



Two tetrahydroquinoline alkaloids from *Galipea officinalis*

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Received 16 September 1998; received in revised form 28 September 1998; accepted 12 January 1999

Abstract

Two tetrahydroquinoline alkaloids have been isolated from the bark of *Galipea officinalis* Hancock. Their structures have been established by spectroscopic methods. The compounds were named angustureine (1,2,3,4-tetrahydro-2(*n*-pentyl)-1-methylquinoline) and galipeine (2-[(3'-hydroxy-4'-methoxy-phenylethyl)]-2,3,4-tetrahydro-1-methylquinoline). © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *Galipea officinalis*; Rutaceae; Angostura; Alkaloids; Tetrahydroquinolines; Angustureine; Galipeine

1. Introduction

The genus *Galipea* Aublet is composed of approximately 20 species that are found primarily in northern South America. *Galipea officinalis* Hancock is a shrub indigenous to the mountains of Venezuela. Its principal action is its influence on the spinal motor nerves; it is therefore a cure for paralytic affections. This is a valuable tonic in dyspepsia, dysentery and chronic diarrhoea (Steinmetz, 1954). The bark, named angostura, is also used in making bitter liquors. The bark has previously been investigated and five quinoline alkaloids have already been reported (Rakotoson et al., 1998). Some other alkaloids have been reported long time ago but without any spectral data (Mester, 1973). We report here the isolation and the structural elucidation of two tetrahydroquinoline alkaloids, named angustureine **1** and galipeine **2**.

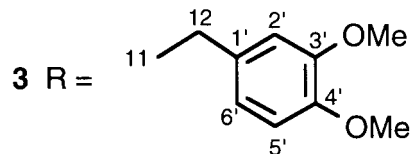
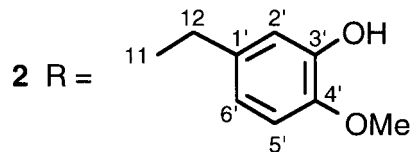
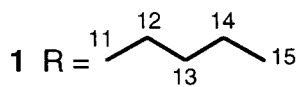
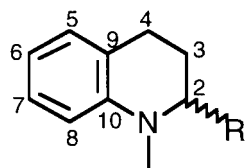
2. Results and discussion

The methods of extraction and purification are described in the Section 3.

The combination of various routine ^1H , ^{13}C NMR and mass spectrometric analyses allowed us to attribute the formulas $\text{C}_{15}\text{H}_{23}\text{N}$ and $\text{C}_{19}\text{H}_{23}\text{NO}_2$ to compounds **1** and **2** respectively. The similarities of the chemical shifts and multiplicities for both compounds, compared with those of the literature (Rakotoson et al., 1954; Vieira, & Kubo, 1990) revealed the presence of a characteristic tetrahydroquinoline moiety, substituted on position 2. This observation was confirmed by the presence of four aromatic protons between δ 6 and δ 7.5 (doublets for H-5 and H-8 and triplets or triplet doublets for H-6 and H-7). The quinoline moiety was saturated on position 2, 3 and 4; the ^1H NMR spectra clearly showed the characteristic multiplets beside δ 3.0, corresponding to H-3 and H-4. Moreover, the ^1H and ^{13}C NMR spectra of **1** and **2** indicated the presence of a characteristic N-Me group (δC 38.2, δH 2.97 ± 0.08). Substitution on position 2 was confirmed by the presence of the tertiary carbon (δC -2 529 ± 0.4) for the two compounds.

For compound **1**, the side chain moiety corresponded to a *n*-pentyl chain, characterized in ^1H NMR by specific multiplets beside δ 2.0 and in ^{13}C NMR by four CH_2 between δ 20 and δ 30 ca. and by one CH_3 at δ 14.4. **1** was then the 1,2,3,4-tetrahydro-2-(*n*-pentyl)-1-methylquinoline.

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For compound **2**, the side chain moiety corresponded to a phenylethyl group itself substituted on position 3' and 4' (Vieira, & Kubo, 1990; Rakotoson et al., 1998). A typical shift for a methoxy group (3H, δ H 3.85, δ C 56) was present. The HMBC spectrum indicated that the methoxy group substituted the aromatic moiety on position 4' ($^3J_{C-4', O-CH_3}$, $^2J_{C-4', H-5'}$, $^3J_{C-6', H-12}$). The 1H and ^{13}C NMR spectra of cuspareine (**3**) (Rakotoson et al., 1998) and compound **2** are

similar except for C-3' which is shielded in case of compound **2**. Comparison of EIMS spectra of both compounds showed a molecular weight difference of 14. This suggested that C-3' was not substituted by a methoxy group as for cuspareine but by a hydroxyl group. The HMBC spectrum indicated that the hydroxyl group substituted the aromatic moiety on position 3' ($^2J_{C-3', H-2'}$, $^3J_{C-2', H-12}$). All these results afforded us to propose the structure 2-[(3'-hydroxy-4'-methoxy)-

Table 1
 1H and ^{13}C -NMR spectral data of compounds **1** and **2** in $CDCl_3$

	1			2		
	δ_C	δ_H	(J in Hz)	δ_C	δ_H	(J in Hz)
<i>Quinoline moiety</i>						
N-CH ₃	38.2	3.04	s 3H	38.2	2.89	s 3H
2	59.3	3.35	m 1H	58.5	3.26	m 1H
3	26.1	2.01	m 2H	24.4	1.92	m 2H
4	23.9	2.94	m 1H	23.6	2.82	m 1H
		2.78	m 1H		2.68	m 1H
5	110.7	6.65	(d 3J 8.2) 1H	110.7	6.51	(d 3J 8.2) 1H
6	127.4	7.21	(t 3J 8.2) 1H	127.2	7.06	(t 3J 8.2) 1H
7	115.5	6.71	(td 7.3–1) 1H	115.4	6.57	(td 7.3–0.9) 1H
8	128.9	7.09	(d 7.2) 1H	128.8	6.96	(d 7.3) 1H
9	122.0	–	–	121.8	–	–
10	145.7	–	–	145.4	–	–
<i>Side chain</i>						
11	31.5	1.73	m 2H	33.2	1.87	–
12	24.8	1.42–1.55	–	32.1	1.70	–
13	32.4	1.42–1.55	–	–	–	–
14	23.0	1.42–1.55	–	–	–	–
15	14.4	1.42–1.55	–	–	–	–
<i>Aromatic moiety</i>						
1'	–	–	–	134.0	–	–
2'	–	–	–	110.8	6.65 super-imposed on H-6'	s 1H
3'	–	–	–	143.7	–	–
4'	–	–	–	146.5	–	–
5'	–	–	–	114.3	6.80	(d, 7.2) 1H
6'	–	–	–	120.9	6.65	(dd, 7.1–1.9) 1H
O-CH ₃	–	–	–	56.0	3.85	s 3H

phenylethyl]-2,3,4-tetrahydro-1-methylquinoline for compound **2**.

To our knowledge and up to now, only one tetrahydroquinoline alkaloid (cuspareine) (Rakotoson et al., 1998) was isolated, from *G. officinalis* Hancock. Angustureine and galipeine are two new natural tetrahydroquinoline alkaloids; these results confirmed the particular alkaloids biosynthetic pathway of this species and tetrahydroquinolines may be used as chemotaxonomic markers of *G. officinalis* Hancock.

3. Experimental

3.1. General

MS: by EI and DCI with NH_3 in CHCl_3 ; HMQC, HMBC 2D-shift correlations, ^1H and J mod. ^{13}C NMR: 400 and 100 MHz respectively, in CDCl_3 , using the solvent peaks at δ 7.23 and δ 77 ppm as standards.

3.2. Plant material

The bark of *G. officinalis* Hancock was obtained from Venezuela. A voucher specimen (93123JHR) has been identified and is deposited at the Pharmacognosy Department, Faculty of Pharmaceutical Sciences, University of Toulouse (France).

3.3. Extraction and isolation

Dried powered trunk bark (1 kg) was extracted with CHCl_3 (5 l). The chloroformic phase was evpd. under low pressure to dryness (39 g). 25 g of this extract were separated on a silica gel (70–200 μm , 170 g) column, eluted with various proportions of hexane, CHCl_3 and MeOH. The fractions were gathered into

three groups (FA, FB and FC) and evaporated to dryness.

FB (5.3 g) was separated on a silica gel (70–200 μm , 75 g) column, eluted with various proportions of hexane, CHCl_3 and MeOH. One fraction contained only **1** (980 mg).

8.5 g of FC were separated on a silica gel (70–200 μm , 120 g) column, eluted with various proportions of hexane, CHCl_3 and MeOH. Repeated chromatography gave three fractions (X1, X2 and X3). X2 provided **2** (14 mg, R_f : 0.8) by prep. TLC (silica gel) using CHCl_3 as development solvent.

3.4. 1,2,3,4-Tetrahydro-2(*n*-pentyl)-1-methylquinoline, **1**

Oil; $[\alpha]_D = -7.16^\circ$; UV $\lambda_{\text{max}}^{\text{CHCl}_3}$ nm ($\log \epsilon$): 259 (3.70) and 311 (3.15); EI-MS m/z (rel. int.): 217 ($[\text{M} + \text{H}]^+$, 22.6), 146 (100); $\text{C}_{15}\text{H}_{23}\text{N}$; ^1H NMR (CDCl_3 , 400 MHz) and ^{13}C NMR (CDCl_3 , 100 MHz): see Table 1.

3.5. 2-[(3'-Hydroxy-4'-methoxy-phenylethyl)]-2,3,4-tetrahydro-1-methylquinoline, **2**

Oil; $[\alpha]_D = -13.6^\circ$; UV $\lambda_{\text{max}}^{\text{CHCl}_3}$ nm ($\log \epsilon$): 259 (3.75) and 311 (3.32); DCI/ NH_3 -MS m/z (rel. int.): 298 ($[\text{M} + \text{H}]^+$, 100), 297 (21.6), 146 (2.7); $\text{C}_{19}\text{H}_{23}\text{NO}_2$; ^1H NMR (CDCl_3 , 400 MHz) and ^{13}C NMR (CDCl_3 , 100 MHz): see Table 1.

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