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ALKALOIDS OF *PHELLINE COMOSA* VAR. *ROBUSTA**

JACQUES PUSSET, STEPHANE LA BARRE,† NICOLE LANGLOIS‡ and JEANNINE HAMON

Institut de Chimie des Substances Naturelles, C N R S, F 91198 Gif sur Yvette, France, †Laboratoire des Plantes Médicinales, C N R S, Montravel, B P 643, Nouméa, New-Caledonia

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Key Word Index—*Phelline comosa*, Phellinaceae; homoerythrinane; comosine; comosidine, 2-*epi*-homoerythratine, comosiline, comosivine, holidinine, robustivine, 1,6-epoxy-comosivine, robustiline, iso-robustiline

Abstract—Ten alkaloids belonging to the homoerythrinane group have been isolated from the leaves of *Phelline comosa* var. *robusta* and identified by spectroscopic methods and chemical correlations

INTRODUCTION

The position of the genus *Phelline* (Phellinaceae) which is at present under review includes about twelve species which are endemic to New-Caledonia The chemotaxonomic investigation of the alkaloids of these species led us to study the alkaloids of a new variety of *Phelline comosa P comosa* Labill var *robusta* (Baill) Loesner [1] The plant, generally a tree between 6 and 8 m high with large and typically dentate leaves, was collected at Mount Oungone on 8 May 1986 in a humid forest on ultrabasic soil

RESULTS

The dried leaves were basified with an aqueous solution of sodium carbonate (10% w/v) to avoid artifact formation in the presence of ammonium hydroxide [2, 3] The extraction was then carried out by standard procedures yielding the crude alkaloid fraction (7 58 g/kg) The known alkaloids were characterized by direct comparison with authentic samples Five of them had been previously identified from *P comosa* Labill [4, 5]. comosine (**1**), comosidine (**2**), 2-*epi*-homoerythratine (**3**), comosiline (**4**) and comosivine (**5**), the last one, holidinine (**6**) had been isolated from *P* sp aff *P lucida* [6]

The elemental composition of the major new alkaloid, robustivine (**7**), was shown to be $C_{20}H_{27}NO_4$ by microanalysis of its hydrochloride Its mass spectrum exhibited a molecular peak at *m/z* 345 and a base peak at *m/z* 301 This fragmentation is consistent with the loss of HO–CH $=CH_2$ by a retro-Diels–Alder reaction in the ring A of a $\Delta^{1(6)}$ homoerythrinane skeleton [4, 5, 7] indicating the presence of a hydroxyl group at C-3 All the MS fragmentations were similar to those of comosivine **5** with a shift of 14 units for the fragments containing the substituent at C-3 (See Table 1) This alkaloid and comosivine **5** presented the same chromophore as shown by their identical UV spectra Thus, the plane structure **7** was assigned to this new alkaloid ^{13}C NMR (Table 2) and ^{1}H NMR confirmed this attribution. The coupling constants between H-C-3 and the two protons at C-4 agreed with a pseudoaxial proton at C-3 The comparison of molecular rotations of **5** and **7** allowed the same configuration to be assigned to the *spiro* carbon C-5

A second new alkaloid **8** of elemental composition $C_{21}H_{29}NO_5$ by microanalysis was named 1,6-epoxy-comosivine on the basis of its spectrocopic data absence of OH, NH and carbonyl groups in its IR spectrum, molecular peak $[M]^+$ as the base peak at *m/z* 375 in its mass spectrum (16 units more than for comosivine **5**). Identical UV spectra of **5** and **8** and close chemical shifts of their aromatic carbons (Table 2) suggested the same substitutions on the aromatic ring The ^{13}C NMR spectrum also showed signals characteristic of a quaternary carbon at δ66 9 and a methine carbon at δ57 4 demonstrating the presence of a trisubstituted epoxide ring Absence of an ethylenic proton in its ^{1}H NMR spectrum in which a signal at δ3.79 was partially masked by the signal of one of the three aromatic methoxyl groups Systematic decoupling experiments showed that this was due to the proton on C-1, the high chemical shift of the C-1 proton on the epoxide ring agreed with the previously reported configuration [8]

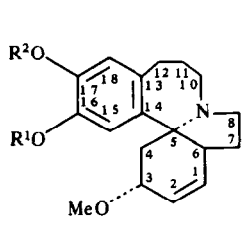
Two minor alkaloids, robustiline and *iso*-robustiline, difficult to separate, were obtained in small amounts Spectroscopic comparisons showed that they had the same functional groups and closely related structures Their identical mass spectra had the molecular peak at *m/z* 329 Their UV spectra showed a phenolic group Their ^{1}H NMR spectra indicated the presence of a disubstituted double bond, an aliphatic and an aromatic

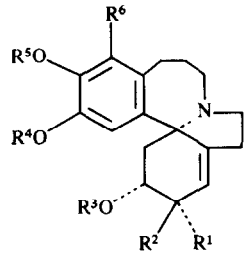
Table 1 MS fragmentations for alkaloids **5** and **7**

5	359 (M^+)	328	301	286	178	165	146
7	345 (M^+)	328	301	286	164	151	146

*This work is dedicated to Professor E Lederer on the occasion of his 80th birthday

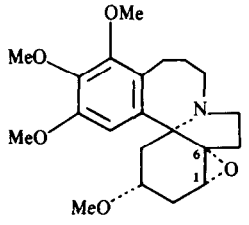
‡Author to whom correspondence should be addressed

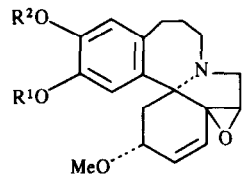




1 $R^1 = R^2 = CH_2$
2 $R^1 = R^2 = Me$

3 $R^1 = OH$, $R^2 = R^6 = H$, $R^3 = R^4 = R^5 = Me$
5 $R^1 = R^2 = H$, $R^3 = R^4 = R^5 = Me$, $R^6 = OMe$
6 $R^1 = R^2 = R^4 = H$, $R^3 = R^5 = Me$, $R^6 = OMe$
7 $R^1 = R^2 = R^3 = H$, $R^4 = R^5 = Me$, $R^6 = OMe$





8

4 $R^1 = R^2 = Me$
9a or **9b** $R^1 = H$, $R^2 = Me$
9b or **9a** $R^1 = Me$, $R^2 = H$

methoxyl groups. The chemical shifts for the two singlets of *para* aromatic protons were the major difference between the spectra of these two alkaloids which differed only in the pattern of their substituents (hydroxyl and methoxyl) on the aromatic ring. To confirm the plane structure of alkaloids **9a** and **9b**, the latter was treated with an excess of diazomethane to furnish the known comosiline (**4**) [5]

This investigation shows that the alkaloid composition of this new variety of *Phelline comosa* is rather different from those of the *P. comosa* Labill [4, 5] previously studied, the major alkaloids bearing three oxygenated substituents on their aromatic ring.

EXPERIMENTAL

Optical rotations $CHCl_3$ soln g/100 cm^3, UV spectra C_2H_5OH, λ_{max}, nm (ε) IR spectra. ν, cm^{-1}, $CHCl_3$) ^1H NMR spectra $CDCl_3$, $\delta = 0$, TMS, coupling constants, J, are given in Hz Prep TLC was performed on silica gel HF 254 Merck and CC on silica gel (70–230 mesh) Merck

Plant material Leaves of *Phelline comosa* Labill. var. *robusta* were collected at Mount Oungone in New-Caledonia A voucher specimen (Radjibaly-La Barre 126) has been deposited in the Herbarium at the ORSTOM Center of Noumea.

Extraction The powdered plant was wetted with a 10% Na_2CO_3 soln and extracted with CH_2Cl_2 in a Soxhlet apparatus until a negative Mayer's test was obtained. The concd organic

Table 2 ^{13}C NMR of alkaloids **5**, **7** and **8** ($CDCl_3$ $\delta = 0$ TMS)

	C Arom.	C C_6	C Arom	CH C_1	CH C_{15}	CH C_3	C C_5	C C_6	OMe	CH C_1	OMe–C_3	CH_2N	CH_2	CH_2
	151 7	143.2	141 3	116 2	111 5	74 4	69 4		61 2		55 7	50 4	38 3	27.9
5	149.4		137 9						60.7			46.8	32 1	25 9
			128.4						56 3					23 5
	151 7	142 6	141 3	116 9	111 4	65 7	70.0		61 3			50.4	41 6	27 7
7	149.8		137 5						60.8			46 7	35 5	25 8
			128.5						56 2					23.2
	151 9		141 4		108 8	73.0	70 5	66 9	61 3	57 4	55 8	49.7	41 6	28 0
8	149 9		137 4						60.8			45.9	30.1	25.8
			129 4						56 2					22.8

soln was then extracted with 2% HCl, the acidic phases made alkaline with Na_2CO_3 and extracted with CH_2Cl_2 giving the crude alkaloid mixture (6 06 g)

Isolation of alkaloids The alkaloids (6 g) were chromatographed on silica gel with CH_2Cl_2–MeOH (99 1 to 17 3) as eluent Among the constituents of the fraction eluted with CH_2Cl_2–MeOH 49 1 (1 86 g), comosivine **5** (0 83 g) was separated through its solubility in hexane The other alkaloids, comosiline **4** (98 mg) and 1,6-epoxy-comosivine **8** (373 mg) were obtained after prep TLC (eluent hexane–EtOAc 1 4 and 2 3). The alkaloids **9a** (20 mg) and **9b** (40 mg) were separated by prep. TLC (eluent hexane–ether–MeOH 3 20 2, 4 successive elutions) From the fraction eluted with CH_2Cl_2 -MeOH 97 3 (1 11 g) the following alkaloids were isolated after prep TLC comosine **1** (134 mg), comosidine **2** (43 mg), 2-*epi*-homoerythratine **3** (335 mg) and holidinine **6** (78 mg) Robustivine **7** (1 335 g) was isolated from the fractions eluted with CH_2Cl_2–MeOH 24 1 (1 12 g) and 19 1 (1 05 g)

Robustivine **7** $[\alpha]_D$ +103 7° ($CHCl_3$, *c* 0 7), hydrochloride mp =234°, $C_{20}H_{28}NO_4Cl$, calculated % C=62 9, H=7 39, N=3 67, found % C=62 73, H=7 18, N=3 40 IR 3350, 2920, 1580, 1480, 1440, UV 212 (13 800), 280 (850) ^{1}H NMR (200 MHz) 6 67 (*s*, 1H, H-15), 5 60 (*m*, 1H, H-1), 3 90 (*s*, 3H, arom OMe), 3 81 and 3 80 (2S, 6H, arom OMe) ^{13}C NMR (Table 2), MS (Table 1)

1,6-*Epoxy comosivine* **8** Mp=136°, $[\alpha]_D$+103 ($CHCl_3$, *c* 0 55), $C_{21}H_{29}NO_5$ calculated % C=67.18, H=7 79, N=3 73, found % C=67 10, H=7 97, N=3.60, IR 3025, 1625, 1540, 1490, 1450, 1360, UV 215 (11 800), 282 (1600), ^{1}H NMR (400 MHz, attribution after decoupling experiments) 6 55 (*s*, 1H, H-15), 3 89 and 3 82 (2*s*, 6H, 2 arom OMe), 3 79 (*d*, 1H, H-1), 3 78 (*s*, 3H, arom OMe), 3 48 (*m*, 2H, H-10a and H-12a), 3 32 (*br d*, 1H, $J_{10a\ 10b}$=13 5, H-10b), 3 16 (*s*, 3H, C_3- OMe), 3 01 and 2 96 (2*m*, 2H, H-8a and H-3), 2 82 (*m*, 1H, H-8b), 2 59 (*m*, 1H, H-12b), 2 54 (*dd*, 1H, H-4a), 2 29 (*m*, 2H, H-2a and H-7a), 2 05 (*dd*, 1H, $J_{2a,2b}$ =15 5, $J_{2b\ 3}$=6 7, H-2b), 1 83 (*m*, H-7b), 1 81 (*dd*, $J_{4a\ 4b} \sim J_{3,4b} \sim$ 11 3, H-4b), 1 78 (*m*, 1H, H-11a), 1 58 (*m*, 1H, H-11b) ^{13}C NMR (Table 2), MS *m/z* 375 (M^+), 344, 288, 194, 181 (100%), 180

Alkaloid **9a** Mp=228°, $[\alpha]_D$ +71 2° ($CHCl_3$, *c* 0 48), IR 3550, 2950, 1600, 1515, UV (neutral) 208 (17 900), 282 (2000), (basic) 251 (9100), 293 (4530). ^{1}H NMR (200 MHz) 6 90 (*s*, 1H, arom), 6 64 (*s*, 1H, arom), 6 02 and 5 76 (2 *br d*, 2H, *J* = 10, H-1 and H-2), 5 42 (OH), 3 80 (*s*, 3H, arom OMe), 3 30 (*s*, 3H, C-3 OMe), 1 67 (*dd*, H-4ax), MS (*m/z*) 329 (M^+, 100%), 314, 298, 242

Alkaloid **9b** Mp=205°, $[\alpha]_D$+69 7° ($CHCl_3$, *c* 0 46), IR 3550, 3010, 1600, 1515, UV (neutral) 211 (14250), 282 (3350); (basic) 251 (10 900), 297 (6400) ^{1}H NMR (200 MHz) 6 97 (*s*, 1H, arom), 6 56 (*s*, 1H, arom), 5 99 and 5 76 (*br d* and *dd J* = 10, *J'* = 2, H-1 and H-2), 5 33 (OH), 3 81 (*s*, 3H, arom OMe), 3 30 (*s*, 3H, C-3 OMe), 1 68 (*dd*, H-4ax), MS (*m/z*) 329 (M^+), 314 (100%), 298, 242

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