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ALKALOIDS OF *ASPIDOSPERMA PYRIFOLIUM*

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Key Word Index—*Aspidosperma pyrifolium*; Apocynaceae; root bark; leaves; alkaloids; structure and configuration; (+)-aspidospermine; 6-demethoxypyrifoline.

Abstract—Two new alkaloids have been isolated from root bark and leaves of *Aspidosperma pyrifolium* and identified as (+)-aspidospermine and 6-demethoxypyrifoline.

INTRODUCTION

Several studies on *Aspidosperma pyrifolium* have reported the isolation of pyrifoline (**1**) [1, 2] and pyrifolidine (**2**) [1, 3] from trunk bark, and aspidofiline (**3**) [4, 5] from leaves. As part of a chemical and pharmacological screening of Brazilian plants a strong hypotensive effect of the crude alkaloids from root bark and leaves of *A. pyrifolium* was detected on the arterial blood pressure of the dog.

As the roots of the plant have not been investigated before, it was decided to carry out a chemical investigation of these parts as well as to reinvestigate the alkaloids in the leaves because of their pharmacological properties.

RESULTS AND DISCUSSION

A. pyrifolium, a tree popularly known as 'pereiro-preto', is widely distributed in north-east Brazil. The plant studied was collected in Sobral, Ceará in August 1980. The crude alkaloids were isolated from an ethanolic extract of the leaves and three alkaloids were purified by prep. TLC on Si gel. The major alkaloid was identified as pyrifoline (**1**) by comparison of its ^{1}H NMR and mass spectra with those recorded for pyrifoline previously isolated from the trunk bark of the same species [1, 2].

The second substance presented spectral data similar to pyrifoline, except for the absence in the ^{1}H NMR spectrum of the aliphatic methoxyl peak (δ 3.31), suggesting the structure 6-demethoxypyrifoline (**4**) for this alkaloid. The mass spectrum exhibited a $M^{+\cdot}$ 352 in agreement with the molecular formula, $C_{22}H_{28}N_2O_2$, and peaks at *m/z* 324 $[M^+ - 28]^{+\cdot}$, 309, 281, 124 and 109 (base peak) all characteristic of the aspidosperma alkaloid skeleton.

The third alkaloid was identified as aspidofiline (**3**) by analysis of spectral data and by comparison with an authentic sample.

From a chloroform extract of the roots was isolated aspidospermine identified by its spectral data (mass and ^{1}H NMR spectra) and mp [6]. To establish the configuration of 6-demethoxypyrifoline (**4**), it was necessary to compare its ORD curve with similar data from (+)-pyrifoline with a known configuration [7]. The ORD curve of (+)-aspidospermine was also obtained and compared with data recorded for (−)-aspidospermine [8]. The three alkaloids exhibited positive Cotton effects and showed almost superimposable curves. From these observations it is possible to conclude that the aspidospermine isolated from *A. pyrifolium* belongs to the (+) series and that it is the antipodal isomer of the known (−)-aspidospermine (**6**). Determination of $[\alpha]_D^{25}$ gave a value of +92° whereas the lit. value for the laevo isomer is −92°. The occurrence of the new aspidosperma-type 6-demethoxypyrifoline could be biosynthetically associated with the presence of pyrifoline, which is the major base present in the leaves of *A. pyrifolium*.

Although the isolation of aspidospermine from *A. pyrifolium* has already been reported [6], on the basis of its optical rotation it is now possible to report the natural occurrence of the dextrorotatory isomer for the first time.

In spite of the fact that (−)- and (+)-quebrachamine (**7**) are biosynthetic precursors of the aspidospermine skeleton presumably by C-12 → C-19 ring closure [9–11] it is surprising that only (−)-aspidospermine is reported in the lit. The present isolation of the dextro aspidospermine (**5**) gives a strong support for the above hypothesis.

EXPERIMENTAL

Leaves of *A. pyrifolium* Mart. (10 kg, dry wt) were extracted with EtOH in a Soxhlet apparatus. The EtOH extract was concd at 45–50° in a rotatory evaporator. To the residue was added 1 N H_2SO_4 (500 ml) with stirring. The aq. phase was extracted with Et_2O at different pH values (3,5,7,9 and 12). The Et_2O extracts obtained at pH 9 and 12 were combined and concd under red. pres. giving 54 g of a dark residue. This residue (10 g) was chromatographed on prep. Si gel $H + PF_{254+366}$ (3:1) plates using C_6H_6–Me_2CO–MeOH (9:2.5:1) as eluent. Three fractions of prepurified alkaloids were obtained. Each fraction was further chromatographed by prep. TLC at pH 6 with Pi buffer. From *ca* 500 plates were isolated three pure alkaloids (1 g each).

(+)-*Pyrifoline* (**1**). White crystals from petrol, mp 138–140° (lit. [1], 141–144°). $[\alpha]_D$ +105° (lit. [1] $[\alpha]_D$ +102°), IR ν_{max}^{KBr} cm^{-1}: 2920, 1660, 1550, 1480, 1200, 1068, 750, 720. UV λ_{max}^{EtOH} nm (log ε): 218 (4.35), 260 (3.93), 284–292 (infl.) (3.50); λ_{min} 238 (3.70). ORD $\lambda^{MeOH}(\phi)$: λ_{max} 258 (+92 444); λ_{min} 228 (−29 032); $\lambda_{infl.}$ 288 (+23 000), a = 1214. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.0–2.1

Taken in part from the M.Sc. thesis of Leila Máriam Serur presented to the Universidade Federal do Ceará.

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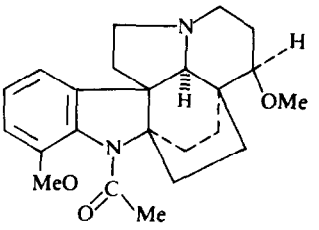

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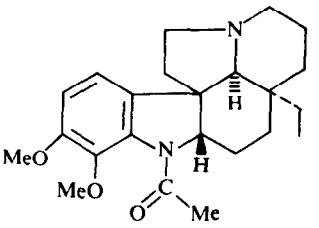

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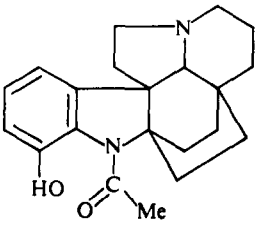

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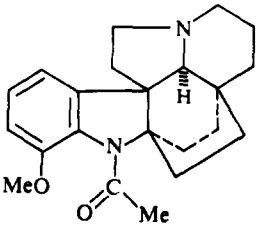

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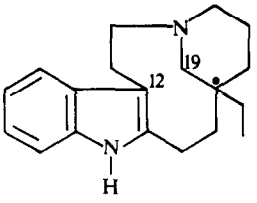

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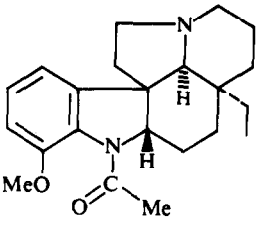

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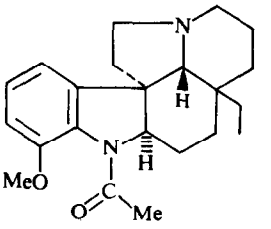

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(12H, *m*), 2.11 (1H, *s*), 2.12 (CO<u>Me</u>, *s*), 2.4–3.30 (5H, *m*), 3.31 (O<u>Me</u>, *s*), 3.81 (*ϕ*-O<u>Me</u>, *s*), 6.8–7.1 (3Ar-<u>H</u>, *m*). MS, *m/z* 382 $[M]^{+\cdot}$, 354, 339, 310, 139, 154.

6-*Demethoxypyrifoline* (**4**). White crystals from petrol, mp 121–123°, IR ν_{max}^{KBr} cm^{-1}: 2920, 1660, 1590, 1215, 750 and 720. UV λ_{max}^{MeOH} nm (log ε): 216 (4.34), 259 (3.97), 285–295 (infl.) (3.60); λ_{min} 235 (3.74). ORD λ^{MeOH} (*ϕ*): λ_{max} 259 (+81 840); λ_{min} 228 (−22 000); $\lambda_{infl.}$ 285 (+22 000), *a* +1038. ^{1}H NMR (60 MHz, $CDCl_3$): *δ* 1.0–2.1 (14H, *m*), 2.11 (1H, *s*), 2.12 (CO<u>Me</u>, s), 2.4–3.3 (4H, *m*), 3.81 (*ϕ*-O<u>Me</u>, s), 6.8–7.1 (3Ar-<u>H</u>, *m*). MS *m/z* 352 $[M]^{+\cdot}$, 324, 309, 281, 124, 109.

(−)-*Aspidofiline*(**3**). White crystals from petrol, mp 181–184° (mmp with authentic sample no depression). $[\alpha]_D$ −170° (lit. [5] $[\alpha]_D$ −174°). IR ν_{max}^{KBr} cm^{-1}: 2920, 1640, 1550, 1460, 755, 725. ^{1}H NMR (100 MHz, $CDCl_3$): *δ* 1.2–2.27 (14H, *m*), 2.34 (1H, *s*), 2.35 (–CO<u>Me</u>, *s*), 2.4–3.3 (4H, *m*), 6.7–7.2 (3Ar-<u>H</u>, *m*), 10.1 (*ϕ*-O<u>H</u>, *s*). MS *m/z* 338 $[M]^{+\cdot}$, 310, 295, 266, 109.

(+)-*Aspidospermine* (**5**). Isolated from root bark of *A. pyrifolium* as reported in ref. [9], mp 206.5–207°. $[\alpha]_D$ +92°. IR ν_{max}^{KBr} cm^{-1}: 2930, 1640, 1590, 1490, 1180, 780, 740. UV λ_{max}^{EtOH} nm(log ε) 218 (4.44), 256 (3.39), 286–296 (infl.) (3.49); λ_{min} 236 (3.72). ORD λ^{MeOH} (*ϕ*): λ_{max} 255 (+79 650); λ_{min} 227 (−40 562); $\lambda_{infl.}$ 280 (+11 062), *a* = +1212. ^{1}H NMR (60 MHz, $CDCl_3$): *δ* 0.62 (–CH_2<u>Me</u>, *t*), 0.7–2.1 (12H, *m*), 2.21 (1H, *s*), 2.22 (–CO<u>Me</u>, *s*), 3.00–3.24 (4H, *m*). 3.88 (*ϕ*-O<u>Me</u>, *s*), 4.5 (1H, *m*), 6.74–7.14 (3Ar-<u>H</u>, *m*). MS *m/z* 354 $[M]^{+\cdot}$ 339, 326, 312, 152, 124.

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