^{1}H- AND ^{13}C-NMR SPECTRAL DATA OF FIVE SARPAGINE-TYPE ALKALOIDS

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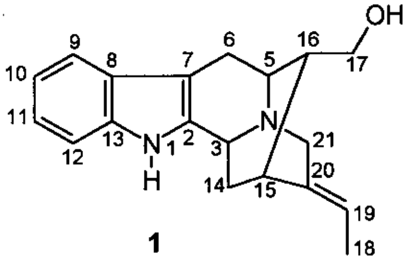
Abstract - Revised ^{1}H- and ^{13}C-nmr spectral data are presented for normacusine B (**1**), *E*-akuammidine (**2**), pericyclivine (**3**), polyneuridine (**4**), and voachalotine (**5**).

As part of our continuing effort to obtain useful spectroscopic data of indole alkaloids, we analysed the ^{1}H- and ^{13}C-nmr spectra of five important sarpagine-type alkaloids: normacusine B (**1**), *E*-akuammidine (**2**),[1] pericyclivine (**3**), polyneuridine (**4**), and voachalotine (**5**) (Table 1).



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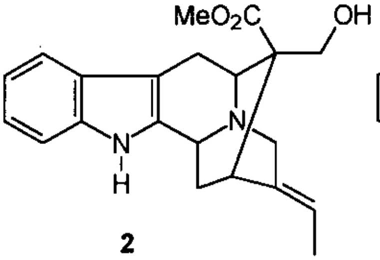

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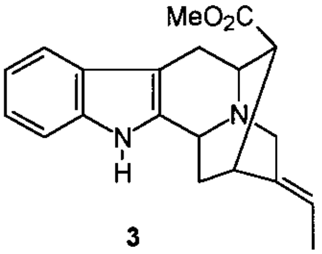

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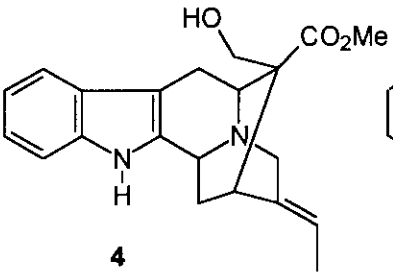

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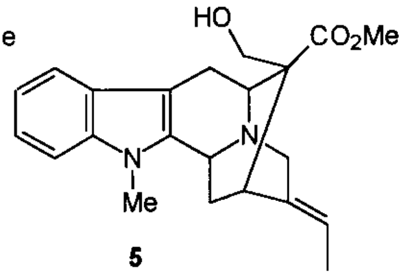

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For the most part, the ^1H-nmr spectra of the sarpagine-type alkaloids (1)-(5) can be found in the literature.[2-12] However, there are several misinterpretations of the ^1H chemical shifts, which are now corrected. The published ^{13}C-nmr spectra contain major mistakes and the ^{13}C-nmr values for polyneuridine (4) appear to be totally unknown. In this paper, our intention is to put the ^1H- and ^{13}C-nmr data of the five alkaloids (1)-(5) of sarpagine-type on a firm basis and remove the confusion existing in the literature (*vide infra*).

We have previously introduced the ^1H-nmr spectral data of compounds (1)-(5).[2] According to homonuclear COSY- and some nOe-measurements, our chemical shift values for compounds (1)-(4) are corrected (Table 1), but a few corrections need to be made to the chemical shifts of voachalotine (5). The accurate chemical shifts for H-17,17' are 3.57 and 3.68 ppm ($J_{17,17'}=11$ Hz) (Table 1), and not 3.67 ppm and 3.67 ppm as earlier indicated.[2] For H-21α and β the chemical shifts are ~ 3.7 ppm (Table 1).

The ^1H-nmr spectral values for compounds (1)-(4) have also been given by other authors.[3-12] Most of their reports contain partly incorrect or insufficient ^1H-nmr data.[3-5,7-12] The structure referred to in Ref. 8 as polyneuridine actually represents *E*-akuammidine, which is a C-16 epimer of polyneuridine. Thus the ^1H-nmr data given for polyneuridine are those of akuammidine. The ^1H-nmr data for polyneuridine given in Ref. 9 are erroneous as well. The chemical shifts reported for H-5 (2.65 ppm) and CO_2Me (2.85 ppm) point to a different stereochemistry at C-16 (*cf.* Table 1), so the compound cannot be polyneuridine.

Regarding the assignment of the ^{13}C-nmr data of compounds (1)-(5),[6,7,9,10,12-17] the situation is even more confusing than for the ^1H-nmr data (*vide supra*), although correct ^{13}C chemical shifts for compounds (1),[6] (2)[7,14,15], and (5)[16] are known.

Our new ^{13}C-nmr data for normacusine B (1) are in accordance with those of Clivio *et al.*[6]

The chemical shifts for *E*-akuammidine (2) reported by Jewers *et al.*[13] are misleading. The values presented are those of an unknown compound, which definitely is not akuammidine.[18] For the correct ^{13}C-nmr data of *E*-akuammidine (2), see Table 1.

As far as we know, the only ^{13}C-nmr data introduced for pericyclivine (3) are those of Mukhopadhyay and Cordell.[10] Several of the ^{13}C-nmr values must be interchanged, however. We have confirmed our ^{13}C-nmr data for pericyclivine (3) by heteronuclear correlation spectroscopy.

Table 1. ^{1}H- and ^{13}C-nmr data for compounds (1) - (5).

	1		**2**		**3**		**4**		**5**	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1	7.91 br s		7.90 br s		7.78 br s		7.81 br s			
2		136.4*		136.6*		136.6*		136.2*		136.2*
3	4.16 br d	50.5	4.24 br d	51.4	4.21 br d	50.4	4.06 dd	49.0	4.16 dd	47.9
5	2.8 m	54.3	3.1 m	58.0	3.68 ddd	53.0	4.27 br d	53.6	4.28 br d	53.6
6α	3.07 dd	27.0	2.94 dd	24.7	2.91 dd	24.2	3.10 dd	22.3	3.11 dd	22.3
6β	2.64 br d		3.30 dd		3.24 dd		2.94 br d		2.94 br d	
7		104.8		106.2		105.7		106.2		104.9
8		127.8		126.9		127.1		126.5		126.1
9	7.46 d	118.1	7.42 d	118.0	7.41 d	117.8	7.48 d	118.3	7.47 d	118.3
10	7.09 t	119.4	7.05 t	119.4	7.04 t	119.2	7.10 t	119.5	7.09 t	118.9
11	7.14 t	121.5	7.11 t	121.5	7.10 t	121.3	7.15 t	121.6	7.19 t	121.1
12	7.31 d	110.9	7.28 d	110.9	7.28 d	110.8	7.31 d	110.8	7.28 d	108.7
13		138.1*		137.0*		137.4*		136.5*		137.2*
14α	2.04 ddd	33.6	1.85 ddd	29.2	1.76 ddd	26.9	1.91 ddd	28.9	1.98 ddd	28.3
14β	1.74 ddd		2.67 ddd		2.58 ddd		1.85 ddd		1.79 ddd	
15	2.8 m	27.8	3.1 m	29.4	2.98 m	27.2	3.21 dd	30.6	3.22 dd	30.3
16	1.85 dddd	44.3		50.3	2.82 dd	43.8		53.4		53.3
17	3.52 dd	65.1	3.67 d	68.8			3.61 d	63.2	3.57 d	63.1
17'	3.59 dd		3.83 d				3.71 d		3.68 d	
18	1.63 br d	12.8	1.65 ddd	13.0	1.62 ddd	12.9	1.60 br d	12.7	1.61 ddd	12.7
19	5.38 br q	116.7	5.39 br q	116.8	5.27 br q	114.4	5.28 br q	116.0	5.30 br q	116.2
20		139.5*		137.1*		139.5*		136.9*		138.3*
21α	3.55 def	56.1	3.58 def	55.5	3.6 m	56.0	3.6 m	55.8	3.7 m	55.9
21β	3.55 def		3.58 def		3.6 m		3.6 m		3.7 m	
CO$_2$*Me*			2.94 s	50.6	3.07 s	50.8	3.73 s	52.2	3.73 s	52.2
CO$_2$Me				173.8		172.9		176.4		176.4
NCH$_3$									3.61 s	29.2

* Assigments for these signals within a vertical column may be reversed

Table 1 (continued). Coupling constants for compounds (**1**) - (**5**).

Compound **1**.

$J_{3,14\alpha} = 11$ Hz; $J_{3,14\beta} \approx 2$ Hz; $J_{5,6\alpha} = 5$ Hz; $J_{5,6\beta} \approx 1,5$ Hz; $J_{5,16} \approx 1$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 13$ Hz; $J_{14\alpha,15} = 2$ Hz; $J_{14\beta,15} \approx 3$ Hz; $J_{15,16} \approx 1.5$ Hz; $J_{16,17} = 8.5$ Hz; $J_{16,17'} = 6$ Hz; $J_{17,17'} = 11$ Hz; $J_{18,19} = 7$ Hz

Compound **2**.

$J_{3,14\alpha} = 11$ Hz; $J_{3,14\beta} \approx 2$ Hz; $J_{5,6\alpha} = 5$ Hz; $J_{5,6\beta} = 1.5$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 12.5$ Hz; $J_{14\alpha,15} \approx 2$ Hz; $J_{14\beta,15} \approx 3$ Hz; $J_{17,17'} = 11$ Hz; $J_{18,19} = 7$ Hz; $J_{18,21\alpha} = 2$ Hz; $J_{18,21\beta} = 2$ Hz

Compound **3**.

$J_{3,14\alpha} = 10.5$ Hz; $J_{3,14\beta} = 2$ Hz; $J_{5,6\alpha} = 5$ Hz; $J_{5,6\beta} = 1.5$ Hz; $J_{5,16} = 11$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} \approx 13$ Hz; $J_{14\alpha,15} \approx 2$ Hz; $J_{14\beta,15} = 4.5$ Hz; $J_{15,16} = 2.5$ Hz; $J_{18,19} = 7$ Hz; $J_{18,21\alpha} = 2$ Hz; $J_{18,21\beta} = 2$ Hz

Compound **4**.

$J_{3,14\alpha} = 9.5$ Hz; $J_{3,14\beta} = 4$ Hz; $J_{5,6\alpha} = 6.5$ Hz; $J_{5,6\beta} \approx 1$ Hz; $J_{6\alpha,6\beta} = 16.5$ Hz; $J_{14\alpha,14\beta} = 13.5$ Hz; $J_{14\alpha,15} = 2.5$ Hz; $J_{14\beta,15} = 3.5$ Hz; $J_{17,17'} = 11.5$ Hz; $J_{18,19} = 6.5$ Hz

Compound **5**.

$J_{3,14\alpha} = 10.5$ Hz; $J_{3,14\beta} \approx 3.5$ Hz; $J_{5,6\alpha} = 6.5$ Hz; $J_{5,6\beta} \approx 1$ Hz; $J_{6\alpha,6\beta} = 16.5$ Hz; $J_{14\alpha,14\beta} = 13.5$ Hz; $J_{14\alpha,15} = 2.5$ Hz; $J_{14\beta,15} \approx 3$ Hz; $J_{17,17'} = 11$ Hz; $J_{18,19} = 6.5$ Hz; $J_{18,21\alpha} \approx 2$ Hz; $J_{18,21\beta} \approx 2$ Hz

Cordell *et al.* have presented the ^{13}C-nmr spectrum of a compound they call polyneuridine (**4**).[9] In fact, the chemical shifts belong to a compound that cannot be polyneuridine (**2**) (*vide supra*, ^{1}H-nmr). The new and correct ^{13}C chemical shifts for polyneuridine (**4**) are reported in Table 1.

Our ^{13}C chemical shift values for voachalotine (**5**) are in accordance with those of Reis *et al.*[16]

As we can see, there has been much confusion in the literature about the ^{1}H- and ^{13}C-nmr spectral data of alkaloids (**1**)-(**5**). Their chemical shifts are now revised, and they can be used as reliable reference data in analyzing the nmr spectra of other alkaloids of sarpagine type.

EXPERIMENTAL

^{1}H-and ^{13}C-nmr spectra were measured with a Varian Unity-400 NMR spectrometer working at 399.952

MHz (^{1}H) and 100.577 MHz (^{13}C). The solvent in all measurements was $CDCl_3$ (the solubility of *E*-akuammidine is poor). Chemical shifts are given in ppm by reference to TMS (^{1}H-nmr; δ_H = 0.00 ppm) and $CDCl_3$ (^{13}C-nmr; δ_C = 77.00 ppm). Signal assignments were confirmed by APT- and ^{1}H,^{1}H-COSY measurements, and when there was enough of the sample also by ^{1}H,^{13}C-correlation spectroscopy. Abbreviations s, d, t, q, m, def, and br are used to designate singlet, doublet, triplet, quartet, multiplet, deformed, and broad, respectively.

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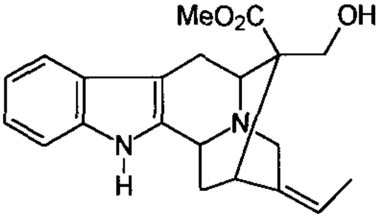

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