ($C_7H_{11}N^+$) in its GC/MS spectrum, arising from a *retro-Diels–Alder* reaction, which is characteristic for a hexahydroindole ring in the homolycorine series lacking substitution at C(2) [4]. Although the basic structure of a homolycorine-type alkaloid for compound **1** was readily established by NMR evidence, the unusual chemical shift and splitting pattern were ratified *via* comparisons with the data for 8-*O*-demethyl-6-*O*-methyllycorenine found in the literature [6]. The ^{1}H-NMR data of **1** was atypical in the following three ways: *i*) two *para*-oriented aromatic H-atoms attributed to H–C(7) and H–C(10), the latter of which was assignable to the highly deshielded resonance *singlet* at δ(H) 8.41 (confirmed by NOESY correlation with the MeN group); *ii*) an uncommon coupling constant (J = 4.5 Hz) observed between H–C(1) and H–C(10b) and the absence of the distinctive *trans*-diaxial coupling (J ~ 10 Hz) between H–C(10b) and H–C(4a); *iii*) a NOESY correlation between H–C(4a), H–C(10b), and H–C(1). This data was thus pivotal in assigning both H–C(1) and H–C(10b)

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Table 1. *GC/MS Analysis of the Alkaloid Content of* Hippeastrum papilio

Alkaloid	*RI*	% A[a])	% B[b])	M^+	MS
Apogalanthamine (**8**)	2253	–	3.12	269 (88)	268 (32), 254 (26), 226 (61), 211 (54), 194 (32), 193 (50), 166 (29), 165 (100), 152 (30)
Hippapiline (**1**)	2301	–	1.68	317 (–)	110 (8), 109 (100), 108 (18), 107 (2), 94 (24), 81 (2), 77 (2), 42 (2)
Galanthamine (**5**)	2335	86.26	39.01	287 (82)	288 (14), 286 (100), 270 (13), 244 (26), 230 (13), 216 (36), 174 (30), 115 (13)
Narwedine (**6**)	2402	1.31	0.52	285 (85)	286 (15), 284 (100), 242 (22), 216 (23), 214 (10), 199 (26), 185 (13), 181 (12), 178 (15), 174 (43), 161 (11), 153 (13), 141 (10), 128 (22), 115 (22), 77 (13), 42 (22)
9-*O*-Demethyllycosinine B (**9**)	2499	0.24	5.72	283 (100)	284 (19), 256 (11), 255 (70), 254 (72), 240 (30), 239 (13), 223 (11), 222 (33), 210 (11), 194 (17), 167 (10), 44 (16)
11β-Hydroxygalanthamine (**7**)	2510	traces	7.02	303 (21)	302 (12), 231 (21), 230 (100), 213 (28), 181 (13), 174 (13), 115 (13), 44 (13)
Haemanthamine (**4**)	2556	1.92	26.87	301 (12)	273 (18), 272 (100), 242 (15), 240 (16), 214 (13), 212 (14), 211 (15), 181 (26), 153 (10), 128 (12), 115 (11)
Papiline (**2**)	2565	1.08	10.98	345 (–)	286 (3), 177 (3), 165 (1), 122 (1), 110 (6), 109 (100), 108 (14), 96 (1), 82 (3), 81 (2), 44 (1), 43 (3), 42 (2)
3-*O*-Demethyl-3-*O*-(3-Hydroxy-butanoyl)-haemanthamine (**3**)	3030	–	1.00	373 (5)	345 (21), 344 (95), 270 (24), 269 (37), 268 (25), 240 (55), 226 (20), 225 (30), 224 (25), 212 (53), 211 (27), 210 (16), 182 (20), 181 (100), 153 (33), 128 (16), 115 (17), 45 (21)

[a]) % A: Alkaloid percentage in the total mixture of alkaloids extracted with hexane. [b]) % B: Alkaloid percentage in the total mixture of alkaloids extracted with AcOEt. All values are expressed as a relative percentage of TIC.

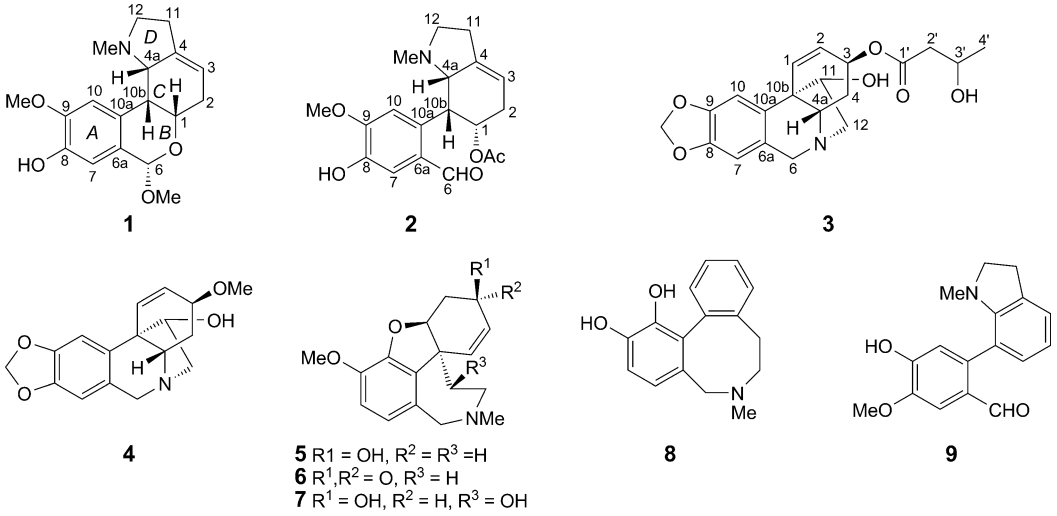

Figure. *Alkaloids identified in* Hippeastrum papilio

to the β-face. CD Analysis showed that there were positive, negative, and positive *Cotton* effects at around 225, 250, and 290 nm, respectively, which are antipodal to those observed for typically *cis-B*/*C*-ring-fused homolycorine-type alkaloids [7]. Taken together, the CD and NMR data (*Table 2*) are in agreement with this novel stereochemical arrangement involving *cis-B*/*C*-ring fusion in **1**, for which the name hippapiline is proposed.

The HR-ESI-MS of **2** suggested a molecular formula $C_{19}H_{24}NO_5^+$ for $[M+H]^+$ with the parent ion at *m*/*z* 346.1643 (calc. 346.1649). The EI-MS showed a signal ion at *m*/*z* 286 ($[M-59]^+$) diagnostic for the loss of an AcO group. Characteristic NMR signals included: *i*) a *singlet* H-atom resonance at δ(H) 9.91, indicative of an aldehyde functionality which appeared in nonfused dihydroindole lycosinine derivatives [8][9], with the corresponding signal at δ(C) 191.7 (*d*) in the ^{13}C-NMR; *ii*) two *para*-orientated aromatic H-atoms at δ(H) 7.32 and 7.29, the more deshielded of which was assigned to H–C(7) due to its NOESY correlation with H–C(6); *iii*) the AcO substituent was assigned to C(1) due to the strong deshielding of H–C(1) (δ(H) 5.45), confirmed by HMBC; *iv*) the magnitude of the coupling constant (J(4a,10b) = J(1,10b) = 4.5 Hz) together with the observed NOESY correlations were congruent with the *syn*-disposition for H–C(1), H–C(10b), and H–C(4a). The IR spectrum of **2** displayed strong absorbances at 1738 and 1674 cm^{-1} for two C=O groups ascribed to the AcO and conjugated CHO moieties, respectively. All spectroscopic data together were in agreement with a new compound bearing a nonfused

Table 2. *NMR Data* (500 MHz for ^{1}H- and 125 MHz for ^{13}C-NMR, $CDCl_3$) *of* **1**. δ in ppm, J in Hz.

Position	δ(H)	COSY	NOESY	δ(C)	HMBC
1	4.29 (*ddd*, *J* = 9.8, 6.8, 4.5)	H-2α, H-2β, H-10b	H-2α, H-2β, H-4a, H-10b	70.5 (*d*)	
2α	2.41 – 2.47 (*m*)	H-1, H-2β, H-3, H-4a, H-11	H-1, H-2β, H-3, 6-MeO	28.9 (*t*)	
2β	2.25 – 2.29 (*m*)	H-1, H-2α, H-3, H-4a, H-11	H-1, H-2α, H-3		
3	5.07 (br. *s*)	H-2α, H-2β, H-4a, H-11	H-2α, H-2β, H-11	115.2 (*d*)	
4				138.4 (*s*)	
4a	2.94 (br. *s*)	H-2α, H-2β, H-3, H-10b, H-11	H-1, H-10b, H-12β, MeN	70.6 (*d*)	
6β	5.44 (*s*)	H-7	H-7, H-10b, 6-MeO	97.1 (*d*)	C-1, C-10a, 6-MeO
6a				127.8 (*s*)	
7	6.88 (*s*)	H-6β	H-6β	112.4 (*d*)	C-6, C-8, C-9, C-10a
8				143.7 (*s*)	
9				145.9 (*s*)	
10	8.41 (*s*)	H-10b	9-MeO, MeN	110.6 (*d*)	C-6a, C-8
10a				126.7 (*s*)	
10b	3.32 (*t*, *J* = 4.5)	H-1, H-4a, H-10	H-1, H-4a, H-6β, MeN	35.4 (*d*)	C-1, C-4, C-4a, C-6a
11 (2 H)	2.28 – 2.36 (*m*)	H-2α, H-2β, H-3, H-4a, H-12α, H-12β	H-3, H-12α, H-12β	28.6 (*t*)	
12α	3.21 (*ddd*, *J* = 8.7, 6.7, 2.0)	H-11, H-12β	H-11, H-12β, MeN	56.1 (*t*)	C-4,C-4a
12β	2.18 (*dt*, *J* = 9.8, 8.6)	H-11, H-12α	H-4a, H-11, H-12α, MeN		
6-MeO	3.57 (*s*)		H-2α, H-6β	55.3 (*q*)	C-6
9-MeO	3.80 (*s*)		H-10	55.7 (*q*)	C-9
MeN	2.44 (*s*)		H-4a, H-10, H-10b, H-12α, H-12β	40.0 (*q*)	C-4a, C-12

hexahydroindole nucleus, for which the name papiline has been proposed. The complete NMR data for compound **2** are listed in *Table 3*.

The new alkaloid **3** exhibited a parent ion $[M+H]^+$ at *m*/*z* 374.1603 in its HR-ESI-MS spectrum, suggesting the molecular formula $C_{20}H_{24}NO_6^+$ (calc. 374.1598). The EI-MS fragmentation showed the loss of 105 mass units characteristic of a 3-hydroxybutanoyl substituent [10], which was confirmed by corresponding resonances in the ^{1}H- and ^{13}C-NMR spectra (*Table 4*). The remaining NMR data were very similar to those of haemanthamine [3]. Furthermore, the loss of 29 mass units from the molecular ion observed by GC/MS (*m*/*z* 344, $[M-29]^+$) is typical of haemanthamine derivatives bearing a OH group at C(11) [4]. The magnitude of the coupling constant between H–C(2) and H–C(3) ($J(2,3) = 5.1$ Hz) suggested a *trans* relationship between the substituent at C(3) and the 5,10b-ethano bridge [3]. The CD spectrum confirmed **3** as a haemanthamine-type derivative, showing positive and negative *Cotton* effects at 275 and 249 nm, respectively. A

Table 3. *NMR Data* (500 MHz for ^{1}H- and 125 MHz for ^{13}C-NMR, $CDCl_3$) *of* **2**. δ in ppm, J in Hz.

Position	δ(H)	COSY	NOESY	δ(C)	HMBC
1	5.45 (*ddd*, *J* = 10.0, 5.0, 5.0)	H-2α, H-2β, H-10b	H-2β, H-4a, H-10b	70.9 (*d*)	C-10a, Me*C*O
2α	2.00 – 2.06 (*m*)	H-1, H-2β, H-3, H-4a, H-11	H-2β, H-3, H-10	27.9 (*t*)	Me*C*O
2β	2.44 (*dddd*, *J* = 16.5, 5.5, 4.5, 2.5)	H-1, H-2α, H-3, H-4a, H-11	H-1, H-2α, H-3		
3	5.54 (*m*)	H-2α, H-2β, H-4a, H-11	H-2α, H-2β, H-11	116.1 (*d*)	
4				131.1 (*s*)	
4a	3.10 (*s*)	H-2α, H-2β, H-3, H-10b, H-11	H-1, H-10b, H-12β, MeN	69.5 (*d*)	
6	9.91 (*s*)		H-7, H-10b	191.7 (*d*)	
6a				127.2 (*s*)	
7	7.32 (*s*)		H-6	116.2 (*d*)	C-8, C-9, C-10a
8				144.6 (*s*)	
9				150.1 (*s*)	
10	7.29 (*s*)	9-MeO	H-2α, H-11, 9-MeO	112.5 (*d*)	C-6a, C-8, C-9, C-10b
10a				129.0 (*s*)	
10b	4.74 (*dd*, *J* = 4.5, 4.5)	H-1, H-4a	H-1, H-4a, H-6, MeN	35.3 (*d*)	C-1, C-4a, C-10
11 (2 H)	2.55 (*m*)	H-2α, H-2β, H-3, H-4a, H-12α, H-12β	H-3, H-10, H-12α,„H-12β	28.0 (*t*)	
12α	3.26 (br. *s*)	H-11, H-12β	H-11, H-12β, MeN	56.3 (*t*)	
12β	2.33 (*q*, *J* = 9.0)	H-11, H-12α	H-4a, H-11, H-12α, MeN		MeN
9-MeO	3.84 (*s*)	H-10	H-10	55.8 (*q*)	C-9
*Me*CO	1.90 (*s*)			21.2 (*q*)	Me*C*O
Me*C*O				170.6 (*s*)	
MeN	2.20 (*s*)		H-4a, H-10b, H-12α, H-12β	40.9 (*q*)	C-4a, C-12

Table 4. *NMR Data* (500 MHz for ^{1}H- and 125 MHz for ^{13}C-NMR, $CDCl_3$) *of* **3**. δ in ppm, J in Hz.

Position	δ(H)	COSY	NOESY	δ(C)	HMBC
1	6.52 (*d*, *J* = 10.1)	H-2	H-2, H-10	129.3 (*d*)	C-3, C-4a, C-10a, C-10b
2	6.31 (*ddd*, *J*= 10.1, 5.1, 0.7)	H-1, H-3	H-1, H-3	130.2 (*d*)	C-3, C-4, C-10b
3	5.44 (*td*, *J* = 4.8, 1.7)	H-2, H-4α, H-4β	H-2, H-4α, H-4β	67.2 (*d*)	C-1, C-2, C-4a, C-1′
4α	2.37 (*td*, *J* = 14.0, 4.6)	H-3, H-4β, H-4a	H-3, H-4β, H-4a, H_{exo}-12	29.5 (*t*)	C-4a
4β	1.91 (*dd*, *J* = 14.0, 4.6)	H-3, H-4α, H-4a	H-3, H-4α, H-4a		C-2, C-3, C-4a, C-10b
4a	3.36 (*dd*, *J* = 13.5, 4.5)	H-4α, H-4β	H-4α, H-4β, H-6β	63.0 (*d*)	C-6, C-12, C-11
6α	3.72 (*d*, *J* = 17.0)	H-6β, H-7	H-6β, H_{endo}-12, H-7	61.5 (*t*)	C-4a, C-6a, C-7, C-10a
6β	4.35 (*d*, *J* = 17.0)	H-6α, H-7	H-4a, H-6α, H-7		C-6a, C-7, C-8, C-10a, C-11, C-12
6a				126.9 (*s*)	
7	6.51 (*s*)	H-6α, H-6β	H-6α, H-6β	107.1 (*d*)	C-6, C-9, C-10a
8				146.6 (*s*)	
9				146.8 (*s*)	
10	6.84 (*s*)		H-1	103.4 (*d*)	C-6a, C-8, C-10b
10a				134.8 (*s*)	
10b				50.2 (*s*)	
11	4.03 (*ddd*, *J* = 6.5, 3.5, 1.5)	H_{exo}-12, H_{endo}-12	H_{endo}-12	80.3 (*d*)	C-4a
12_{exo}	3.27 (*dd*, *J* = 14.0, 3.0)	H-11, H_{endo}-12	H-4α, H_{endo}-12	63.6 (*t*)	C-4a, C-6, C-11
12_{endo}	3.41 (*dd*, *J* = 14.0, 6.5)	H-11, H_{exo}-12	H-6α, H-11, H_{exo}-12		C-6, C-4a, C-10b, C-11
OCH_2O	5.91 (*d*, *J* = 7.5)			101.1 (*t*)	C-8, C-9
1′				172.4 (*s*)	C-2′
2′a	2.45 (*dd*, *J* = 16.5, 3.0)	H-2′b, H-3′	H-2′b	43.0 (*t*)	C-1′, C-3′, C-4′
2′b	2.36 (*dd*, *J* = 16.5, 9.0)	H-2′a, H-3′	H-2′a		C-1′, C-3′, C-4′
3′	4.17 (*ddq*, *J* = 9.5, 6.3, 3.3)	H-2′a, H-2′b, H-4′	H-4′	64.4 (*d*)	
4′	1.19 (*d*, *J* = 6.3)	H-3′	H-3′	22.6 (*q*)	C-2′, C-3′

full set of NMR data for 3-*O*-demethyl-3-*O*-(3-hydroxybutanoyl)haemanthamine (**3**) is shown in *Table 4*.

In summary, a new phytochemical investigation of *H. papilio* led to the identification of nine alkaloids, among which hippapiline, papiline, and 3-*O*-demethyl-3-*O*-(3-hydroxybutanoyl)haemanthamine are reported for the first time. The unusual β-orientation for both H–C(1) and H–C(10b) in the homolycorine-type skeleton of hippapiline was confirmed by NMR and CD spectroscopy. This finding provides new insight on the biosynthesis of homolycorine compounds in particular and Amaryllidaceae alkaloids in general.

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Experimental Part

General. Thin layer chromatography (TLC): silica gel F_{254} as the stationary phase with plate dimensions of 20 cm × 20 cm × 0.20 mm for anal. TLC, and 20 cm × 20 cm × 0.25 mm for semi-prep. TLC (SPTLC; Val-de-Reuil, France). Vacuum liquid chromatography (VLC): silica gel (*Kieselgel* – mesh 0.15/0.30, Val-de-Reuil, France). Optical rotations: *PerkinElmer 241* polarimeter (*Waltham*, MA, USA) in $CHCl_3$ at 22°. CD Spectra: *Jasco-J-810* spectrophotometer (*Easton*, MD, USA) in MeOH. UV Spectra: *Dinko UV2310* instrument (Barcelona, Spain); λ_{max} (log ε) in nm. IR Spectra: *Nicolet Avatar 329* FT-IR spectrophotometer (Waltham, MA, USA); $\tilde{\nu}_{max}$ in cm^{-1}. NMR Spectra: *Varian VNMRS 500* MHz (Palo Alto, CA, USA), using $CDCl_3$ as solvent; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS: *Agilent 6890 + MSD 5975* GC/MS spectrometer (*Agilent Technologies*, Santa Clara, CA, USA) operating in EI mode at 70 eV. An *HP-5* MS column (30 m × 0.25 mm × 0.25 μm) was used. The temp. program was as follows: 100 – 180° at 15° min^{-1}, 1 min hold at 180°, 180 – 300° at 5° min^{-1}, and 1 min hold at 300°. The injector temp. was 280°. The flow rate of carrier gas (He) was 0.8 ml min^{-1}. The 1 : 20, 1 : 10, and 1 : 5 split ratios were applied, depending on sample concentration. GC/MS Results were analyzed using AMDIS 2.64 software (NIST). HR-ESI-MS: *LC/MSD-TOF* spectrometer (*Agilent Technologies*, Santa Clara, CA, USA) through direct injection of pure compounds dissolved in H_2O/MeCN (1 : 1).

Plant Material. Hippeastrum papilio was collected during the flowering period (May, 2012) in the south of Brazil (Caxias do Sul - RS). A voucher specimen (ICN-149428) was authenticated by Dr. *Julie Dutilh* (University of Campinas) and deposited with the Institute of Botany, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre.

Identification of Alkaloids by GC/MS. The alkaloids were identified by comparing their GC/MS spectra and *Kovats* retention index (*RI*) with those of authentic Amaryllidaceae alkaloids previously isolated and identified by spectrometric methods (NMR, UV, CD, MS) [5][8][11], the NIST 05 Database or literature data. *RI* Values of compounds were measured with a standard *n*-hydrocarbon mixture (C_9 – C_{36}) using AMDIS 2.64 software. The proportion of each individual compound in the alkaloid fractions analyzed by GC/MS (*Table 1*) is expressed as a percentage of the total alkaloids (TIC – total ion current). The area of the GC/MS peaks depends on the concentration of the corresponding compound and the intensity of their mass spectral fragmentation. Although data given in *Table 1* do not express a real quantification, they can be used for a relative comparison of the amount of the respective alkaloids present in *Hippeastrum papilio*.

Extraction and Isolation of Alkaloids. Dried bulbs (220 g) of *H. papilio* were crushed and extracted with MeOH at r.t. as following: twice using 900 ml for 48 h and twice with 400 ml for 72 h. The extract was evaporated under reduced pressure to yield 55 g. This crude extract was acidified to pH 2 with H_2SO_4 (2% *v*/*v*), and extracted with Et_2O (170 ml × 6) to remove neutral material. The aq. soln. was basified with

25% $NH_3 \cdot H_2O$ up to pH 10, and extracted with hexane (170 ml × 13) to give extract *A* (1.3 g). Another extraction using AcOEt (170 ml × 20) gave extract *B* (1.5 g). Extract *A* yielded galanthamine (**5**; 130.71 mg) and haemanthamine (**4**; 49.5 mg) by SPTLC (CH_2Cl_2/acetone 10 : 7; in NH_3 atmosphere). Extract *B* was subjected to vacuum liquid chromatography (VLC) using a silica gel (7 g) column with a diameter of 2.5 cm and a height of 4.5 cm, eluting with hexane gradually enriched with AcOEt (0 → 100%), and then with AcOEt gradually enriched with MeOH (0 → 20%). Fractions of 40 ml were collected (340 in total) monitored by TLC (*Dragendorff*'s reagent, UV 254 nm) and combined according to their profiles. From fractions *11 – 20*, hippapiline (**1**; 22.2 mg) was directly obtained as a crystal. Fractions *90 – 160* were subjected to SPTLC (hexane/AcOEt 1 : 2; and a second time hexane/AcOEt/MeOH 5 : 10 : 7; in NH_3 atmosphere) to give papiline (**2**; 26.7 mg). 9-*O*-Demethylycosinine B (**9**; 7.4 mg) was isolated from fractions *61 – 85* by SPTLC (hexane/AcOEt 4 : 1; in NH_3 atmosphere), while 11*β*-hydroxygalanthamine (**7**; 1.2 mg) was obtained *via* SPTLC (hexane/AcOEt/MeOH 10 : 3 : 3; in NH_3 atmosphere) from fractions *206 – 210*. A third VLC column (1.5 × 4.5 cm) was performed with fractions *161 – 205* yielding 176 fractions (10 ml each), of which fractions *69 – 92* were further purified by SPTLC (hexane/AcOEt/MeOH 2 : 4 : 1; in NH_3 atmosphere) to furnish 3-*O*-demethyl-3-*O*-(3-hydroxybutanoyl)haemanthamine (**3**; 12.5 mg). In addition, a small amount of narwedine (**6**) and apogalanthamine (**8**) was identified by comparing their GC/EI-MS spectra and *Kovats* retention indices (*RI*) with our own library database. All known alkaloids isolated were identified by comparing their physical and spectroscopic data with those of alkaloids previously isolated and characterized by our group [5][8][11].

Hippapiline (*=(7α,13β,16β)-7,10-Dimethoxy-1-methyllycorenan-9-ol*; **1**). White crystals. $[\alpha]_D^{24} = +33$ ($c = 0.15$, $CHCl_3$). UV (MeOH): 316 (2.90), 282 (3.30), 228 (3.64). CD (MeOH, 20°): $\Delta\varepsilon_{227}$ +1330, $\Delta\varepsilon_{247.5}$ −455, $\Delta\varepsilon_{281.5}$ +89, $\Delta\varepsilon_{305.5}$ −176. IR ($CHCl_3$): 3380, 2924, 1733, 1509, 1449, 1275, 1130, 1058, 1043, 960, 913, 880, 802, 758. ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): *Table 2*. EI-MS: *Table 1*. HR-EI-MS: 318.1706 ($[M+H]^+$, $C_{18}H_{24}NO_4^+$; calc. 318.1700).

Papiline (*=(6*S*,7*R*,7a*S*)-7-(2-Formyl-4-hydroxy-5-methoxyphenyl)-2,3,5,6,7,7a-hexahydro-1-methyl-1*H*-indol-6-yl Acetate*; **2**). Amorphous solid. $[\alpha]_D^{24} = -29$ ($c = 0.26$, $CHCl_3$). UV (MeOH): 318 (3.27), 280 (3.48), 236 (3.76). IR ($CHCl_3$): 2925, 2854, 1738, 1674, 1595, 1557, 1514, 1455, 1378, 1260, 1148, 1099, 1020, 800. ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): *Table 3*. EI-MS: *Table 1*. HR-EI-MS: 346.1643 ($[M+H]^+$, $C_{19}H_{24}NO_5^+$; calc. 346.1649).

*3-*O*-Demethyl-3-*O*-(3-Hydroxybutanoyl)haemanthamine* (*=(3β,13β)-1,2-Didehydro-11-hydroxycrinan-3-yl 3-Hydroxybutanoate*; **3**). Amorphous solid. $[\alpha]_D^{24} = -13$ ($c = 0.49$, $CHCl_3$). UV (MeOH): 292 (3.46), 238 (3.36). CD (MeOH, 20°): $\Delta\varepsilon_{249}$ −2375, $\Delta\varepsilon_{275}$ +1569. IR ($CHCl_3$): 3377, 2925, 1727, 1504, 1484, 1376, 1295, 1239, 1173, 1064, 1037, 988, 936, 853, 758. ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): *Table 4*. EI-MS: *Table 1*. HR-EI-MS: 374.1603 ($[M+H]^+$, $C_{20}H_{24}NO_6^+$; calc. 374.1598).

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