ALKALOIDS ISOLATED FROM THE LEAVES OF PHELLINE SP. AFF. P. LUCIDA (PHELLINACEAE)‡

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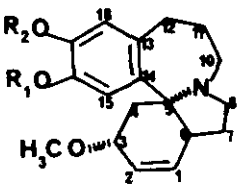
Abstract — Holidine 6, a new example of homoazaerythrinan skeleton was isolated from the leaves of Phelline sp. aff. P. lucida along with several other homoerythrinan and homoerythroidine type alkaloids.

Systematic chemical study of the alkaloids of the genus Phelline (Phellinaceae)[1,2] led us to investigate the alkaloid content of Phelline sp. aff. P. lucida collected in New Caledonia. Indeed the genus Phelline has a biosynthetic potency obviously closely related to that of Cephalotaxus from which the antitumor derivatives of cephalotaxine were isolated[3].

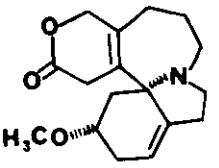
The extraction of the leaves (3 kg) with methylene chloride afforded crude alkaloids (4.13 g) which were separated by chromatography on silica gel and purified by classical methods.

The major component was identified by spectroscopic data to comosidine 1 (a name attributed to the alkaloid n° 2 from Phelline comosa[4]) together with two minor components : 3-epischelhammericine 2[4,5] and 2,7-dihydrohomoerysotrine 3[6,7].



1 $R_1=R_2=CH_3$

7 R_1(or R_2) = H, R_2(or R_1)=CH_3



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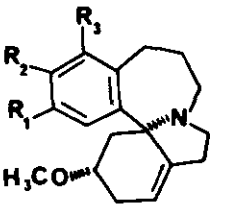


2 R_1-R_2=O-CH_2-O, R_3=H

3 R_1=R_2=OCH_3, R_3=H

8 R_1,R_2,R_3=OH,OCH_3,OCH_3

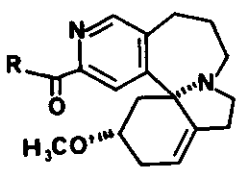
9 R_1=R_2=R_3=OCH_3

‡ N° 91 in series "Plantes de Nouvelle-Calédonie" ; for the n° 90 see : T. Batchily, H. Mehri, M. Plat, T. Sévenet and J. Pusset, Planta Medica, 1984, in press.

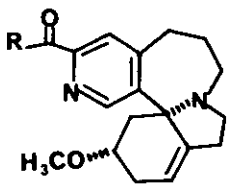
O-Methylisophellibiline 4, one of the alkaloids isolated from Phelline billiardieri[8], was also characterized : therefore the presence of members of homoerythrinan and homoerythroidine groups is reported for the first time in the same species.

It is quite probable that the biosynthetic intermediate between these two structural groups does exist in the plant. Thus phellinamide 5 was also isolated from this species ; phellinamide : $C_{18}H_{23}N_3O_2$ [9], mp : 206°C (acetone) ; $[\alpha]_D$ = + 180° ($CHCl_3$, c = 1.0) ; ir($CHCl_3$, νcm^{-1}) : 3350, 1680 ; uv (EtOH), λ_{max}nm (ε) : 232(9800), 272(4500) ; cd (EtOH), λ_{max}nm($\Delta\varepsilon$) : 235(- 1.5), 275(+ 2.4) ; ms (table 1) ; pmr($CDCl_3$, δ) : 8.34 (s, 1H; C_{18}-H or C_{15}-H, α to the nitrogen atom), 7.94 (s, 1H, C_{15}-H or C_{18}-H), 7.83 (1H, NH), 5.79 (1H) and 5.69 (1H) C_1-H and NH, 3.23 (s, 3H, OCH_3), 3.13 (m, 1H, C_3-H), 2.68 (dd, $J_{4eq,4ax}$ = 12 Hz and $J_{3,4eq}$ = 3 Hz, C_{4eq}-H), 1.68 (dd, $J_{4eq,4ax}$ = $J_{3,4ax}$ = 12 Hz, C_{4ax}-H) ; ^{13}C nmr (table 2), was previously obtained from Phelline billiardieri and structure 5a (or 5b) has been assigned to it constituting the first example of homoazaerythrinan skeleton[10].

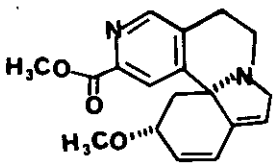
In addition, a new compound named holidine [$C_{19}H_{24}N_2O_3$ [9], $[\alpha]_D$ = + 175° ($CHCl_3$, c = 1.0) ; ir ($CHCl_3$, cm^{-1}) : 1715, 1580 ; uv (EtOH), λ_{max}nm (ε) : 233(8500), 272(4300) ; cd (EtOH), λ_{max}nm ($\Delta\varepsilon$) : 234(- 4.0), 278(+ 3.9) ; pmr ($CDCl_3$, δ), 8.50 (s, 1H, C_{18}-H or C_{15}-H, α to the nitrogen atom), 7.88 (s, 1H, C_{15}-H or C_{18}-H), 5.70 (1H, C_1-H), 3.99 (s, 3H, CO_2CH_3), 3.22 (s, 3H, OCH_3), 3.14 (m, C_3-H), 2.70 (dd, 1H, $J_{4eq,4ax}$ = 12 Hz, $J_{3,4eq}$ = 3 Hz, C_{4eq}-H), 1.66 (dd, $J_{4ax,4eq}$ = $J_{3,4ax}$ = 12 Hz, C_{4ax}-H)] having a characteristic pyridine ring appears to be structurally closely related to phellinamide 5 (tables 1 and 2). Its spectral data led us to propose structure 6 including a methoxycarbonyl group instead of the amide group of 5.



5a R=NH_2



5b R=NH_2



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6a R=OCH_3

6b R=OCH_3

Table 1 : Mass spectral fragmentations of phellinamide 5 and holidine 6

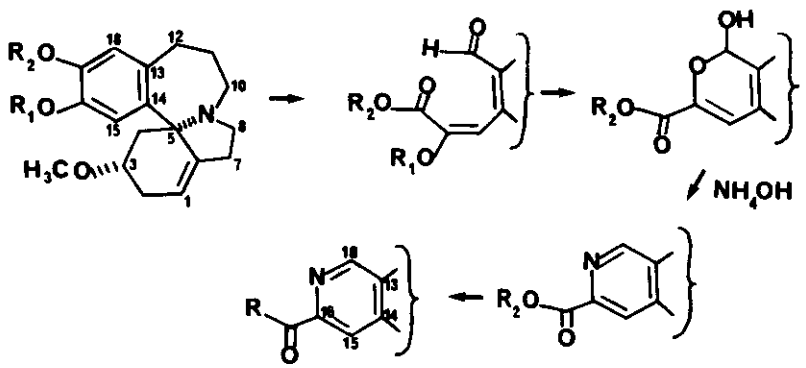
5	313 $M^{+\cdot}$	282	255	211	178(100%)	165	146
6	328 $M^{+\cdot}$	297	270	211	178(100%)	165	146

Table 2 : ^{13}C nmr of phellinamide 5 and holidine 6 ($CDCl_3$ δ ppm)

n° of C	C_1	C_3	C_4	C_5	C_6	C_8 C_{10}	C_{13} C_{14}	C_{15}	C_{16} C_{18}	OCH_3	$CO_2\underline{CH}_3$	CO
5(a)	117.8	73.9	37.8	68.7	147.6	49.5 46.6	140.4 140.5	123.3	150.1 153.5	55.9		167.4
6	118.1	74.0	37.7	68.8	147.1	49.5 46.7	140.7 141.3	126.2	151.7 153.5	56.1	52.9	166.3

This hypothesis was verified by chemical correlation : hydrolysis of the amide group of phellinamide 5 with 1N HCl followed by esterification with diazomethane[11] afforded a compound identical in all respects with holidine 6. This correlation confirms that the configurations at carbons 3 and 5 are the same in both compounds.

Phellinamide 5 and holidine 6 result probably from the reaction of ammonia on aldehydes formed from the cleavage of the aromatic ring of homoerythrinan precursors (scheme 1) thus following one of the hypotheses proposed by Barton[12]. Compounds 5 and 6 are therefore probably artefacts formed during the contact of powdered leaves with ammonia before extraction, though this fact has not yet been definitely proved. The analogy with the azaerythrinan alkaloid erymelanthine 10 recently described[13] supports the structures 5a and 6a with the nitrogen atom of the pyridine ring in the 17 position.



5a R = NH_2

6a R = OCH_3

Scheme 1

Two new phenolic alkaloids lucidinine 7 and holidinine 8 were also isolated in small amounts.

Lucidinine 7 has the following spectral properties : $[\alpha]_D$ = + 73° ($CHCl_3$, c = 1.03) ; ir ($CHCl_3$, cm^{-1}) : 3270, 1582, 1510, 1485, 1450 ; uv (EtOH), λ_{max} nm (ε) : neutral medium 234(6700), 283(3300), alkaline medium 252(8100), 299(4700) ; cd (EtOH), λ_{max} nm ($\Delta\varepsilon$) : 241(-0.7), 282(-0.3) ; ms (m/z) : 315.1836 $M^{+\cdot}$, $C_{19}H_{25}NO_3$, 300, 284, 270, 179 ; pmr ($CDCl_3$, δ) : 6,82 (s, 1H) and 6.65 (s, 1H) C_{15}-H and C_{18}-H , 6.09 (m, 1H, C_1-H), 5.85 (bd, $J_{1,2}$ = 10 Hz, C_2-H), 3.87 (s, 3H OCH_3 arom.), 3.30 (s, 3H, C_3-OCH_3), 2.62 (dd, 1H, $J_{4eq,4ax} \sim 11.5$ Hz, $J_{3,4eq} \sim 4.5$ Hz, C_{4eq}-H) ; 1.61 (dd, $J_{3,4ax} \sim J_{4eq,4ax} \sim 11.5$ Hz, C_{4ax}-H). These data, including cd characteristics, show that it differs only from comosidine 1 by the substitution of one of the methoxyl groups on the aromatic ring by a hydroxyl group.

In the same way, the physical and spectral data of holidinine 8 : mp : 164 - 165°C (ether) ; $[\alpha]_D$ = + 91° ($CHCl_3$, c = 1.03) ; ir ($CHCl_3$, νcm^{-1}) 3320, 1580, 1480 ; uv (EtOH), λ_{max} nm (ε) : neutral medium : 276(1900), 284(2000), alkaline medium 249(6800), 298(3000) ; dc (EtOH), λ_{max} nm ($\Delta\varepsilon$) : 224(-1.5), 240(+ 2.6), 283(-0.4) ; ms (m/z) : 345.1952 $M^{+\cdot}$, $C_{20}H_{27}NO_4$, 314, 287, 286, 272, 178(100%), 165, 146 ; pmr ($CDCl_3$ δ) : 6.63 (s, 1H arom.), 5.58 (1H, exchangeable with D_2O, OH), 5.56 (1H, C_1-H), 3.93 (s, 3H) and 3.76 (s, 3H) OCH_3 arom., 3.25 (s, 3H, C_3-OCH_3), indicated the structure 8 where one of the methoxyl groups of comosivine 9 (a name assigned to the alkaloid n° 5 of Phelline comosa, is replaced by a hydroxyl group.

The extraction of larger quantities of plant should allow to ascertain the position of the phenolic groups in 7 and 8.

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