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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], tropoloisoquinolines [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, (−)-daurisoline **1** and (−)-lindoldhamine **3**.

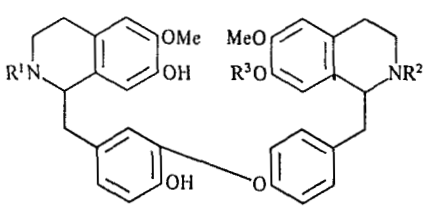
The three remaining alkaloids are new. They are all of the single bridged *bis*-benzylisoquinoline type, as suggested by mass spectroscopy by the very low intensity of the $[M]^+$ peak [9]. The ^1H NMR spectra (360 MHz, FT) (*cf.* Table 1) display much analogy. There appears, in particular, the constant 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 daurisoline **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 (−)-daurisoline **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. ^{1}H NMR chemical shifts of compounds 1–6 (δ ppm, 360 MHz, $CDCl_3$, 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_3O-6	3.80* *s*	3.81† *s*	3.86‡ *s*	3.85§ *s*	3.85‖ *s*	3.85¶ *s*
CH_3O-6′	3.83* *s*	3.86† *s*	3.85‡ *s*	3.81§ *s*	3.81‖ *s*	3.84¶ *s*
CH_3O-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 CH_2Cl_2 in a Soxhlet apparatus. The alkaloidal mixture was further purified by the usual acid–base treatment, then separated by CC on Merck 60 silica gel or by TLC on Merck 60 H silica gel and by prep. TLC on Merck HF_{254} silica gel.

Identification of compounds. Data (^{1}H 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 (−)-daurisoline 1 to [3], for (−)-lindoldhamine 3 to [2] and for *N,N*-dimethyllindoldhamine 6 to [11] (except 360 MHz ^{1}H NMR data of 1, 3 and 6: *cf.* Table 1).

2′-N-*Nordaurisoline* 2. $[\alpha]_D$: negative. MS *m/z* (rel. int.): 596 $[M]^+$ (< 1), 192 (100). 360 MHz ^{1}H NMR: *cf.* Table 1. Main observed NOEs: 2-*N*-CH_3 on H-1: +4% (reciprocal); H-1 on H-8: +2% (reciprocal); H-1 on H-10: +1.2% (reciprocal).

2-N-*Methyllindoldhamine* 4. $[\alpha]_D = -185°$ (MeOH; $c = 0.10$). UV (EtOH) λ_{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 ^{1}H NMR: *cf.* Table 1. Main observed NOEs: 2-*N*-CH_3 on H-10: +1.5% (reciprocal); H-1′ on H-8′: +5% (reciprocal); H-1′ on H-10′,14′: +2.5% (reciprocal).

2′-N-*Methyllindoldhamine* 5. $[\alpha]_D = -47°$ (MeOH; $c = 0.17$). MS *m/z* (rel. int.): 582 $[M]^+$ (< 1), 192 (47), 178 (100) 360 MHz ^{1}H 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. $NaBH_4$ (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 NH_3 and then extd with $CHCl_3$. Solvent was removed in vacuum, and the residues purified by prep. TLC.

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