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AN ACRIDONE ALKALOID FROM THE ROOT BARK OF *ATALANTIA MONOPHYLLA*

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Key Word Index—*Atalantia monophylla*; Rutaceae; alkaloid; atalaphylline 3,5-dimethyl ether.

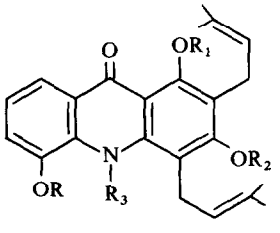
Abstract—Atalaphylline 3,5-dimethyl ether, a new acridone alkaloid from *Atalantia monophylla*, has been characterized on the basis of spectral data and chemical transformations.

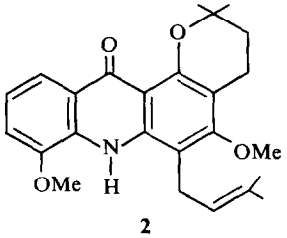
Atalantia monophylla Correa [1] is a thorny tree which has been reported to contain a number of acridone alkaloids [2–6] and limonoids [7–9] in its root bark. We present here the isolation and structure elucidation of another minor acridone alkaloid from the root bark of the plant collected from Orissa (India).

The mother liquor obtained by chilling the hot petrol (bp 60–80°) extract of the root bark on column chromatography over silica gel furnished an alkaloid fraction, TLC examination of which showed three further spots in addition to those of the six alkaloids already reported [2–6]. Exhaustive column chromatographic separation of this alkaloid fraction led to the isolation of a new alkaloid, atalaphylline 3,5-dimethyl ether (**1a**).

1a $C_{25}H_{29}NO_4$ (M^+ at *m/e* 407), mp 145–6° shows characteristic absorption of acridones [10] in its UV and IR (Nujol) bands at ν_{max}3350 sharp (NH), 1640 (chelated C=O) and 1605 (aromatic). The presence of a phenolic hydroxyl group is suggested by the deep green ferric reaction. Further, this hydroxyl group must be situated peri to the carbonyl group since the alkaloid is insoluble in alkali, could not be methylated by diazomethane and no band attributable to hydroxyl group is present in its IR. The band due to hydroxyl group must have been merged with C-H stretching as it is strongly hydrogen bonded to carbonyl group [11, 12]. Further, it is evident from the IR of the compound (**1d**) which did not show any bands in the region of 3000–3500 cm^{-1}. Such a low field absorption of hydroxyl group is also found in similar compounds reported earlier [13]. Its NMR spectrum showed two sharp singlets at δ 3.93 and 3.8 integrated for 3 protons each due to two methoxy groups. The presence of two prenyl groups is indicated by δ 1.64 (3 H, *s*), 1.76 (6 H, *s*) and 1.92 (3 H, *s*) corresponding to four methyls, δ 3.40 (4 H, *m*) benzylic and δ 5.14 (2 H, *br.*) vinylic protons. Two low field signals at δ 14.2 (1 H, *s*) and 8.78 (1 H, *br.*, *s*) which disappear in the presence of D_2O are assigned to chelated hydroxyl at C_1 and NH respectively. The aromatic region of the spectrum showed the presence of three protons of ABX pattern, δ 7.75 (1 H, *dd*, J = 7.5 and 3.0 Hz) must belong to H_8 [14]. The multiplet at δ 6.8–7.2 arises from H_6 and H_7; this region of the spectrum shows a striking similarity to that of atalaphylline (**1b**) and *N*-methylatalaphylline (**1c**). The mass spectrum of the alkaloid further confirms the presence of two prenyl groups by showing strong peaks at *m/e* 352 ($M^+ - 55$) and at *m/e* 296 (352 − 56) due to the cleavage of prenyl groups.

The alkaloid (**1a**) on treatment with boiling formic acid gave a cyclized product (**2**) mp 139–40°. It resembles compound **1a** in its UV spectrum, NMR signals at δ 1.5 (6H, *s*), 2.78 (2H, *t*, J = 7 Hz) indicating the formation of a 2,2-dimethylchroman. Methylation of the alkaloid under forcing conditions gave a *N*-methyl derivative (**1d**) and *N*-methyl tri-*O*-methylatalaphylline (**1e**). Their physical data are identical with those reported [2] earlier. Their IR spectra were superimposable with the authentic





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1a R = R_2 = Me, R_1 = R_3 = H
1b R = R_1 = R_2 = R_3 = H
1c R = R_1 = R_2 = H, R_3 = Me
1d R = R_2 = R_3 = Me, R_1 = H
1e R = R_1 = R_2 = R_3 = Me

samples obtained by methylation of *N*-methylatalaphylline with CH_2N_2 and complete methylation of atalaphylline under forcing conditions respectively.

All the above mentioned spectral data and reactions lead to the structure **1a** for the new alkaloid. Further atalaphylline 3,5-dimethyl ether was found to be identical with synthetic material prepared by treating atalaphylline with diazomethane (mp, mmp and superimposable IR).

EXPERIMENTAL

Mps are uncorrected; NMR spectra were recorded at 100 MHz using TMS as internal standard in $CDCl_3$ and MS were recorded at 70 eV.

Isolation of atalaphylline 3,5-*dimethyl ether* (**1a**). The powdered root bark was extracted in a Soxhlet with petrol (bp 60–80°). The extracts were pooled and chilled. The mother liquor was chromatographed over silica gel (1:30). The column was eluted with petrol, petrol–EtOAc (2.5, 5 and 7.5% VV) and then with C_6H_6, Et_2O and MeOH. The fractions collected with C_6H_6 and Et_2O (TLC similar) gave a yellow solid. This fraction was rechromatographed over silica gel (1:50). The fractions collected with petrol–EtOAc (10:1) (TLC single spot) on concentration gave yellow crystalline needles (78 mg); recrystallization from hexane–ether yielded (75 mg) bright yellow needles, mp 145–6° insoluble in aq. NaOH. The compound gave a green colour with $FeCl_3$ in MeOH solution and has λ_{max}^{MeOH} 215, 262, 280, 310, 323 and 405 nm (log ε 4.10, 4.58, 4.42, 3.94, 3.99 and 3.43), IR (Nujol): 3350, 1640, 1605, 1590 and 1570 cm^{-1}. (Found: C, 73.90; H, 7.46. $C_{25}H_{29}NO_4$ requires: C, 73.71; H, 7.13%.) MS *m/e* (rel. int.): 407 (M^+, 78), 392 (10), 364 (84), 352 (100), 336 (5), 308, 296 (40) and 282 (26).

Cycloatalaphylline 3,5-*dimethyl ether* (**2**). Atalaphylline 3,5-dimethyl ether (100 mg) was heated at 80–100° for 3 hr with formic acid (85%, 3 ml) then left at room temp. overnight. Water was added, extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $NaHCO_3$ aq., H_2O, dried and evapd. The residue was chromatographed over Si gel and eluted with C_6H_6–EtOAc (4:1). Fractions of 25 ml were collected and monitored by TLC. Fractions (10–20) yielded cycloatalaphylline 3,5-dimethyl ether (60 mg) pale yellow crystalls from petrol–EtOAc, mp 139–40°, alcoholic and chloroform solutions gave bright blue fluorescence. λ_{max}^{MeOH} 218, 232, 263, 306, 317 and 398 nm (log ε 4.24, 4.15, 5.15, 4.02, 4.05 and 3.85), IR (Nujol): 3375, 1640, 1625, 1600 and 1575 cm^{-1}. (Found: C, 73.61; H, 7.23. $C_{25}H_{29}NO_4$ requires: C, 73.71; H, 7.13%), NMR: δ 8.50 (NH, *br.s*), 7.94 (1H, *dd*, *J* = 7.5 and 2 Hz), 6.82–7.1 (2H, *m*), 5.16 (1H, *t*, *J* = 7 Hz), 3.97 (3H, *s*, OMe), 3.82 (3H, *s*, OMe), 3.54 (2H, *d*, *J* = 6 Hz), 2.78 (2H, *t*, *J* = 7 Hz), 1.8–1.98 (8 H, *m*) and 1.52 (6 H, *s*, O—C=Me_2. MS *m/e* (rel. int.): 407 (M^+, 35), 392 (95), 379 (5), 364 (8), 352 (100), 296 (10) and 284 (13).

N-*Methyl-atalaphylline* 3,5-*dimethyl ether* (**1d**) *and* N-*methyl tri*-O-*methylatalaphylline* (**1e**). Atalaphylline 3,5-dimethyl ether (0.100 g) in acetone (50 ml) was refluxed with 10 ml MeI and 10 g K_2CO_3 (anhydrous) for 76 hr. Filtered, evaporated, the residue was chromatographed over silica gel and eluted with petrol–EtOAc (10:1), and then with benzene–EtOAc (10:1). Fractions collected with petrol–EtOAc gave compound **1d** as a gum (23 mg) and the fractions collected with benzene–EtOAc gave compound **1e** which showed green fluorescence and was an uncrystallizable gum (40 mg).

Compound **1d** showed λ_{max}^{MeOH} 217, 272, 325 and 410 nm (log ε 3.9, 4.0, 3.5 and 3.1). IR (CCl_4): 1630, 1600, 1573 and 1500 cm^{-1}. (Found: C, 74.28; H, 7.1, $C_{26}H_{31}NO_4$ requires: C, 74.11; H, 7.36%). NMR: δ 14.2 (*s*, OH), 7.9 (1H, *dd*, *J* = 7 and 3 Hz), 7.08–7.26 (2H, *m*), 5.28 (2H, *br.*), 4.0 (3H, *s*, OMe), 3.81 (3H, *s*, OMe), 3.58 (3H, *s*, N – Me), 3.38–3.51 (4H, *m*), 1.79 (6H, *s*, 2C – Me) and 1.7 (6 H, *s*, 2C – Me). MS *m/e* (rel. int.): 421 (M^+, 45), 406 (80), 393 (30), 366 (100) and 310 (15).

Compound **1e** showed λ_{max}^{MeOH} 218, 270, 323 and 405 nm (log ε 3.8, 4.1, 3.4 and 3.0), IR (CCl_4): 1640, 1600, 1575 and 1500 cm^{-1}. (Found: C, 74.21; H, 7.33, $C_{27}H_{33}NO_4$ requires: C, 74.45; H, 7.64%). NMR: δ 7.83 (1H, *dd*), 7.08–7.3 (2H, *m*), 5.14–5.44 (2H, *m*), 3.98 (3 H, *s*, OMe), 3.91 (3 H, *s*, OMe), 3.82 (3 H, *s*, OMe), 3.52 (3 H, *s*, N – Me), 3.45 (4 H, *br.*), 1.8 (6 H, *s*, 2C – Me), and 1.68 (6 H, *s*, 2C – Me). MS *m/e* (rel. int.): 435 (M^+, 45), 420 (80), 380 (100), 367 (70) and 324 (8).

Atalaphylline dimethyl ether. Atalaphylline (**1b**) 100 mg in 3 ml of MeOH was treated with excess of ethereal CH_2N_2 and left at room temp. overnight. Evaporation and crystallization of the residue from Et_2O–hexane gave yellow needles (60 mg), mp 145–7°.

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