

BIS-BENZYLISOQUINOLINE ALKALOIDS FROM *ABUTA PAHNI*

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Key Word Index—*Abuta pahni*; Menispermaceae; bis-benzylisoquinoline alkaloids; 2'-*N*-nordaurisoline; 2-*N*-methyllindoldhamine; 2'-*N*-methyllindoldhamine.

Abstract—From the stems of *Abuta pahni*, eight isoquinoline alkaloids were isolated and identified by spectroscopic methods and chemical correlations. Three of the bis-benzylisoquinoline alkaloids are new and were assigned the structures 2'-*N*-nordaurisoline, 2-*N*-methyllindoldhamine and 2'-*N*-methyllindoldhamine. The other known alkaloids were coclaurine, daurisoline, lindoldhamine, dimethyllindoldhamine, stepharine and thalifoline.

INTRODUCTION

The genus *Abuta* (Menispermaceae, Anomospermae) spreads widely throughout tropical America. Out of its 30 species [1] only a few have been studied from a chemical point of view. They all contain isoquinoline alkaloids of several types, namely bis-benzylisoquinolines [2, 3], oxoaporphines [4, 5], azafluoranthenes [5], tropoisoquinolines [6] and isoquinolobenzazepines [7]. As *A. pahni* [8] is part of Amazonian curare mixtures, we thought it worthwhile carrying out the analysis of the alkaloidal composition of this species.

RESULTS AND DISCUSSION

Extraction and separation of the non-quaternary alkaloids, according to a conventional process, led to the isolation and characterization of eight alkaloids. Five of them are known, an isoquinolone, thalifoline, a benzylisoquinoline, (+)-coclaurine, a proaporphine, (+)-stepharine and two bis-benzylisoquinolines, (–)-daurisolone 1 and (–)-lindoldhamine 3.

The three remaining alkaloids are new. They are all of the single bridged bis-benzylisoquinoline type, as suggested by mass spectroscopy by the very low intensity of the $[M]^+$ peak [9]. The 1H NMR spectra (360 MHz, FT) (cf. Table 1) display much analogy. There appears, in particular, the constant presence of an ABX system, and of an A_2B_2 system, respectively, assigned to the protons in the 10,13,14 and 10',11',13',14' positions, a characteristic feature of the 11,12' single bridged bis-coclaurine [2, 3]. Each of the three spectra also shows only one singlet assignable to a *N*-methyl group at ca 2.5 ppm. The other nitrogen atom is therefore engaged in a secondary amino function as established by the very strong deshielding of the 1- or 1'-proton (ca 4.1–4.2 ppm).

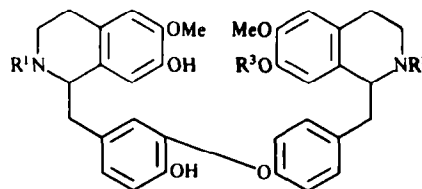
Alkaloid 2, $C_{36}H_{40}N_2O_6$, $[M]^+$ m/z 596, presents a 1H NMR spectrum that differs little from that of daurisolone 1. Methylation of 2 ($HCHO-NaBH_4$) affords a compound identical in every respect to 1. The use of NOEs helps establish the respective positions of the *N*-H

and of the *N*-Me. Irradiation of the *N*-Me singlet induces a 4% increase of the signal at 3.61 ppm; when this last signal is irradiated, increases of 2% on the H-8 signal (at 6.31 ppm) and of 1.2% on the doublet of the X proton of the ABX system in the ring C (H-10 at 6.49 ppm) can be observed. Therefore, the nitrogen in position 2 carries the methyl group and alkaloid 2 is assigned the structure 2'-*N*-nordaurisoline.

Alkaloids 4 and 5 exhibit the same molecular formula $C_{35}H_{38}N_2O_6$, $[M]^+$ m/z 582. Like 2, they both carry a secondary amino function, which on methylation ($HCHO-NaBH_4$) gives one product only, the (–)-*N,N*-dimethyllindoldhamine 6 (= guattegaumerine [10]), identified by comparison with authentic samples [11]. As above, the respective positions of the secondary amino and tertiary amino groups in alkaloid 4 are determined through NOE measurements (cf. values in the Experimental). It can then be given the structure 2-*N*-methyllindoldhamine. Consequently alkaloid 5 corresponds to 2'-*N*-methyllindoldhamine.

Like (–)-daurisolone 1 and (–)-lindoldhamine 3 the three new alkaloids have a 1*R*,1'*R* configuration as established by the superimposability of their CD curves.

Thus, *A. pahni* displays an array of isoquinoline alkaloids close in composition to other *Abuta* species. Yet



- | | | | |
|---|-------------|-------------|------------|
| 1 | $R^1 = Me,$ | $R^2 = Me,$ | $R^3 = Me$ |
| 2 | $R^1 = Me,$ | $R^2 = H,$ | $R^3 = Me$ |
| 3 | $R^1 = H,$ | $R^2 = H,$ | $R^3 = H$ |
| 4 | $R^1 = Me,$ | $R^2 = H,$ | $R^3 = H$ |
| 5 | $R^1 = H,$ | $R^2 = Me,$ | $R^3 = H$ |
| 6 | $R^1 = Me,$ | $R^2 = Me,$ | $R^3 = H$ |

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Table 1. ¹H NMR chemical shifts of compounds 1–6 (δ ppm, 360 MHz, CDCl₃, TMS as internal standard)

	1	2	3	4	5	6
2-N-CH ₃	2.47 s	2.43 s	—	2.46 s	—	2.50 s
2'-N-CH ₃	2.53 s	—	—	—	2.47 s	2.45 s
H-1	3.62 dd	3.61 dd	4.05 dd	3.61 dd	4.16 dd	3.62 dd
H-1'	3.77 dd	4.15 dd	4.15 dd	4.11 dd	3.61 dd	3.72 dd
H-5	6.46 s	6.45 s	6.51 s	6.45 s	6.45 s	6.48 s
H-5'	6.57 s	6.60 s	6.58 s	6.57 s	6.62 s	6.54 s
H-8	6.34 s	6.32 s	6.69 s	6.30 s	6.66 s	6.24 s
H-8'	6.14 s	6.69 s	6.69 s	6.77 s	6.35 s	6.32 s
H-10	6.53 d	6.49 d	6.66 d	6.48 d	6.48 d	6.61 d
H-13	6.90 d	6.90 d	6.89 d	6.87 d	6.90 d	6.87 d
H-14	6.84 dd	6.84 dd	6.91 dd	6.84 dd	6.85 dd	6.76 dd
H-10' and 14'	7.03 d	7.16 d	7.17 d	7.14 d	7.17 d	7.02 d
H-11' and 13'	6.81 d	6.83 d	6.87 d	6.82 d	6.84 d	6.82 d
CH ₃ O-6	3.80* s	3.81† s	3.86‡ s	3.85§ s	3.85 s	3.85¶ s
CH ₃ O-6'	3.83* s	3.86† s	3.85‡ s	3.81§ s	3.81 s	3.84¶ s
CH ₃ O-7	3.62 s	3.84 s	—	—	—	—

*†‡§||¶ Assignments with the same superscript are interchangeable for a given compound.

only *A. candicans* and *A. grisebachii* contain bis-quaternary alkaloids which could be responsible for a muscle relaxant activity and therefore for a curare-like toxicity. Due to the lack of detailed investigations on the activity of tertiary bis-benzylisoquinolines on muscle, the part played by the other *Abuta* species in the arrow poison mixtures still remains unclear.

EXPERIMENTAL

Plant material. Stems of *Abuta pahni* (Martius) Krukoff and Barneby (1.5 kg) were collected in August 1984 by one of us (A.F.) in Alto-Beni, Marimono, Bolivia, at 850 m altitude.

Extraction and chromatography. After removal of lipids with petrol, the stem powder was made alkaline and extracted with CH₂Cl₂ in a Soxhlet apparatus. The alkaloidal mixture was further purified by the usual acid-base treatment, then separated by ¹⁸C on Merck 60 silica gel or by TLC on Merck 60 H silica gel and by prep. TLC on Merck HF₂₅₄ silica gel.

Identification of compounds. Data (¹H NMR, MS, UV, comparative TLC) of the known compounds were in total accordance with those published. For thalifoline refer to [12], for (+)-coclaurine and (+)-stepharine to [13], for (–)-daurisolone 1 to [3], for (–)-lindoldhamine 3 to [2] and for *N,N*-dimethylindoldhamine 6 to [11] (except 360 MHz ¹H NMR data of 1, 3 and 6: cf. Table 1).

2'-N-Nordaurisolone 2. [α]_D: negative. MS *m/z* (rel. int.): 596 [M]⁺ (< 1), 192 (100). 360 MHz ¹H NMR: cf. Table 1. Main observed NOEs: 2-N-CH₃ on H-1: +4% (reciprocal); H-1 on H-8: +2% (reciprocal); H-1 on H-10: +1.2% (reciprocal).

2-N-Methylindoldhamine 4. [α]_D = –185° (MeOH; *c* = 0.10). UV (EtOH) X_{max} nm (log): 213 (4.965), 225 sh (4.829), 285 (4.364). MS *m/z* (rel. int.): 582 [M]⁺ (< 1), 192 (100), 178 (20). 360 MHz ¹H NMR: cf. Table 1. Main observed NOEs: 2-N-CH₃ on H-10: +1.5% (reciprocal); H-1' on H-8': +5% (reciprocal); H-1' on H-10', 14': +2.5% (reciprocal).

2'-N-Methylindoldhamine 5. [α]_D = –47° (MeOH; *c* = 0.17). MS *m/z* (rel. int.): 582 [M]⁺ (< 1), 192 (47), 178 (100) 360 MHz ¹H NMR: cf. Table 1.

N-Methylation reactions. 37% formalin (1 ml) was added slowly into samples of 2, 4 and 5 (10 mg) in MeOH (5 ml) and the solns stirred under reflux for 45 min, then cooled. NaBH₄ (50 mg) was then added and the solns stirred under reflux for another 45 min. After cooling, HOAc was added to decompose excess reagent and the mixtures made alkaline with NH₃ and then extd with CHCl₃. Solvent was removed in vacuum, and the residues purified by prep. TLC.

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