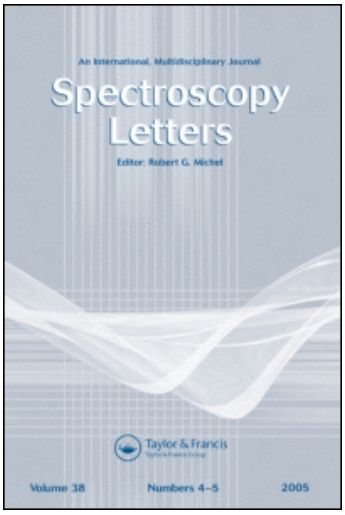


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Complete ^{1}H and ^{13}C NMR Chemical Shift Assignments for Some Pentacyclic Oxindole Alkaloids

H. Toure[a]; A. Babadjamian[b]; G. Balansard[a]; R. Faure[b]; P. J. Houghton[c]
[a] Laboratoire de Pharmacognosie, Faculté de Pharmacie, Cedex, France [b] ensSPICam, Université d'Aix-Marseille III, Marseille, Cedex, France [c] Chelsea Department of Pharmacy, King College London, University of London, London, SW, England

To cite this Article Toure, H. , Babadjamian, A. , Balansard, G. , Faure, R. and Houghton, P. J.(1992) 'Complete ^{1}H and ^{13}C NMR Chemical Shift Assignments for Some Pentacyclic Oxindole Alkaloids', Spectroscopy Letters, 25: 2, 293 — 300
To link to this Article: DOI: 10.1080/00387019208020694
URL: http://dx.doi.org/10.1080/00387019208020694

SPECTROSCOPY LETTERS, 25(2), 293-300 (1992)

COMPLETE ^{1}H AND ^{13}C NMR CHEMICAL SHIFT ASSIGNMENTS FOR SOME PENTACYCLIC OXINDOLE ALKALOIDS.

Key Words: Mitraphylline Isomitraphylline Speciophylline Pteropodine ^{1}H homonuclear correlation ^{1}H homonuclear J-resolved 2D NMR spectra ^{1}H and ^{13}C NMR chemical shifts.

H. TOURE†, A. BABADJAMIAN*††, G.BALANSARD† R. FAURE†† and P.J. HOUGHTON‡

(†) Laboratoire de Pharmacognosie, Faculté de Pharmacie, 27 Boulevard Jean Moulin, 13385 Marseille Cedex 5, France.

(††) ensSPICam, Université d'Aix- Marseille III, Avenue Escadrille Normandie-Niemen, 13397 Marseille Cedex 13, France.

(‡) Chelsea Department of Pharmacy, King College London, University of London, Mauresa Road, London SW 36 LX, England.

Abstract:

The complete analysis of the ^{1}H and ^{13}C NMR has been performed for four pentacyclic oxindole alkaloids: mitraphylline, isomitraphylline, speciophylline and pteropodine. The total assignment of the ^{1}H NMR parameters was achieved from combined evaluation of homonuclear shift correlation and J-resolved diagrams, while DEPT spectra and selective decoupling experiments provided all carbon chemical shifts.

* To whom correspondance should be addressed)

INTRODUCTION

As part of an investigation of the medicinal properties of natural products extracted from the leaves of Mitragyna inermis (willd.) O. Kuntze, a plant used in african folk medicine, we have isolated a mixture of four alkaloids which possess the pentacyclic oxindole skeleton. Comparison with previously reported physico-chemical data[1] indicated that these compounds were mitraphylline **1a**, isomitraphylline **1b**, speciophylline **1c** and pteropodine **1d** (figure 1).

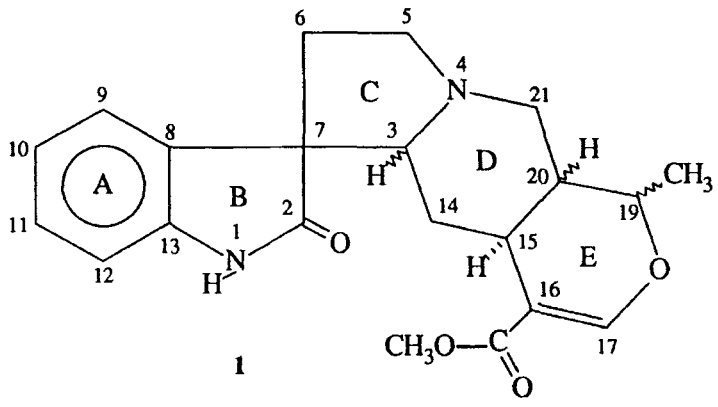
We report in this paper the complete ^{1}H and ^{13}C NMR assignment of the **1a-1d** compounds using two-dimensional NMR spectroscopic techniques.

RESULTS AND DISCUSSION

^{1}H NMR spectroscopy

^{1}H NMR spectral assignments for pentacyclic oxindole alkaloids **1a-1d** were deduced from the concerted application of autocorrelated[2-4] and homonuclear J-resolved[5, 6] two-dimensional NMR spectroscopy. Chemical shift information is provided by the 2D-J technique while the proton connectivity is easily available from the COSY diagram. The complete ^{1}H NMR spectrum analysis of mitraphylline **1a** illustrates this approach.

A convenient starting point for the interpretation and utilization of the COSY spectrum of **1a** is provided by the resonances which can be assigned with certainty from the one-dimensional ^{1}H spectrum: H-17, H-19 and the methyl protons. It is evident from the contour plot of the homonuclear shift correlation that the H-17 doublet presents correlated peaks with the proton resonating at 2.02 ppm (H-15) via a long range coupling, while H-19 correlates vicinally with H-20 which, in turn, is coupled with the methylenic protons H-21 α and H-21 β. The H–15 resonance is also coupled with the signal at 0.91ppm which can be easily identified as H-14 β from its coupling pattern (q, J = 11.2 Hz). As a consequence, the H-14 α and H-3 chemical shifts were determined in a straightforward manner from their spin multiplicities extracted from the corresponding slices of the 2D-J spectrum.



1

compound	Alkaloid	Type	configuration of asymetric centres			
			C-3 H	C-20 H	C-19 CH_3	C-7[a]
1a	Mitraphylline	normal	α	β	α	B
1b	Isomitraphylline	normal	α	β	α	A
1c	Speciophylline	epiallo	β	α	α	A
1d	Pteropodine	allo	α	α	α	B

[a] A: lactam carbonyl group below the plane of C/D rings;
B: lactam carbonyl group above the plane of C/D rings.

FIGURE 1. Configurational terminology for oxindole alkaloids

Deshielding of H-5 β (and H-21 β) was supported by the examination of Dreiding models and the ^1H assignments of isopteropodine[7]. Although the protons of C ring form a complex spin system, their coupling connectivities can be easily established from the ^1H-^1H homonuclear correlation spectrum. Finally, additional support for these assignments was also provided by double resonance experiments.

A complete summary of the proton chemical shifts of **1a-1d** is presented in table 1. As stated by Yagudaev *et al* [8], it can be seen from the table, that in **1c** (epiallo type) the signals in the 19-CH_3 and 1H protons appear in a stronger field than those of the corresponding protons in **1d** (allo type).

^{13}C NMR spectroscopy

The complete ^{13}C data are given in table 2. The limited quantities of material available precluded the use of the 2D-heteronuclear shift correlation. The ^{13}C chemical shift assignments of **1a-1d** were, therefore, assigned a) by comparison with literature data of representative oxindole[7, 9] or other alkaloid[10] models, b) on the basis of their multiplicities in the DEPT[12] spectra and c) from selective decoupling experiments using previously reported ^1H chemical shifts for ^{13}C ambiguous assignments: CH-3 and CH-19; CH_2-5 and CH_2-21. It should be point out that our attribution for the cited carbons, for pteropodine **1d** and for speciophylline **1c**, do not agree with the interpretation of Borges del Castillo *et al* [13].

EXPERIMENTAL

Mitraphylline **1a**, isomitraphylline **1b**, speciophylline **1c** and pteropodine **1d** were isolated from the plant according to the operating process previously reported[1, 11]. All NMR spectra were recorded with a multinuclear Bruker AM-200 spectrometer (Centre Interuniversitaire de RMN de Marseille). The NMR spectra were measured as solutions in $CDCl_3$ (DMSO-d_6 for **1a**) in 10mm and 5mm o.d. tubes for ^{13}C and ^1H respectively. Tetramethylsilane was used as an internal standard in both measurements.

Resonance multiplicities for ^{13}C were established via the acquisition of DEPT spectra obtained for proton pulses $P\theta = 90°$ (CH only) and $P\theta = 135°$ (CH and CH_3 differentiated from CH_2). For the DEPT sequence the with of ^1H 90° pulse was 29 μs, the width of a ^{13}C 90° pulse was 13 μs and the $(2J)^{-1}$ delay was set equal to 3.7 ms.

TABLE 1. ^{1}H NMR chemical shifts of oxindole alkaloids **1a** - **1d** [a]

	δ^1H			
Atoms	**1a**[a]	**1b**	**1c**	**1d**
1	10.17	8.99	9.15	9.15
3	2.33	2.65	2.18	2.47
5α	3.16	3.32	3.39	3.36
5β	2.18	2.41	2.45	2.35
6α	1.89	2.06	2.05	1.99
6β	2.45	2.56	2.45	2.40
9	7.28	7.38	7.16	7.21
10	6.99	6.97	7.18	7.18
11	7.18	7.18	7.02	7.03
12	6.81	6.91	6.94	6.90
14α	2.12	2.23	2.21	1.74
14β	0.91	0.66	1.63	1.53
15	2.02	2.19	2.86	2.36
17	7.42	7.40	7.39	7.49
19	4.46	4.39	4.21	4.55
20	1.76	1.90	2.05	1.60
21α	1.81	1.95	2.12	2.40
21β	3.08	3.16	3.12	3.35
OCH_3	3.50	3.58	3.37	3.50
CH_3	1.04	1.12	1.26	1.39

[a] in ppm from TMS
[b] DMSO-d_6 as solvent

TABLE 2. ^{13}C NMR chemical shifts of oxindole alkaloids **1a** - **1d** [a]

Atoms	$\delta^{13}C$			
	1a[a]	**1b**	**1c**	**1d**
2	179.44	181.21	181.95	181.41
3	73.62	71.88	70.52	74.47
5	52.79	53.40	53.37	55.18
6	34.35	35.37	34.16	34.83
7	54.85	56.60	56.00	56.34
8	133.65	133.95	133.44	133.62
9	122.85	125.00	122.59	123.04
10	121.40	122.38	122.15	122.59
11	127.50	127.65	127.80	127.99
12	108.69	109.61	109.85	109.70
13	141.80	140.57	141.59	141.10
14	28.01	29.33	26.45	29.73
15	29.73	30.29	25.21	31.20
16	106.74	107.59	105.20	109.38
17	153.29	153.88	153.66	155.30
19	73.22	74.09	74.8	172.28
20	40.23	41.14	36.60	38.10
21	53.31	54.39	54.90	53.72
CO	165.94	167.06	167.47	167.73
OCH_3	50.30	50.67	50.45	50.86
CH_3	14.53	14.90	18.80	18.94

[a] in ppm from TMS
[b] DMSO-d_6 as solvent

The homonuclear ^1H-^1H shift correlated two-dimensional diagrams were obtained using the COSY-45 pulse sequence. The spectral withs were F_2 = 2000Hz and F_1= ± 1000 Hz, allowing a digital resolution of 1.95 Hz. The spectra were collected as 2048x1024 blocks of data, and were processed using sinusoidal multiplication in each dimension followed by symmetrization of the final data matrix. Other parameters were as follows: number of increments in t_1, 512; scans, 32; phase cycling, 16; and relaxation delay, 2s.

The basic pulse sequence was used for the two-dimensional homonuclear proton J-resolved diagram. The F_2 spectral with was 2000 Hz and F_1 was ± 62 Hz. A 16 phase cycling , with 16 scans and 64 increments, followed by zero filling and weighting with sine bell functions in both directions, providing a digital resolution of 1.95 Hz in F_2 and 0.97 Hz in F_1; the recycle delay was 2s.

References

1. J. D. Phillipson and S. R. Hemingway, *J. Chromatogr.*, **105**, 163 (1975).
2. W.P. Aue, E. Bartholdi and R.R. Ernst, *J. Chem. Phys.*, **64**, 2229 (1976).
3. K. Nagayama, A. Kumar, K. Wüthrich and R.R. Ernst, J. *Magn. Reson.*, **40**, 321 (1980).
4. R. Freeman, G.A. Morris and A. Bax, *J. Magn. Reson.*, **42**, 164 (1981).
5. W.P. Aue, J. Karhan and R.R. Ernst, *J. Chem. Phys.*, **64**, 4226 (1976.
6. K. Nagayama, K. Wüthrich, P. Bachman and R.R. Ernst, *Biochem. Biophys. Res. comm.*, **78**, 99 (1977).
7. G. E. Martin, R. Sanduja and M. Alam, *J. Nat. Prod.*, **49**, 406 (1986).
8. M. R. Yagudaev and S. Y. Yunusov, *Khim. Prir. Soedin.*, (3), 345 (1976).
9. E. Wenkert, J. S. Bindra, C. J. Chang, D. W. Cochran and F. M. Schell, *Acc. Chem. Research* , **7**, 46 (1974).
10. E. Wenkert, C. J. Chang, H.P.S. Chawla, D. W. Cochran, E.W. Hagaman , J.C. King and K. Orito, *J. Am. Chem. Soc.*, **98**, 3645 (1976).
11. D. M. Doddrell, D.T. Pegg and M. R. Bendall, *J. Magn. Reson.*, **48**, 323 (1982).

12. E. S. Shellard and K. Sarpong, *J. Pharm. Pharmacol.*, **21**, suppl. 113S (1969).

13. J. Borges del Castillo, M. T. Manresa ferrero, J.L. Martin Ramon, F. Rodriguez Luis, P. Vazquez Bueno and P. Joseph-Nathan, *An. Quim., Ser. C*, **78** (1), 126, 1982.

Date Received: 10/03/91
Date Accepted: 11/06/91