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NOVEL BENZOPYRIDOQUINOLIZINE BASES FROM ALANGIUM LAMARCKII THW.[1]

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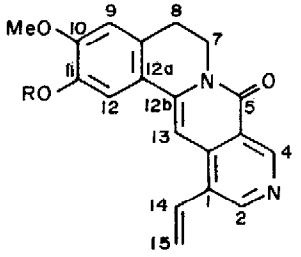
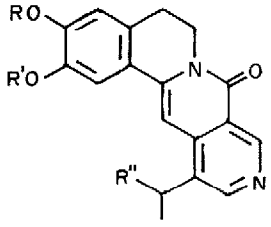
Abstract: Alangimarine (1), alamarine (2) and alangimaridine (3), isolated from the seeds of the title plant, have been characterised as a new class of alkaloids. Presence of isoalamarine (13) in the stem-bark is indicated.

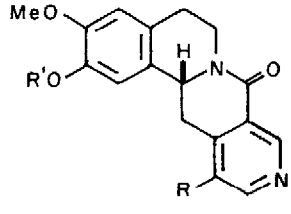
Several benzoquinolizine bases have so far been isolated[2] from Alangium lamarckii Thw.(Alangiaceae). We now report the structure elucidation of the novel benzo[a] pyrido[3,4-g]quinolizine alkaloids alangimarine (1), alamarine (2) and alangimaridine (3), isolated from the weakly basic fraction of the seeds.



1. R = H
6. R = Ac



2. R=Me,R'=H,R"=OH
7. R=Me,R'=Ac,R"=OAc
8. R=Me,R'=R"=H
13. R=H,R'=Me,R"=OH



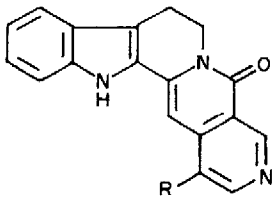
3. R= $-CH=CH_2$,R'=H
9. R= Et,R'=H
10. R= $-CH=CH_2$,R'=Ac

Alangimarine (1),m.p. 247°, $C_{19}H_{16}N_2O_3$ (high resolution MS), ν_{max}^{nujol} 1650 cm^{-1} (-CO-N<), showed no significant fragments in its mass spectrum except for a M-Me peak, indicating the presence of a highly conjugated aromatic system. The pronounced bathochromic shift of the long wavelength UV absorption maximum (Table 1) in acid, reminescent[3] of the indole bases angustine (4) and angustoline (5), gave the first indication of its benzopyridoquinolizine skeleton. Similar shift of the same band in alkali further suggested its phenolic nature, confirmed by the formation (Ac_2O/Py) of an O-monoacetate (6),m.p. 202°, MS: m/e 362(M^+), ν_{max}^{KCl} 1750,1625 and 1600 cm^{-1}.

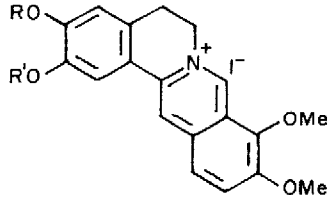
The PMR spectrum (Table 2) of the acetate 6 exhibited characteristic signals for Ar-OCH_3, Ar-$CH=CH_2$ and Ar-CH_2-CH_2-N< groups besides singlets for five aromatic protons. The assignments for the pyridoquinolizine part were in good accord with those reported[3] for 4. Therefore, the structure of alangimarine could be deduced as 1 except for the relative positions of the OH and OMe groups.

Alamarine (2), $C_{19}H_{18}N_2O_4$ (M^+338), m.p. 288°, $[\alpha]_D \pm 0°$, closely resembled 1 in mass spectral fragmentation pattern as well as in its UV spectra (Table 1). It formed an amorphous diacetate, 7[MS: m/e 422(M^+); ν_{max}^{KCl} 1765,1735,1660 and 1600 cm^{-1}], the PMR spectrum of which differed from that of 6 only with respect to the signals for a MeCH(OAc)- in place of the vinyl group.

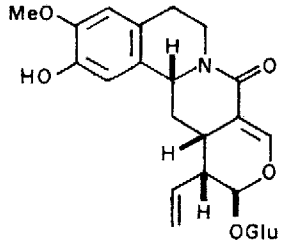
Dehydration (H_2SO_4/MeOH) of 2 smoothly afforded 1, while hydrogenolysis (5% Pd/C, EtOH, 10 hr) of 7 and subsequent saponification yielded the dihydro-derivative 8 [m.p. 222°, MS: m/e 322(M^+); ν_{max}^{nujol} 3500,1655,1595 cm^{-1}] obtained by catalytic hydrogenation (5% Pd/C, EtOH, 6 hr) of 1. Thus, 1 and 2 are correlated. Incidentally, the absence of any Cotton effect in the CD spectrum of 7 placed alamarine (2) in the rare group of racemic alkaloids.



4. R=-CH=CH_2
5. R=-CH(OH)Me



11. R=Me,R'=H
12. R=H,R'=Me



14.

The main breakthrough for the structure establishment of 1 and 2, particularly the location of the amide group in ring C rather than D, was however provided by the mass spectral fragmentation of the co-occurring base alangimaridine (3), m.p. 278°, $[\alpha]_D$ + 429° (c 0.35, $CHCl_3$), $C_{19}H_{18}N_2O_3$ (M^+322), that also clearly differentiated it from its isomer 8. The fragment pairs at m/e 177 and 175 and at m/e 145 and 117 in the mass spectrum of 3 evidently arose from isoquinoline and pyridine moieties, respectively, by the collapse of ring C. This requires saturation of the 12b,13 double bond, a conclusion also borne out by the absence of any absorption maximum above 320 nm. That the fragments at m/e 145 and 117 were indeed derived from the pyridine part with a vinyl side chain was further corroborated by the shift of these two peaks by 2 mass units in the mass spectrum of its dihydro-derivative (9), m.p. 232°, ν_{max}^{nujol} 3100,1650,1590 cm^{-1}, prepared by catalytic hydrogenation of 3 (10% Pd/C, EtOH, 1 hr).

The PMR spectrum of the acetate 10 [m.p. 232°, ν_{max}^{KCl} 1752,1650,1600 cm^{-1}] was in excellent agreement with the structure assigned to 3, a signal at δ 3.37 (1H,dd,J=16,4 Hz) clearly showing the 12b-proton to be axial.

Alangimaridine (3) was partially converted to 1 on long standing, the dehydrogenation being more readily brought about by refluxing with iodine in ethanol for 2 hr. All the three bases could, therefore, be correlated.

Table 1. UV spectra of alangimarine and related compounds

Comp. No.	λ_{max}(log ε), nm		
	EtOH	0.1 N NaOH	0.1 N HCl
1	220(4.37),261(4.11), 290sh(3.83),365(4.42)	225(4.27),272(4.17), 364(4.22),402(4.18)	230(4.22),275(4.04), 290(3.79),429(4.41)
2	220(4.37),253(4.20), 363(4.44)	231(4.37),259(4.36), 360(4.23),400(4.19)	220(4.32),269(4.12), 301(3.78),422(4.53)
3	220(4.53),255(4.00), 284(3.84)	221(4.54),246(4.25), 301(3.76)	220(4.42),254(4.00), 284(3.90)
8	220(4.51),255(4.24), 299(3.71),357(4.45), 373sh(4.40)	215(4.54),252(4.33), 358(4.32),367sh(4.29), 411(3.77)	213(4.48),224(4.45), 266(4.14),420(4.54)
13	220(4.25),253(4.04), 364(4.29)	223(4.25),259(4.03), 306(3.74),418(4.42)	220(4.21),266(3.97), 301(3.60),424(4.41)

Table 2. PMR chemical shifts* of alangimarine and related compounds

Comp. No.	H-2	H-4	H-7	H-8	H-9, H-12	H-13	H-14	H-15	OMe
6	8.77	9.50	4.37t (6)	3.01t (6)	6.86, 6.94	7.52	7.13dd (18,11)	5.84dd(18,1.2) 5.68dd(11,1.2)	3.91
7	8.84	9.61	4.40t (6)	3.01t (6)	6.91, 7.00	7.58	6.40q (6)	1.70d(6)	3.93
8	8.53	9.47	4.35t (6)	2.96t (6)	6.75, 6.90	7.41	2.92q (7.3)	1.36t(7.3)	3.98
10	8.82	9.24	4.90m	2.94m	6.83, 6.93	2.94	6.87dd (18,12)	5.76d(18) 5.55d(12)	3.84

* In δ units from internal TMS standard. Coupling constants (in Hz) in parentheses. Comp. nos. 6 & 8 were analysed in a 100 MHz and 7 & 10 in a 90 MHz instrument in $CDCl_3$.

The β(axial) configuration of the 12b-H in 3 could be deduced in analogy with the closely related tetrahydroprotoberberines [cf.(+)-tetrahydropalmatine] which exhibit high specific rotations, the sign of which determines the absolute stereochemistry irrespective of aromatic ring substitutions.

The location of the OMe and OH groups in all the three alkaloids could be tentatively fixed at C-10 and C-11 respectively from the UV spectral behaviour of 1 and 2 in basic media. On this criterion, they resemble columbamine (11) rather than the isomeric jatrorrhizine (12). It has been shown[5] that while the long wavelength maximum of 12 undergoes considerable bathochromic shift in presence of even a weak base ($NaHCO_3$), the spectrum of 11 remains unaffected. Again, while the same maximum in 12 is shifted completely in presence of alkali,

only partial shift has been noted in case of 11. A behaviour analogous to 12 was indeed observed in case of an isomer (high resolution MS) of alamarine isolated from the stem-bark of the same plant. Although paucity of material precluded its full characterization, isoalamarine, otherwise showing identical UV spectra as 1 (Table 1), has been assigned the structure 13.

It is noteworthy that the benzene ring substitution pattern of 1 to 3 and the absolute stereochemistry of alangimaridine (3) are the same as in alangiside[6] (14), the co-occurring glycoside. That the compounds were not artefacts formed by amination of 14 or its aglycone during work up was confirmed by their isolation by total exclusion of ammoniacal reagents.

These benzo[a]pyrido [3,4-g]quinolizine bases, therefore, constitute a new class of alkaloids, biogenetically derivable from 14 (or isomer for 13).

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