Fontaineine, a New Alkaloid from *Fontainea pancheri*

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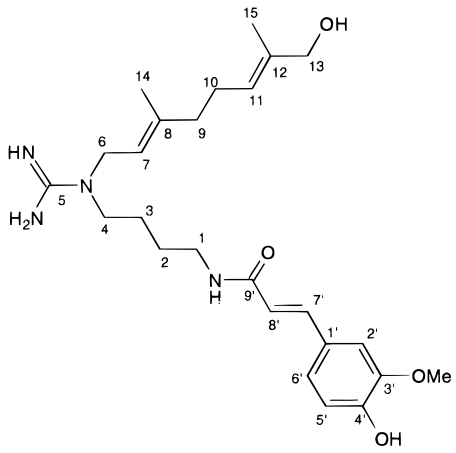
A new guanidine-type alkaloid, fontaineine (**1**), was isolated from the leaves of *Fontainea pancheri* and its structure elucidated by 2D NMR.

During the course of a systematic search of alkaloids in New Caledonian plants,[1] we have isolated from the leaves of *Fontainea pancheri* (Baillon) Heckel, a new acyclic guanidine-type alkaloid, fontaineine (**1**). The genus *Fontainea* belongs to the family Euphorbiaceae, subfamily Crotonoidae. Guanidine alkaloids with related structures were reported from two plants of this subfamily, *Alchornea floribunda*[2] and *Alchornea javanensis*.[3] However, they differ from compound **1**, showing the guanidine included in two rings or only simple chains.



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The alkaloids were extracted from the powdered leaves using the usual organic solvent−aqueous acid partitioning method (see the Experimental Section). Fontaineine (**1**) was isolated from an *n*-butanol extract of the basified aqueous phase (pH 8.5) and was the only alkaloid obtained from the alkaline organic extracts.

Fontaineine (**1**) gave a MH^+ peak in the HRFABMS at *m*/*z* 459.2975, which matched the molecular formula $C_{25}H_{38}N_4O_4$ (Δ 0.4 mmu). The IR exhibited intense C=O (amide) or C=N bands at 1652 and 1613 cm^{-1} and a large band of exchangeable protons at 3380 cm^{-1}. The ^1H NMR (CD_3OD, Table 1) showed singlets at δ 1.60 and 1.70 corresponding to two methyl groups each attached to a trisubstituted double bond with the olefinic protons appearing at δ 5.46 and 5.32, respectively. The spectrum also revealed signals of methylene or methine groups between δ 1.6 and 3.8 and, in addition, the typical resonances of an *O*-methylcaffeic amide residue: two doublets at δ 7.11 and δ 6.78 (J = 8.2, 1.5 Hz, respectively) and a double doublet at δ 7.01 (J = 8.2, 1.5 Hz) for the aromatic ring, together with two doublets at δ 7.42 and 6.45 (J = 16 Hz) for the unsaturated amide *E*-double bond, and finally the OMe singlet (3H, δ 3.86). In the spectrum registered in DMSO-d_6, the amide NH appeared as a triplet (δ 8.30, J = 1.5 Hz), and the presence of a broad singlet (δ 7.50) of three other exchangeable protons suggested a guanidine group accounting for the three remaining nitrogens. This was confirmed by the ^{13}C spectrum (Table 1), which disclosed at low field, apart from the caffeic amide and the double bond resonances, a quaternary carbon signal with the characteristic chemical shift of a guanidine group (δ 157.9). The high-field shift of the methyls on the double bonds (δ 14.0 and 16.7) indicated an *E* stereochemistry.[4] All the aliphatic signals were methylenes with one of them at δ 69.0 linked to an oxygen. Finally, the chemical shift of the C-2′ (δ 111.8) and C-5′ (δ 116.7) in the aromatic amide part indicated that the methoxy

Table 1. ^{13}C (75 MHz) and ^1H (400 MHz) Data for Fontaineine (**1**)[a]

position	δ C	δ H (*J*, Hz)	HMBC[b]
1	39.9	3.32 m	2, 3, 9′
2	28.0	1.60 m	1, 3, 4
3	25.6	1.65 m	4
4	49.3	3.32 m	3, 5, 6
5	157.9		
6	47.7	3.86 m	4, 5, 7, 8
7	119.2	5.32 m	6, 9, 14
8	142.9		
9	40.3	2.10 m	7, 8, 10, 12
10	26.9	2.14 m	8, 9, 11,12
11	126.0	5.46 m	9, 10, 13, 15
12	136.6		
13	69.0	3.81 m	11,12,15
14	16.7	1.70 s	7, 8, 9
15	14.0	1.60 s	11, 12, 13
1′	128.4		
2′	111.8	7.11, d (1.5)	1′,3′,4′,6′,7′
3′	149.5		
4′	150.1		
5′	116.7	6.78, d (8.2)	1′, 3′,4′,6′
6′	123.6	7.01, dd (8.2, 1.5)	2′, 4′, 5′,7′
7′	142.5	7.42, d (16.0)	1′,2′,6′,8′,9′
8′	118.9	6.45, d (16.0)	1′, 7′, 9′
9′	169.6		
OMe	56.7	3.86 s	3′
NH_2[c]		7.50 br s	
NH[c,d]		7.50 br s	
NH[ce]		8.30 t (1.5)	

[a] In CD_3OD except otherwise stated. Assignments based on 2D experiments. [b] Carbon atoms (see **1** for numbering) correlated with H on position number. [c] In DMSO-d_6. [d] NH of the guanidine function. [e] NH of the amide.

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group was at position 3′ and thus revealed the presence of a ferulic amide moiety.[5,6]

The COSY spectrum showed the spin system of a four-methylene chain (C_1-C_4) with chemical shifts indicating that the chain was placed between two nitrogens. The latter were obviously the ferulic amide NH and one of the guanidine nitrogens. The other observed vicinal and long-range proton correlations were in accordance with an isoprene-type chain (C_6-C_{15}). The heteronuclear multiple bond correlation (HMBC) spectrum (Table 1) confirmed the structure of this chain and revealed that it was linked to the same guanidine nitrogen as the chain C_1-C_4 through CH_2-6, as shown by the cross-peaks H-4/C-5,C-6 and H-6/C-4,C-5. The linkage of the ferulic amide to the C_1-C_4 chain was further supported by the HMBC correlations H-1/C-9′, C-2,C-3 and H-2/C-1,C-2,C-4. The NOESY spectrum showed the cross-peaks H-7/H-9, H-11/H-10, and H-11/H-13, which confirmed the *E* configuration of the double bonds.

The structure of fontaineine (**1**) appears as less common than the one of known related guanidine alkaloids of the Euphorbiaceae family. Only one alkaloid having a similar guanidine system with two chains attached to the same nitrogen has been previously isolated from *A. javanensis*.[3] However, both chains are simple isopentenyl residues.

Experimental Section

General Experimental Procedures. Spectra were recorded on the following equipment: IR, Nicolet 205 FT-IR spectrometer; FABMS, Kratos MS 80; HR-FABMS, VG-Zab-Seq spectrometer; NMR, Bruker AC 300 (^{1}H and ^{13}C NMR spectra) and AM 400 (2D NMR spectra). Column chromatography was performed using Si gel Merck H60.

Plant Material. Leaves of *F. pancheri* (Baillon) Heckel were collected in Port-Boisé-Forêt, New Caledonia, on Jan 18, 1996. The identification was made by one of us (M.L.). Voucher specimens (Lit. 0088) are deposited in the Herbarium of the Centre ORSTOM, Noumea, New Caledonia.

Extraction and Isolation. The dried ground leaves of *F. pancheri* (630 g) were extracted, after basification (NH_4OH 40%), with CH_2Cl_2 in a Soxhlet extractor. The solution was concentrated and diluted with ether. The organic layer was further extracted with 5% HCl. The acidic aqueous layer was washed with ether, basified with NH_4OH, and extracted sucessively with CH_2Cl_2, EtOAc, and *n*-butanol. The CH_2Cl_2 extract (0.50 g) and the EtOAc extract (0.15) were discarded. Repeated column chromatography of the *n*-butanol extract (1.50 g) on Si gel with CH_2Cl_2/MeOH mixtures afforded compound **1** (0.15 g, CH_2Cl_2/MeOH 90:10).

Fontaineine (1): amorphous gum; IR ν_{max} (KBr) 3380, 1652, 1613, 1517, 1458, 1381, 1275, 1157, 1129, 1031, 852, 819 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; FABMS *m/z* 479 $[M + Na]^+$; HRFABMS *m/z* 459.2975 ($C_{25}H_{38}N_4O_4$, Δ 0.4 mmu).

References and Notes

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