

19-Epivoacristine, an Iboga Alkaloid Isolated from *Peschiera affinis*

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Dados de RMN ¹³C foram utilizados para definir a configuração relativa do carbono quiral C-19 de um epímero da voacristina, um alcalóide iboga isolado de *Peschiera affinis*, família Apocynaceae.

¹³C-NMR spectral data were used to define the relative configuration of the chiral carbon C-19 of an epimer of voacristine, an iboga alkaloid isolated from *Peschiera affinis*, family Apocynaceae.

Keywords: *Peschiera affinis*, *Apocynaceae*, alkaloid, 19-epivoacristine, ¹³C-NMR

Introduction

Continuing our chemical investigation of *Peschiera affinis*, family Apocynaceae^{1,2}, an additional quantity of the epimer (**1**)² of (-)-voacristine (**2**)^{3,4} was isolated from a specimen collected in the proximities of Fortaleza, in the state of Ceará, Brazil.

A comparative analysis of the ¹³C-NMR spectra (PND and DEPT) of **1** and the literature values for **3**⁵ revealed that the natural product isolated from *Peschiera affinis* is an isomer of voacristine and allowed us to establish its relative configuration as 19-epivoacristine (**1**).

Results and Discussion

The methanolic extracts from the bark, wood and roots of *Peschiera affinis* (Muell. Arg.) Miers, collected at three different geographical sites (Fortaleza and Ubajara in the state of Ceará and Cocal in the state of Piauí, Brazil) afforded, after chromatographical separation, the alkaloids coronaridine, 19-epivoacristine (**1**), 19-epiheyanine (**3**), voacangine (**5**), affinisine, vobasine, a mixture of 19-hydroxiibogamine and ibogaine and olivacine, together with the terpenoids β -sitosterol, β -amyryn, lupeol and 3-O-acetyl-lupeol².

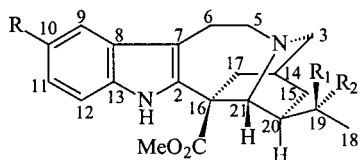
The constitution of **1** was deduced on the basis of the data obtained from the ¹H-NMR spectra [60 MHz, CDCl₃: δ _H 1.28 (d, J = 6.5 Hz, 3H-18), 1.44 - 2.25 (m, 6H), 2.30 - 4.05 (m, 8H), 3.76 (s, COOMe), 3.84 (s, MeO-10), 4.18 (s, OH), 6.60 - 7.60 (m, H-9, H-11, H-12), 8.62 (s, NH)], mass [m/z (rel. int.): 384 (M⁺, 100), 283 (**1b**, 14), 244 (**1c**, 35), 184 (**1d**, 27), 160 (**1e**, 36), 152 (**1f**, 44), 140 (**1g**, 28)], IR [ν _{max}^{KBr} cm⁻¹: 3433 (OH), 1726 (COOMe), 1629, 1600, 1500 (aromatic moiety)] and UV [λ _{max}^{EtOH} nm (ϵ): 226 (26993), 285 (9079), 302i (8098), 313i (3987)]^{2,6} and by comparison with the literature values^{1,7,8}.

The relative configuration and the conformation of the molecule were determined by the use of PND- and DEPT-¹³C-NMR (50.3 MHz) spectra of **1** and by comparison with the literature values described for 19-epiheyanine (**3**)⁵ (Table 1). The ¹³C-NMR spectra of **1**, named 19-epivoacristine, revealed the chemical shifts correlated to sp³ carbon atoms C-3, C-5 [δ _c 51.9 (CH₂) and 50.6 (CH₂)], C-6 [δ _c 21.7 (CH₂)], C-14 [δ _c 26.9 (CH₂)], C-15 [δ _c 28.6 (CH₂)], C-16 [δ _c 53.9 (C)], C-17 [δ _c 36.7 (CH₂)], C-18 [δ _c 22.3 (CH₃)], C-19 [δ _c 70.8 (CH)], C-20 [δ _c 39.9 (CH)] and C-21 [δ _c 54.3 (CH)], practically identical to those reported for 19-epi-

heyneanine (**3**): δ_c 52.0, 50.9 (C-3 and C-5), 21.7 (C-6), 26.0 (C-14), 28.6 (C-15), 54.1 (C-16), 36.5 (C-17), 22.1 (C-18), 70.7 (C-19), 40.2 (C-20) and 54.7 (C-21)⁵ (Table 1). These results pointed to an identical configuration for the chiral carbon C-19 of **1** and **3**, as shown in the conformation **1a**, with an intramolecular hydrogen bond between N-4 and the hydroxyl group. In the epimer heyneanine (**4**), the chemical shifts of the carbon atoms C-15 (δ_c 22.9), C-19 (δ_c 72.3) and C-21 (δ_c 59.7) are significant different, in

agreement with conformation **2a**. The deshielding of carbon C-15 of **3** by 5.7 ppm [$\Delta\delta_c = 28.6$ (**3**) - 22.9 (**4**) = 5.7 ppm] is in accordance with the removal of the γ -effect of the methyl group, which exerts a γ -effect on carbon C-21 of -5.0 ppm [$\Delta\delta_c = 54.7$ (**3**) - 59.7 (**4**) = -5.0 ppm].

The confirmation of the aromatic indole system was obtained by a comparative analysis of the ¹³C-NMR spectral data of **1** and voacangine, **5** (Table 1)⁵ In the ¹H-NMR (200 MHz) spectrum (with CDCl₃ as solvent) of **1** the



- 1** R = OMe, R₁ = OH, R₂ = H
2 R = OMe, R₁ = H, R₂ = OH
3 R = H, R₁ = OH, R₂ = H
4 R = H, R₁ = H, R₂ = OH
5 R = OMe, R₁ = R₂ = H

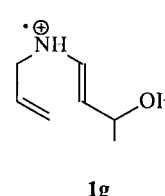
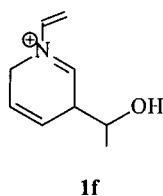
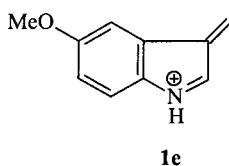
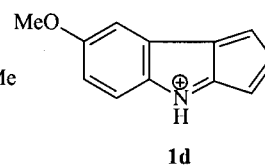
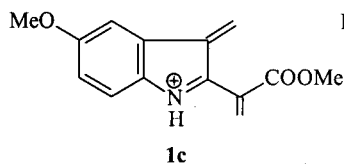
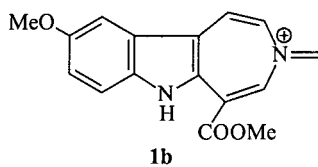
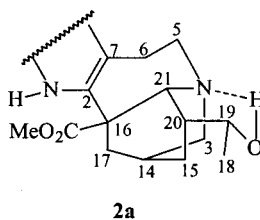
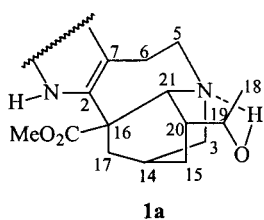
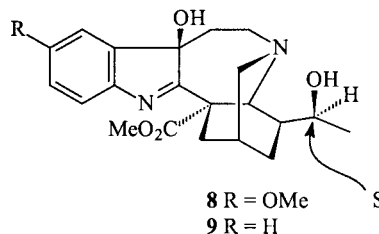
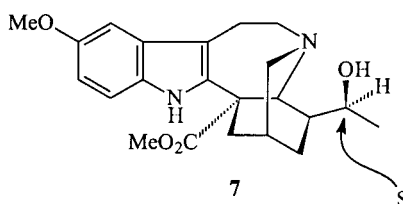
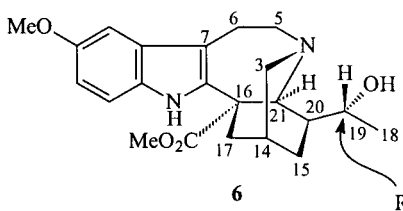


Table 1. ^{13}C -NMR (50.3 MHz) spectral data for alkaloid **1** compared with literature values for **3** and **4**, in CDCl_3 with TMS as the internal standard, chemical shifts in δ (ppm)*.

C	1	3	4	5
2	136.5	135.9 ^a	136.5 ^a	137.3
7	109.5	109.6	110.7	109.7
8	128.9	128.4	129.5	128.7
10	154.1	—	—	153.6
13	130.5	135.6 ^a	136.3 ^a	130.5
16	53.9	54.1	56.8	55.0
COOMe	174.9	174.8	175.7	175.4
CH				
9	100.6	118.3	119.3	100.4
10	—	120.3	119.3	—
11	112.3	122.1	123.2	111.4
12	111.3	110.4	111.4	110.9
14	26.9	26.0	26.7	27.2
19	70.8	70.7	72.3	—
20	39.9	40.2	39.5	38.9
21	54.3	54.7	59.7	57.2
CH₂				
3	51.9 ^a	52.0 ^b	52.1 ^b	53.0
5	50.6 ^a	50.9 ^b	51.1 ^b	51.5
6	21.7	21.6	21.3	22.0
15	28.6	28.6	22.9	31.9
17	36.7	36.5	36.8	36.2
19	—	—	—	26.6
CH₃				
18	22.3	22.1	20.2	11.5
MeO-10	56.0	—	—	55.7
COOMe	52.8	52.6	52.8	52.2

* The multiplicity of the signals of **1** was deduced by comparative analysis of the PND- and DEPT- ^{13}C -NMR spectra.

signals corresponding to three aromatic hydrogens, H-9, H-11 and H-12 were clearly defined: δ_{H} 6.90 (d, $J = 2.2$ Hz, H-9), 6.82 (dd, $J = 2.2$ Hz and $J = 8.6$ Hz, H-11) and 7.14 (d, $J = 8.6$ Hz, H-12).

Thus, the relative configuration at chiral carbon atom C-19 of (-)-epivoacristine (**1**) was defined as S in the enantiomer **1**, or as R in **6** [(+), optical isomer of **1**]. The configuration indicated for (+)-voacristine (**7**), isolated from *Ervatamia coronaria* var. *plena*⁴, is an epimer of **6** at carbon C-19 (R in **6** and S in **7**). On the basis of these data, the isomeric alkaloid isolated from *Peschiera affinis* was named epivoacristine (**1**), leaving the name voacristine for the alkaloid previously described in the literature (e.g.⁴).

The comparative analysis of the chemical shifts of the carbon atoms C-15, C-18 and C-21 of **1** and **3** (Table 1) with **4** (Table 1), **8** and **9**⁴ can also be used to conclude that the alkaloids **8** and **9** adopt an analogous conformation as shown for **2a**, justifying the signal of the methylene group C-15 at δ_{C} 22.8 (γ -effect of the methyl group), and of the methine CH-21 at δ_{C} 59.9 (**8**) and 59.8 (**9**), revealing the absence of this γ -effect, which is observed in **1** and **3** (δ_{C} 54.3 and 54.7, respectively) as shown in **1a**.

Experimental

General experimental procedures: m.p. were determined using a Kofler hot stage instrument and are uncorrected; IR spectra were taken on a Perkin Elmer 257 spectrometer; ^1H -NMR and ^{13}C -NMR spectra were recorded in CDCl_3 employing a Brücker AC 200 (^1H : 200 MHz; ^{13}C : 50.3 MHz) spectrometer.

Plant material: roots of *Peschiera affinis* were collected in Fortaleza, in the state of Ceará, Brazil. A voucher specimen (N^o 9638) is deposited in the herbarium (Herbário Prisco Bezerra), Departamento de Biologia, Universidade Federal do Ceará.

Extraction and isolation of 1: powdered roots (1.5 kg) were extracted with ethanol to afford 120 g of residue. The residue was treated with 8% tartaric acid (150 mL) and partitioned with CHCl_3 (4 x 100 mL). Ammonium hydroxide was added until pH 10, followed by extraction with CHCl_3 , drying with Na_2SO_4 , and concentration, to produce an alkaloid fraction (2 g; 1.6% yield).

A sample of this fraction (1 g) was subjected to column chromatography over silica gel, eluting with hexane, CHCl_3 and EtOAc mixtures of increasing polarities. The fractions eluted with CHCl_3 : EtOAc (4:2) were submitted to preparative TLC over silica gel followed by recrystallization from hexane: CHCl_3 to produce **1** (45 mg).

19-Epivoacristine (1): powder, m.p. 119.1-121.1 °C; IR (KBr) cm^{-1} : 3500 (OH, NH), 1726 (esters), 1629, 1600, 1500 (aromatic moiety). ^{13}C -NMR: Table 1. ^1H -NMR (Results and Discussion).

Acknowledgments

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