

# Isolation and 2D NMR Studies of Alkaloids from *Comptonella sessilifoliola*<sup>1</sup>

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## Abstract

Six known furanoquinoline alkaloids have been isolated from the wood and trunk bark of *Comptonella sessilifoliola* (Guillaumin) Hartley (Rutaceae). 2D NMR experiments gave the assignment of all the signals for both <sup>1</sup>H- and <sup>13</sup>C-NMR spectra. Pteleine and kokusaginine were used as models. The two-dimensional carbon-proton correlation experiments, performed for the first time on furanoquinoline alkaloids, led us to correct <sup>13</sup>C-NMR assignments previously described in the literature.

## Key words

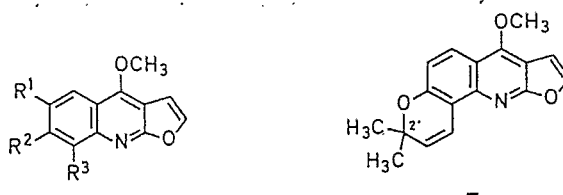
— **RUTACEAE**

— *Comptonella sessilifoliola*, furanoquinoline alkaloids, 2D NMR, dictamnine, pteleine, evolitrine, kokusaginine, dutadrupine, R-(+)-platydesmine.

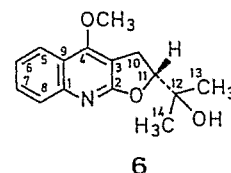
## Introduction

*Comptonella sessilifoliola* (Guill.) Hartley (Rutaceae) is a tree that grows to 8 m high with opposite trifoliated leaves and four-lobed fruits. Phytochemical studies on different parts of the plant (trunk bark and wood) led to the isolation of six alkaloids. Their spectroscopic data (IR, <sup>1</sup>H-NMR, UV, mass) showed that they all belong to the group of furanoquinoline alkaloids. They have been found to be identical with dictamnine (1) (1), pteleine (2) (2), evolitrine (3) (3), kokusaginine (4) (4), dutadrupine (5) (5), and R-(+)-platydesmine (6) (2). From these only for dictamnine were <sup>13</sup>C-NMR data (6) previously available and some assignments of signals from proton spectra were not possible without <sup>13</sup>C-NMR spectra.

Since it is difficult, with the large number of quaternary aromatic carbon atoms, to assign the different <sup>13</sup>C-NMR signals to each atom without error, heteronuclear one bond and long-range carbon-hydrogen correlation experiments have been performed for two of the alkaloids: pteleine (2) and kokusaginine (4). The results of these experiments, shown in Figs. 1 and 2, led us to assign



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
1	H	H	H
2	H <sub>3</sub> CO	H	H
3	H	H <sub>3</sub> CO	H
4	H <sub>3</sub> CO	H <sub>3</sub> CO	H
7	H	H <sub>3</sub> CO	H <sub>3</sub> CO



unambiguously all the signals of both carbon and proton spectra for the six alkaloids (Tables 1 and 2).

For pteleine (2; Fig. 1), each of the signals of the proton spectrum can be identified as all the signals of aromatic protons show different coupling constants. The assignment of <sup>13</sup>C-NMR signals is clearly resolved by examination of the 2D spectra. For example, in the heteronuclear long-range H/C correlation spectrum, the signals at 155.4 ppm and 156.0 ppm in the carbon spectrum are respectively correlated to methoxy signals at 4.30 ppm and 3.88 ppm in the proton spectrum; furthermore, the latter <sup>13</sup>C signal is also correlated with H-8, which led us to assign the signal at 156.0 ppm to C-6 and hence the former (at 155.4 ppm) to C-4.

Two other signals of non-protonated carbons at 103.6 ppm and 119.0 ppm also show several correlations. The signal at 103.6 ppm is correlated with H-10 and H-11, the signal at 119.0 ppm with H-8; the first signal (at 103.6 ppm) can be assigned to C-3 and the second (at 119.0 ppm) to C-9. The other assignments for this substance are shown in Fig. 1.

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Chemical shifts							
PROTONS	H-8	H-11	H-5	H-7	H-10	OMe-4	OMe-6
multiplicity	7.87	7.50	7.36	7.31	6.90	4.30	3.88
CARBONS	<i>d</i> (9.0)	<i>d</i> (2.8)	<i>d</i> (2.9)	<i>dd</i> (9.0,2.9)	<i>d</i> (2.8)	<i>s</i>	<i>s</i>
Assignment							
55.4 CH <sub>3</sub>						*	MeO-6
58.8 CH <sub>3</sub>						*	MeO-4
100.2 CH			*	*			5
103.6 C		*			*		3
104.4 CH		*			*		10
119.0 C	*						9
122.2 CH			*	*			7
129.0 CH	*						8
141.3 C				*			1
143.3 CH		*			*		11
155.4 C						*	4
156.0 C	*					*	6
162.5 C		*			*		2

\* one bond correlations; \* long-range correlations

Fig. 1 Heteronuclear correlations C-H for one bond and long-range couplings for pteleine (2).

Chemical shifts							
PROTONS	H-11	H-5	H-8	H-10	OMe-4	OMe-7	OMe-6
multiplicity	7.32	7.41	7.31	6.97	4.37	4.02	4.00
CARBONS	<i>d</i> (2.7)	<i>s</i>	<i>s</i>	<i>d</i> (2.7)	<i>s</i>	<i>s</i>	<i>s</i>
Assignment							
56.0 <sup>a</sup> CH <sub>3</sub>						*	MeO-6, MeO-7
58.8 CH <sub>3</sub>						*	MeO-4
100.4 CH			*				5
102.3 C	*				*		3
104.5 CH				*			10
106.7 CH			*				8
113.1 C			*				9
142.4 CH	*			*			11
142.7 C		*					1
147.9 C			*			*	6
152.8 C		*				*	7
155.6 C		*				*	4
163.1 C	*			*			2

<sup>a</sup> double intensity; \* one bond correlations; \* long-range correlations

Fig. 2 Heteronuclear correlations C-H for one bond and long-range couplings for kokusaginine (4).

Table 1 <sup>13</sup>C-NMR chemical shifts for compounds 1 to 6.

Carbon	Compounds					
	1	2	3	4	5	6
1	145.9	141.3	142.5	142.7	142.9	147.9
2	168.9	162.5	161.3	163.1	64.5	169.0
3	103.7	103.6	102.2	102.3	101.8	102.4
4	157.0	155.4	157.3	155.6	157.2	159.2
5	122.4	100.2	116.8	100.4	118.8	122.2
6	123.8	156.0	123.6	147.9	122.9	123.5
7	129.6	122.2	147.7	152.8	154.3	129.8
8	128.0	129.0	106.0	106.7	113.8	127.1
9	119.0	119.0	113.6	113.1	114.5	120.4
10	104.8	104.4	104.9	104.5	104.8	29.1
11	143.7	143.3	142.5	142.4	142.5	86.6
OMe-4	59.1	58.8	59.0	58.8	59.0	58.4
OMe-6		55.4		56.0		
OMe-7			55.5	56.0		
2'					76.9	
3'					116.1	
4'					128.4	
Me					28.1	
12						76.1
Me-13						24.8
Me-14						26.1

CDCl<sub>3</sub>, TMS as internal standard, δ, ppm.

For kokusaginine (4; Fig. 2), signals of the <sup>1</sup>H-NMR at 4.00 ppm and 4.02 ppm can be assigned clearly to OMe-6 and OMe-7 respectively because they are connected, in the 2D long-range correlation spectrum, with the quaternary aromatic carbons at 147.9 ppm for the former signal and 152.8 ppm for the latter. These values correspond to carbons C-6 and C-7 respectively as other correlations with H-8 for the former and with H-5 for the latter are observed and this experiment had been optimised for a coupling constant <sup>1</sup>J<sub>H,C</sub> = 8 Hz, corresponding to the approximate value <sup>3</sup>J<sub>H,C<sub>meta</sub></sub> (7 Hz) for benzenic compounds and quite different from the value <sup>2</sup>J<sub>H,C<sub>ortho</sub></sub> (1 Hz) (7).

As the signals of the non-protonated carbons at 102.3 ppm and 113.1 ppm show chemical shifts similar to those observed in the spectrum of pteleine (103.6 and 119.0 ppm) together with identical correlations, they can be assigned to C-3 and C-9 respectively.

The two-dimensional carbon-proton correlation experiments, performed for the first time on furanoquinoline alkaloids led us to complete and to correct the previous data in <sup>13</sup>C-NMR already published. For skim-

Table 2 <sup>1</sup>H-NMR chemical shifts for compounds 1 to 6.

Protons	1	2	3	4	5	6
5	8.27 <i>dd</i> (8.4,1.7)	7.36 <i>d</i> (2.9)	8.15 <i>d</i> (9.3)	7.41 <i>s</i>	8.09 <i>d</i> (9.1)	7.89 <i>d</i> (8.2)
6	7.45 <i>ddd</i> (8.4,8.4,1.7)	—	7.09 <i>dd</i> (9.3,2.6)	—	6.97 <i>d</i> (9.1)	7.23 <i>ddd</i> (8.3,8.2,1.4)
7	7.68 <i>ddd</i> (8.4,8.4,1.4)	7.31 <i>dd</i> (9.0,2.9)	—	—	—	7.49 <i>ddd</i> (8.4,8.3,1.4)
8	8.01 <i>dd</i> (8.4,1.4)	7.87 <i>d</i> (9.0)	7.33 <i>d</i> (2.6)	7.31 <i>s</i>	—	7.67 <i>d</i> (8.4)
10	7.08 <i>d</i> (2.8)	6.90 <i>d</i> (2.8)	7.05 <i>d</i> (2.8)	6.97 <i>d</i> (2.7)	7.00 <i>d</i> (2.8)	3.53 <i>dd</i> (14.5,9.0)
11	7.69 <i>d</i> (2.8)	7.50 <i>d</i> (2.8)	7.57 <i>d</i> (2.8)	7.52 <i>d</i> (2.7)	7.53 <i>d</i> (2.8)	4.64 <i>dd</i> (9.0,7.4)
OMe-4	4.45 <i>s</i>	4.30 <i>s</i>	4.43 <i>s</i>	4.37 <i>s</i>	4.38 <i>s</i>	4.19 <i>s</i>
OMe-6	—	3.88 <i>s</i>	—	4.00 <i>s</i>	—	—
OMe-7	—	—	3.95 <i>s</i>	4.02 <i>s</i>	—	—
3'					5.68 <i>d</i> (10.0)	—
4'					7.47 <i>d</i> (10.0)	—
Me					1.50 <i>s</i>	—
Me-13						1.28 <i>s</i>
Me-14						1.49 <i>s</i>

CDCl<sub>3</sub>, TMS as internal standard, δ, ppm.

mianine (7), the signals at 101.8 ppm and 114.8 ppm were assigned (8) to C-9 and C-3, but we have shown in this work that it was the opposite. Similar assignments have been made for evoxine (6), perfamine (9), (2-isopentenyl-oxy)-4,7-dimethoxyfurano[2,3-*b*]quinoline (10) and have to be corrected.

## Materials and Methods

### General

Melting points were taken on a Kofler apparatus, optical rotations were measured on a Perkin-Elmer 241 instrument and UV spectra ( $C_2H_5OH$ ,  $\lambda_{max}$ , nm) on a Perkin-Elmer Lambda 5 spectrometer. IR spectra ( $\nu$ ,  $cm^{-1}$ ,  $CHCl_3$ ) were recorded on a Perkin-Elmer 297 spectrometer.  $^1H$ -NMR,  $^{13}C$ -NMR spectra at 50.3 MHz and 2-D experiments have been recorded on a Bruker WP 200 SY spectrometer in  $CDCl_3$ . The  $\delta$  values are given in ppm with TMS as internal reference and coupling constants in Hz. Mass spectra were measured on an MS 50 instrument. Flash chromatography was performed on silica gel 60 (Merck) column and TLC on silica gel F 254 (Merck).

### Material

The plant was collected on Mount Koniambo in New-Caledonia around 800 m on October 21, 1982. A voucher is kept in the Herbarium of ORSTOM Center in Noumea under the reference Puset-Chauviere 453.

### Extractions and purifications

The sawdust (8.7 kg), wet with  $NH_4OH$ , was extracted with methylene chloride during 24 h yielding the crude alkaloids (2.4 g, 0.027 % from starting material). Chromatography on silica gel H60 Merck (with  $CH_2Cl_2$ -MeOH, 99:1) led to compounds 1 (22 mg, 3 %), 2 (30 mg, 4.25 %), 3 (38 mg, 5.4 %), and 6 (600 mg, 25 %).

The trunk bark (6.4 kg), wet with  $NH_4OH$ , was extracted with methylene chloride during 48 h yielding the crude alkaloids (16 g, 0.25 % from starting material). Chromatography on silica gel H60 Merck (with  $CH_2Cl_2$ -MeOH, 99:1) led to compounds 2 (1.74 g, 10.8 %), 3 (1.5 g, 9.3 %), 4 (4.23 g, 26 %), and 5 (1.72 g, 10.7 %).

**Dictamnine (1):** m.p. 128–130°C; IR: 3144, 2960, 1627, 1583, 1470; UV (neutral): 330, 315, 241, 237; MS:  $m/z$  = 199 ( $M^+$ ), 184, 156, 128, 101.

**Pteleine (2):** m.p. 136–138°C; IR: 3130, 1623, 1593, 1542, 1383, 1158; UV (neutral) 349, 307, 296, 249; MS:  $m/z$  = 229 ( $M^+$ ), 214, 186, 158, 156, 63.

**Evolitrine (3):** m.p. 114°C; IR: 3122, 2940, 1626, 1590, 1465, 1158; UV (neutral) 333, 320, 308, 247; MS:  $m/z$  = 229 ( $M^+$ ), 214, 186.

**Kokusaginine (4):** m.p. 168–169°C; IR: 3130, 1623, 1592, 1552, 1423; UV (neutral) 336, 322, 296, 251; MS:  $m/z$  = 259 ( $M^+$ ), 244, 216, 201, 186, 173.

**Dutadrupine (5):** all data are identical with those published in the literature (5).

**R-(+)-Platydesmine (6):**  $[\alpha]_D^{25} = +51^\circ$  (c 1, EtOH); m.p. 136–138°C; IR: 3040, 1636, 1590, 1470, 1370; UV (neutral) 321, 307, 283, 263, 237; MS:  $m/z$  = 259 ( $M^+$ ), 200, 59.

### 2-D NMR experiments

**Heteronuclear  $^1H$ - $^{13}C$  (200/50.3 MHz) correlation:** The four experiments have been performed with the XHDEPT pulse sequence from the Bruker DISNMR 87 library program. For the two one bond correlations 128 FIDs of 1200 scans each, with 1 sec recycle delay and incrementing  $t_1$  from 5  $\mu$ sec to 640 msec, were acquired on a 0.5 M solution at 32°C. Polarization transfer was tuned for a value of  $^1J_{C,H} = 135$  Hz. After sine-bell multiplication of the FID in both domains with one degree of zero-filling in  $F_1$ , a matrix of 256/1024 data points with digital resolution (DR) = 7.2 Hz/pt in  $F_2$  and 7.8 Hz/pt in  $F_1$  was obtained. The long-range  $^1H$ - $^{13}C$  correlation was performed in similar manner with  $^nJ_{C,H} = 8$  Hz and 2400 scans per FID.

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