NEW HOMOERYTHRINANE ALKALOIDS FROM *PHELLINE* SPECIES

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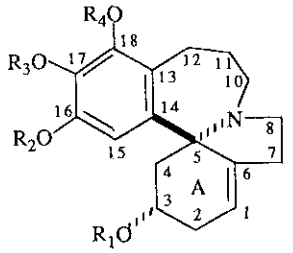
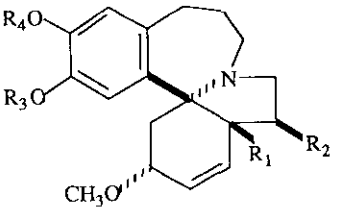
Abstract - Four new homoerythrinane alkaloids have been isolated from the leaves of *Phelline* species. Robustidine 7, robustimine 8, O-methyl-robustimine 9 and robusticine 11 have been characterised using spectroscopic data; the structure of the alkaloid 11 has been confirmed by chemical correlation.

The genus *Phelline*, representative of the family *Phellinaceae*, is endemic to New-Caledonia and comprises about twelve species. Four of these species have already been studied for their alkaloid contents.[1-8] Thus twenty-three alkaloids belonging to the homoerythrinane, homoerythroidine and homoazaerythrinane groups have been characterised. This systematic chemical study is extended here to a new variety of *Phelline comosa* : *P. comosa* Labill. var. *robusta* (Baill.) Loesner. A preliminary examination of the crude alkaloid mixture obtained from the leaves of this new variety has already led to the characterisation of four new bases belonging to the homoerythrinane group : robustivine 1, 1,6-epoxycomosivine 2, robustiline 3 and isorobustiline 4.[9]

The latter two alkaloids, difficult to separate from each other, differ only in the respective positions of their aromatic substituents (hydroxyl and methoxyl).[9] Irradiation of each of the para aromatic protons of the alkaloid 3 (6.97 and 6.56 ppm) indicated nuclear Overhauser effects respectively on the olefinic proton at 5.76 ppm and on the aromatic methoxyl group at 3.81 ppm. These results together with an examination of a Dreiding stereomodel of 3 allowed the signal at 6.97 ppm to be assigned to the proton at C-15 and the singlet at 6.56 ppm to the proton at C-18 (located near the aromatic methoxyl group). These experiments so completed the structural elucidation of robustiline 3 and isorobustiline 4.

Very small amounts of another alkaloid (< 6 mg) could not be completely separated from lucidinine 5, a compound previously isolated from *Phelline* sp. aff. *P. lucida*.[5,8] Although not fully characterised, ^{1}H nmr spectral data (in particular the signals of a disubstituted double bond : m, 1H, 6.04 ppm and bd, 1H, 5.80 ppm, J = 10 Hz) allowed the structure 6 (isolucidinine) to be tentatively assigned to this alkaloid.





1 $R_1 = H$, $R_2 = R_3 = R_4 = CH_3$

11 $R_1 = R_2 = H$, $R_3 = R_4 = CH_3$

12 $R_1 = R_3 = R_4 = CH_3$, $R_2 = H$

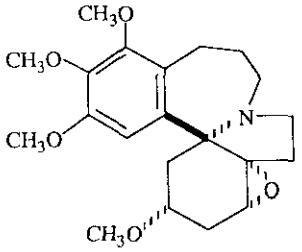
13 $R_1 = R_2 = R_3 = CH_3$, $R_4 = H$

3 $R_1 - R_2 = -O-$, $R_3 = H$, $R_4 = CH_3$

4 $R_1 - R_2 = -O-$, $R_3 = CH_3$, $R_4 = H$

5 $R_1 = R_2 = R_3 = H$, $R_4 = CH_3$

6 $R_1 = R_2 = R_4 = H$, $R_3 = CH_3$



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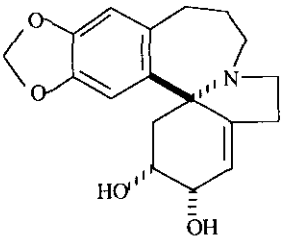

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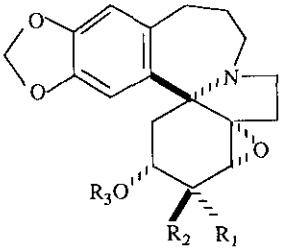

8 $R_1 = R_2 = R_3 = H$

9 $R_1 = R_2 = H$, $R_3 = CH_3$

10 $R_1 = R_3 = H$, $R_2 = OCH_3$

Three minor components (robustidine 7, robustimine 8 and O-methylrobustimine 9) are structurally related to alkaloids isolated from the leaves of *P. brachyphylla*.[4] They have the same chromophore in uv as phellinine 10 and the presence of a methylenedioxy group on the aroma-

tic ring was confirmed by characteristic ^1H nmr signals (7 : 5.90, 8 : 5.93 and 9 : 5.96 ppm). Two of them, 7, and 8, have the same composition $C_{18}H_{21}NO_4$ shown by analysis of molecular peaks in hrms. The presence of a double bond $\Delta^{1(6)}$ in the alkaloid 7, but not in 8, was suggested by the loss of C_2H_4O in ms of 7 (by a retro Diels-Alder fragmentation of ring A[1,10]) and was confirmed by ^1H nmr (δ H-C-1 = 5.75 ppm); this fragmentation indicated also that an hydroxyl group must be located at C-3. The peaks at m/z 180 and 167 are in accord with the presence of a second hydroxyl group in 7,[10b] the allylic position of this group being assigned by ^1H nmr after decoupling experiments on each proton of the substituted cyclohexene ring A. The coupling constants respectively between H-C-2 and H-C-3 (3 Hz[11]) and between H-C-3 and equatorial H-C-4 (3 Hz) and axial H-C-4 (12 Hz) are characteristic of the assigned configurations. A comparison of the ^1H nmr spectral data (Table) of the alkaloids 8 and 9 with the data of the known epoxide phellinine 10[4] allowed their structures to be deduced. These two bases have already been isolated from *P. brachyphylla* but in insufficient quantities to ascertain their structures.

	8	9	10
H-C-1	3.78	3.79	3.81
H-C-2	2.41	2.35	3.47
	1.98	2.01	
H-C-3	3.43	3.0	3.36
Heq-C-4	2.46	2.50	2.30
Hax-C-4	1.85	1.80	1.76
H_a-C-7	2.28	2.26	2.26
H_b-C-7	1.8	1.84	1.83
H_a-C-8	3.01	3.00	2.97
H_b-C-8	2.82	2.82	2.82
H_a-C-10	3.43	3.47	3.42
H_b-C-10	3.30	3.32	3.30
H_a-C-11	1.8	1.84	1.90
H_b-C-11	1.53	1.51	1.49
H_a-C-12	3.12	3.15	3.09
H_b-C-12	2.70	2.71	2.68
H-C-15	6.68	6.71	6.77
H-C-18	6.63	6.66	6.62
O-CH_2O	5.93	5.96	5.92
CH_3O-C-2			3.57
CH_3O-C-3		3.18	

Table : Nmr of the alkaloids 8, 9 and 10, δ ppm/TMS, ($CDCl_3$).

All the spectral data including cd curve of another alkaloid robusticine 11 ($C_{19}H_{25}NO_4$ by hrms) obtained in small amount (13 mg) showed a close resemblance to those of holidinine 12,[7] also present in the same plant.[9] A bathochromic shift was observed in its uv spectrum on addition of alkali indicating the presence of a phenol group. The chemical shifts and multiplicities of all the signals in its ^1H nmr spectrum are very close to those of holidinine 12, except for the absence of an aliphatic methoxyl singlet; the presence of an hydroxyl group at C-3 (instead of the methoxyl group in 12) is also confirmed by the loss of C_2H_4O (peak at m/z 287.1492 in hrms of 11) by a retro Diels-Alder fragmentation. Comparison of the chemical shift of the single aromatic proton of 11 (6.64 ppm) with those of H-C-15 signals in 12 (6.63 ppm) and athrocupressine 13 (6.39 ppm[12]) indicated the phenolic group to be at C-16 in robusticine 11. This assignement was confirmed by the methylation of the alkaloid 11 with an excess of diazomethane which led to robustivine 1, while the phenolic hydroxyl group at C-18 in athrocupressine 13 was unreactive in these conditions.[12]

The other alkaloids produced by this new variety of *Phelline comosa* are currently under investigation.

EXPERIMENTAL

Melting points were measured with a Kofler apparatus and are corrected. Optical rotations ($CHCl_3$) were measured on a Perkin-Elmer 241 polarimeter. Ir spectra ($CHCl_3$, νcm^{-1}) were recorded on a Perkin-Elmer 297 spectrophotometer and uv spectra [ethanol, λ_{max} nm, (ε)] on a λ5 Perkin-Elmer spectrophotometer. Cd curves (ethanol, λ_{max} nm, $\Delta\varepsilon$) were recorded on a Jobin-Ybon V dichrograph. ^1H Nmr spectra were obtained in $CDCl_3$ on a Bruker WM 400 or WP 200 Sy spectrometer with tetramethylsilane as the internal reference; coupling constants J are given in hertz; s, d, t and m indicate singlet, doublet, triplet and multiplet, respectively. Mass spectra were measured on a MS50. Preparative tlc was performed with Kieselgel HF 254 + 366 Merck.

The leaves of *Phelline comosa* Labill. var *robusta* (0.8 kg) were collected at Mount Oungone in New-Caledonia and the alkaloids (6.06 g) extracted by classical method[9].

Isolation of alkaloids

The crude alkaloid mixture (6.0 g) was chromatographied on silica gel with dichloromethane-methanol as eluent. The alkaloid 9 (26 mg) was separated from the fraction eluted with 2% of methanol after preparative tlc (hexane-ethyl acetate, 1-4). From the fraction eluted with 3% of methanol, the alkaloid 8 (12 mg) was isolated after 2 successive preparative tlc (hexane-ether-methanol, 4-15-1 and ethyl acetate). From the fractions eluted with 5 and 6%

of methanol (1.25 g) were isolated robustinine 1 (0.59 g) and, after 2 successive preparative tlc (hexane-ether-methanol, 4-15-1 and dichloromethane-methanol, 93-7), the alkaloids 7 (90 mg), 11 (13 mg) and a mixture of the alkaloids 5 and 6 (12 mg). Preparative tlc of the mixture of 5 and 6 (hexane-ether-methanol, 5-14-1, 4 successive elutions) led to a mixture of the products and to lucidinine 5 (5 mg) identified by comparison with an authentic sample.

Isolucidinine 6 (+ 5) : Ir: 3300, 1500; uv: 237, 282, alkaline medium: 251, 295. ^{1}H Nmr: 6.73 and 6.64 (2s, H-C-15 and H-C-18 of 6), 6.04 and 5.80 (m and d, J = 10, H-C-1 and H-C-2), 3.78 (s, aromatic CH_3O), 3.28 (s, aliphatic CH_3O).

Robustidine 7 : mp = 200-202°C, $[\alpha]_D$ = +141° (c = 0.83); ir: 3300, 2920; uv: 235(4500), 288(3500). ^{1}H Nmr: 6.62 and 6.59 (2s, 2H, H-C-15 and H-C-18), 5.90 (m, 2H, OCH_2O), 5.75 (m, 1H, H-C-1), 4.12 (m, 1H, $J_{2,3}$~3, H-C-2), 3.54 (m, 1H, H-C-3), 3.44 (dd, 1H, J~J'~13.5), 3.15 (m, 2H), 2.72 (m, 2H), 2.47 (m, 1H), 2.42 (dd, 1H, $J_{3,4eq}$ = 3 and $J_{4eq,4ax}$ = 12, H_{eq}-C-4), 2.30 (m, 1H), 1.85 (m, 1H, H_a-C-11), 1.78 (dd, 1H, $J_{4eq,4ax}$ ~ $J_{3,4ax}$ ~ 12, H_{ax}-C-4), 1.55 (m, 1H, H_b-C-11); ms (m/z): 315.1458 $M^{+\cdot}$, $C_{18}H_{21}NO_4$, 271.1232 $C_{16}H_{17}NO_3$, 255, 242, 180 (100%), 167, 77.

Robustimine 8 : mp = 134-136°C, $[\alpha]_D$ = +94° (c = 0.76); ir: 3400, 2925, 1600, 1350, 1100; uv: 236(sh), 290(4200). ^{1}H Nmr (see table); ms (m/z): 315.1464 $M^{+\cdot}$, $C_{18}H_{21}NO_4$ (100%), 298.1371, $C_{18}H_{20}NO_3$, 180, 166, 162, 135.

O-Methylrobustimine 9 : mp = 146-148°C, $[\alpha]_D$ +113° (c = 0.66); ir: 2925, 1600, 1350, 1100; uv: 235(sh), 290(5000). ^{1}H Nmr (see table); ms (m/z): 329($M^{+\cdot}$), 298 (100%), 194, 180, 162, 135.

Robusticine 11 : $[\alpha]_D$ +100° (c = 0.83); ir: 3200(b), 2900, 1575; uv: 278(2660), alkaline medium: 245(sh), 294(8000); dc: 208(+ 16), 225(-0.7), 241(+ 4.7), ^{1}H Nmr: 6.64 (s, 1H, aromatic H), 5.53 (m, 1H, H-C-1), 3.92 and 3.77 (2s, 6H, aromatic CH_3O), 2.69 (dd, 1H, $J_{3,4eq}$ = 3.5 and $J_{4eq,4ax}$ = 11.5, H_{eq}-C-4), 1.71 (dd, 1H, $J_{3,4ax}$ ~ $J_{4ax,4eq}$ = 11.5, H_{ax}-C-4); ms: 331.1782 $M^{+\cdot}$, $C_{19}H_{25}NO_4$, 314, 287.1495, $C_{17}H_{21}NO_3$, 286, 164(100%), 151, 146.

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