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

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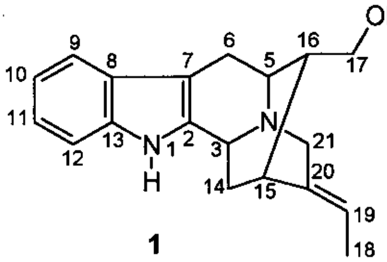
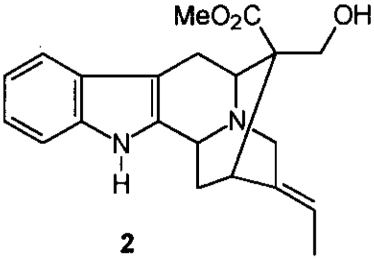
***Abstract*** - Revised $^{1}$H- and $^{13}$C-nmr spectral data are presented for normacusine B (**1**), *E*-akuammidine (**2**), pericyclivine (**3**), polyneuridine (**4**), and voachalotine (**5**).

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).



**1**



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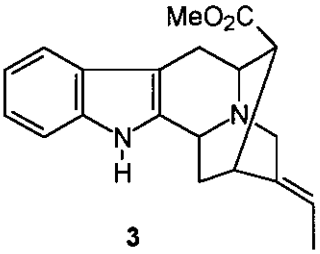

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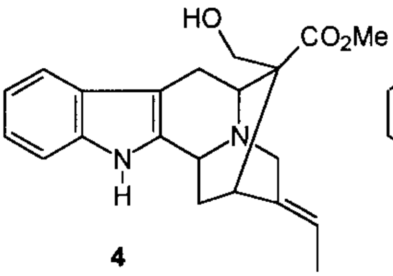

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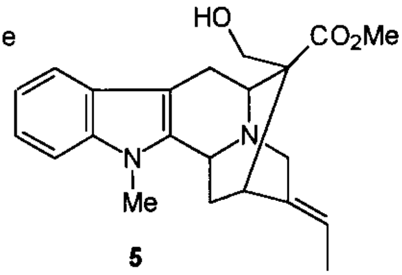

**5**

For the most part, the $^1$H-nmr spectra of the sarpagine-type alkaloids (**1**)-(**5**) can be found in the literature.[2-12] However, there are several misinterpretations of the $^1$H 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 $^1$H- 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 $^1$H-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-21$\alpha$ and $\beta$ the chemical shifts are $\sim 3.7$ ppm (Table 1).

The $^1$H-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 $^1$H-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 $^1$H-nmr data given for polyneuridine are those of akuammidine. The $^1$H-nmr data for polyneuridine given in Ref. 9 are erroneous as well. The chemical shifts reported for H-5 (2.65 ppm) and $CO_2$*Me* (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 $^1$H-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; $J_{3,14\beta}$ ≈ 2 Hz; $J_{5,6\alpha}$= 5 Hz; $J_{5,6\beta}$ ≈ 1,5 Hz; $J_{5,16}$ ≈ 1 Hz; $J_{6\alpha,6\beta}$ = 16 Hz; $J_{14\alpha,14\beta}$ = 13 Hz; $J_{14\alpha,15}$ = 2 Hz; $J_{14\beta,15}$ ≈ 3 Hz; $J_{15,16}$ ≈ 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; $J_{3,14\beta}$ ≈ 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; $J_{14\alpha,15}$ ≈ 2 Hz; $J_{14\beta,15}$ ≈ 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; $J_{14\alpha,14\beta}$ ≈ 13 Hz; $J_{14\alpha,15}$ ≈ 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; $J_{5,6\beta}$ ≈ 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; $J_{3,14\beta}$ ≈ 3.5 Hz; $J_{5,6\alpha}$ = 6.5 Hz; $J_{5,6\beta}$ ≈ 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 Hz; $J_{17,17'}$ = 11 Hz; $J_{18,19}$ = 6.5 Hz; $J_{18,21\alpha}$ ≈ 2 Hz; $J_{18,21\beta}$ ≈ 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; $\delta_H = 0.00$ ppm) and $CDCl_3$ ($^{13}$C-nmr; $\delta_C = 77.00$ 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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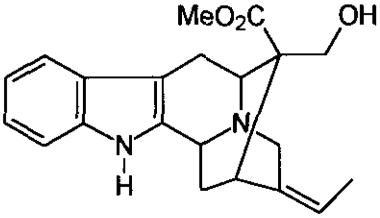
## REFERENCES

1. Since also *Z*-akuammidine (**6**) is known as a naturally occurring compound,[19] we prefer to use the prefix *E*- for the "normal" akuammidine (**2**) in order to avoid confusion.



**6**

2. M. Lounasmaa, R. Jokela, A. Tolvanen, and S.-K. Kan, *Planta Med.*, 1985, 519.
3. T. A. van Beek, F. L. C. Kuijlaars, P. H. A. M. Thomassen, R. Verpoorte, and A. Baerheim Svendsen, *Phytochemistry*, 1984, **23**, 1771.
4. T. A. van Beek, R. Verpoorte, and A. Baerheim Svendsen, *J. Nat. Prod.*, 1985, **48**, 400.
5. J. Garnier and J. Mahuteau, *Planta Med.*, 1986, 66.
6. P. Clivio, B. Richard, J.-R. Deverre, T. Sévenet, M. Zèches, and L. Le Men-Olivier, *Phytochemistry*, 1991, **30**, 3785.

7. A. K. Bashir, A. A. Abdalla, E. S. Hassan, I. A. Wasfi, M. A. Amiri, and T. A. Crabb, *Arab Gulf J. Scient. Res.*, 1994, **12**, 119.
8. S. Mukhopadhyay, G. A. Handy, S. Funayama, and G. A. Cordell, *J. Nat. Prod.*, 1981, **44**, 696.
9. L.-Z. Lin and G. A. Cordell, *Phytochem. Anal.*, 1990, **1**, 26.
10. S. Mukhopadhyay and G. A. Cordell, *J. Nat. Prod.*, 1981, **44**, 335.
11. M. P. Cava, S. K. Talapatra, J. A. Weisbach, B. Douglas, R. F. Raffauf, and J. L. Beal, *Tetrahedron Lett.*, 1965, 931.
12. Atta-ur-Rahman, M. M. Qureshi, K. Zaman, S. Malik, S. S. Ali, *Fitoterapia*, 1989, **60**, 291.
13. K. Jewers, D. F. G. Pusey, S. R. Sharma, and Y. Ahmad, *Planta Med.*, 1980, **38**, 359.
14. D. Ponglux, S. Wongseripipatana, S. Subhadhirasakul, H. Takayama, M. Yokota, K. Ogata, C. Phisalaphong, N. Aimi, and S. Sakai, *Tetrahedron*, 1988, **44**, 5075.
15. E. A. Abdel Sattar, M. M. El Olemy, and J. S. Mossa, *Saudi Pharm. J.*, 1994, **2**, 135.
16. R. Braga and F. Reis, *Phytochemistry*, 1987, **26**, 833.
17. M. R. Yagudaev, *Chem. Nat. Comp.*, 1986, **22**, 1.
18. The erroneous $^{13}$C chemical shifts were included in our earlier review[20] of the sarpagine-ajmaline group of indole alkaloids.
19. S. Sakai, S. Wongseripipatana, D. Ponglux, M. Yokota, K. Ogata, H. Takayama, and N. Aimi, *Chem. Pharm. Bull.*, 1987, **35**, 4668.
20. A. Koskinen and M. Lounasmaa, "Progress in the Chemistry of Organic Natural Products", eds. W. Herz, H. Grisenbach, G. W. Kirby, Vol 43, Springer Verlag, Wien, New York, 1983, pp. 267-346.

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