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ALKALOIDS OF *ATALANTIA MONOPHYLLA*

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Key Word Index—*Atalantia monophylla*; Rutaceae; acridone alkaloid; atalaphyllidine.

Abstract—From *Atalantia monophylla* Correâ (Rutaceae) a new acridone alkaloid atalaphyllidine has been isolated. Its structure has been derived from spectroscopic studies and chemical reactions and is the first acridone alkaloid having an *o*-prenyl moiety in both rings A and B.

INTRODUCTION

Atalantia monophylla Correâ (Family: Rutaceae) a shrub endemic to different parts of India has been examined for alkaloidal constituents. From the petrol extract of the dried roots, the occurrence of a new acridone alkaloid, *N*-methylbicycloatalaphylline [1] was reported. Subsequent investigation by the present authors led to the isolation of another new alkaloid, atalaphyllidine (1) and this communication deals with the details of our work on this alkaloid.

RESULTS AND DISCUSSION

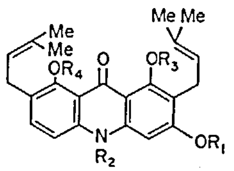
On cooling the concentrated petrol extract of the roots of *Atalantia monophylla* a yellow solid was obtained which was later identified as atalantin [2]. Chromatographic resolution of the mother liquor over silica gel yielded a new acridone base, atalaphyllidine, besides several known components. Atalaphyllidine was purified by preparative-TLC using a multiple development technique.

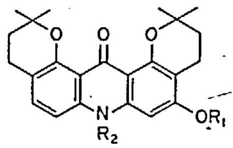
Atalaphyllidine, $C_{23}H_{25}NO_4$ (M^+ 379), crystallized from C_6H_6 as light lemon yellow needles, mp 222°. It turned green with alcoholic $FeCl_3$ and a positive Gibbs test (deep green) revealed that the *p*-position of at least one OH function was unsubstituted. The spectral data, particularly the PMR and UV spectra, together with other transformation reactions established the presence of an acridone moiety in atalaphyllidine. On treatment with CH_2N_2, atalaphyllidine afforded a dimethoxy derivative [3], $C_{25}H_{29}NO_4$ (M^+ 407), the PMR spectrum of which showed only one chelated OH group at δ 15.39. In agreement with this observation, prolonged methylation of the base with MeI and K_2CO_3 furnished a *N*-methyl-tri-*O*-methyl ether, $C_{27}H_{33}NO_4$ (M^+ 435). This could indicate the presence of three phenolic OH in the alkaloid.

Additional evidence in support of these observations was provided by the PMR spectrum of the parent base, atalaphyllidine. The occurrence of two chelated OH was apparent from the downfield chemical shifts at δ 13.59 and 14.65 (both disappearing on deuteration), a NH signal being discernible at δ 8.92 (also exchangeable with D_2O). Thus two of the three OH functions occupy the C-1 and C-8 positions [4, 5]. The PMR spectrum further revealed the presence of two 3,3-dimethylallyl side chains, the resonance signals for one of the gem-diMes being observed at δ 1.75 (6H, *s*), whereas the signals for the protons of the other *gem*-diMes appear at δ 1.82 (3H, *s*) and 1.95 (3H, *s*). Four benzylic methylene protons and two vinylic protons assembled at δ 3.55 (4H, *m*) and 5.20 (2H, *m*) respectively. The fact that all four benzylic methylene protons merged near δ 3.50 and that none was at a downfield region near δ 4.10 demonstrated that, unlike mangostin [6], neither of the isopentenyl side chains occupied the C-8 position.

On cyclisation with formic acid, the base furnished a bicyclo derivative (M^+ 379), mp 240°. In the bicyclic compound the two downfield –OH signals were missing though one phenolic OH group survived as revealed from the chemical shift at δ 8.91 disappearing on treatment with D_2O and by the formation of a *mono-O-*Me) ether (M^+ 393), mp 215–17° with CH_2N_2. This observation confirms that the two prenyl side chains are situated at C-2 and C-7 adjacent to the C-1 and C-8 –OH groups, respectively.

As regards the location of the third phenolic –OH not participating in the formation of the bicyclic compound the position, C-4 or C-5 is unlikely as it does not exhibit any downfield shift due to –NH in the vicinity. Hence, in all probability the site of this –OH group is either C-3 or C-6, both positions being equivalent as visualised from the proposed structure (1). The position of the –OH at C-3 or C-6 is also justified from the biogenetic pattern of naturally occurring hydroxylated acridone alkaloids. This inference could be further confirmed from the PMR spectrum of the bicyclic derivative and its *O*-methyl ether. In the spectrum of the bicyclic derivative the vinylic protons were missing and the OMe functions appeared upfield at δ 1.45 (12 H). The newly formed aliphatic methylenes appeared at δ 1.89 (4H, *m*) while the benzylic methylenes resonated at δ 2.83 (1H, *m*); this is characteristic of 2,2-dimethylchromans [5]. These observations can only be explained on the basis of structure (1) for the base. This could also establish the formulation of bicycloatalaphyllidine as (2a), *O*-methyl bicycloatalaphyllidine as (2b) and atalaphyllidine dimethyl ether, *N*-methyl-tri-*O*-methyl-atalaphyllidine and tetrahydroatalaphyllidine as (3a), (3b) and (4) respectively.





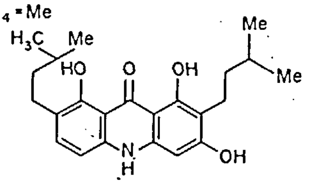
(1): $R_1 = R_2 = R_3 = R_4 = H$

(3a): $R_1 = R_3 = Me, R_2 = R_4 = H$

(3b): $R_1 = R_2 = R_3 = R_4 = Me$

(2a): $R_1 = R_2 = H$

(2b): $R_1 = Me, R_2 = H$



(4)

The MS of atalaphyllidine was in accord with the structure (1) and showed strong peaks at *m/e* 324 (M$^+$-55) and *m/e* 268 (324–56) due to cleavage of the two prenyl groups. Catalytic hydrogenation of the alkaloid with Adam's catalyst furnished tetrahydroatalaphyllidine $C_{23}H_{29}NO_4$, mp 250° whose MS showed a M$^+$ at *m/e* 383 with other significant peaks at *m/e* 326 (M$^+$-57) and 270 (326–56).

EXPERIMENTAL

Mp's are uncorrected. PMR spectra were determined at 100 MHz in $CDCl_3$, a few drops of DMSO-d_6 being added where necessary and the chemical shifts were recorded in δ. Samples were dried over P_2O_5 for 24 hr *in vacuo*.

Isolation. The sun-dried and finely milled roots (20 kg) of *Atalantia monophylla* (collected from Orissa) were exhaustively extracted with petrol (bp 60–80°) in a Soxhlet for 30 hr. After removal of solvent, the concentrated petrol. extract was left at 0° for 1 week when a dirty yellow solid separated out. This solid from later investigations was found to be atalantin [2]. TLC of the mother liquor showed 7 spots of variable intensities. The mother liquor was chromatographed over Si gel and marmesin, xanthyletin and β-sitosterol were eluted from the column with 2, 4 and 6% EtOAc in petrol, respectively. Early C_6H_6 eluates yielded *N*-methyl bicycloatalaphylline (50 mg), R_f 0.61 (in C_6H_6–EtOAc; 9:1) followed by *N*-methylatalaphylline (15 mg), R_f 0.39. The next few fractions of C_6H_6 eluate furnished a lemon yellow solid atalaphyllidine (400 mg), R_f 0.26, followed by atalaphylline (20 mg), R_f 0.26. The latter fractions furnished a tarry mass which still contained a number of less polar components. All the above compounds were identified by the usual procedures, Co-TLC, mmp and IR with the respective authentic samples.

Atalaphyllidine (1). The alkaloid crystallised from C_6H_6–EtOAc (4:1) mixture as yellow needles, mp 222°; λ_{max}^{EtOH} 255, 285, 305, 398 nm (log ϵ 4.39, 4.34, 4.32, 3.74), ν_{max} 3575, 3370, 3150, 1640, 1602, 1530, 1450 cm^{-1} (found: C, 72.91; H, 6.48; N, 3.87. $C_{23}H_{25}NO_4$ requires C, 72.83; H, 6.59; N, 3.69%). MS: *m/e* 379 (M$^+$, 100%), 364, 336, 324, 308, 280, 268 and 257.

Methylation of atalaphyllidine: (*i*) *dimethyl ether* (3a). A soln of (1) (60 mg) in MeOH (8 ml) was treated with excess CH_2N_2 and kept at room temp for 96 hr. The product crystallised from Me_2CO as yellow needles, mp 118° (M$^+$ 407) (Found: C, 73.31; H, 6.88; N, 3.09; OMe, 7.23, $C_{25}H_{29}NO_4$ requires C, 73.70; H, 7.12, N, 3.44; OMe, 7.61%). (*ii*) N-*methyl-tri*-O-*methyl ether* (3b). (1) (50 mg) in Me_2CO (25 ml) was refluxed with MeI and dry K_2CO_3 (400 mg) for 72 hr, filtered, evaporated and chromatographed on Si gel in C_6H_6–$CHCl_3$ (1:1) to yield an uncrystallisable gum, homogeneous by TLC (M$^+$ 435) (Found: C, 73.99; H, 6.96; N, 3.16; OMe, 20.9; $C_{27}H_{33}NO_4$ requires C, 74.48; H, 7.58; N, 3.21; OMe, 20.37%).

Tetrahydroatalaphyllidine (4). A soln of (1) (40 mg) in dry EtOH (10 ml) was stirred with H_2 (1 atm) in the presence of PtO_2 (30 mg) for 6 hr. The soln was filtered, evaporated and the residue crystallised from C_6H_6–EtOAc (2:1) as yellow needles (25 mg), mp 250° (decomp). MS: *m/e* 383 (M$^+$), 340, 326, 270 (Found: C, 72.17; H, 7.65; N, 3.39; $C_{23}H_{29}NO_4$ requires C, 72.06; H, 7.57; N, 3.65%).

Bicycloatalaphyllidine (2a). Atalaphyllidine (100 mg) was heated at 80–100° for 4 hr with formic acid (2 ml) and then left at room temp overnight. H_2O was added and the soln extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with aq. $NaHCO_3$, H_2O, dried and evaporated. The residue was chromatographed on Si gel (5 g) in C_6H_6–EtOAc (4:1). Fractions (10 ml) were collected; 1–5 contained traces of unreacted atalaphyllidine, 6–9 gave white crystals (25 mg), mp 240° (decomp.) which still gave a green colour with $FeCl_3$, (Found: C, 72.68; H, 6.70; N, 3.78; $C_{23}H_{25}NO_4$ requires C, 72.83; H, 6.59; N, 3.69%).

O-*Methylbicycloatalaphyllidine* (2b). A soln of (4a) (20 mg) in MeOH (5 ml) was treated with excess CH_2N_2 and kept at room temp for 72 hr and the product crystallised from C_6H_6–EtOAc as needles, mp 215–17° (M$^+$ 393). (Found, C, 73.55; H, 6.97; N, 3.33; -OMe 7.98; $C_{24}H_{27}NO_4$ requires C, 73.28, H, 6.87, N, 3.56 –OMe 7.88%).

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