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^{13}C-NMR OF SOME AJMALANE ALKALOIDS

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Summary: The ^{13}C-NMR spectra of the alkaloid ajmaline (1) and its stereoisomers isoajmaline (2), sandwichine (3) and isosandwichine (4) are reported. The different stereochemistry at C (17), C(20) and C(21) of the four isomers can be directly ascertained by chemical shifts data.

Ajmaline (1) and its naturally occurring stereoisomers isoajmaline (2), sandwichine (3) and isosandwichine (4) are heteroyohimbine related alkaloids used against heart diseases, in particular for their antiharrhitmic and antifibrillatory properties.

The here reported study of the ^{13}C-NMR spectra of (1),(2),(3) and (4) was undertaken not only for determining the basic carbon shifts of the rigid ajmalane skeleton, but also for assessing by direct analysis the relative stereochemistry at C(17), C(20) and C(21). This would be of particular interest for studies of biological interaction(s) and in view of the facile epimerization at C(21) *via* a ring-opened amino aldehyde intermediate during the formation of some derivatives[1].

Attribution of all ^{13}C-NMR signals in (1),(2),(3) and (4) was greatly assisted by analysis of a series of functional derivatives (acetates, N_b-methiodides, ethers) and structural derivatives (ajmalidine, 21-desoxyajmaline, tetraphyllicine, quebrachidine) and is reported in TABLE[2].

The shifts assignment is limited only to the differentiation of nonaromatic methine and methylene resonances, the remaining signals being easily attributed. Predictably, C(21) is the most deshielded methine and a sound distinction of the close C(2) and C(17) is based on the acetylation shift of the latter. Of the remaining methines, C(15) is expected upfield, while C(3) and C(5) in spite of their α-position to N_b show a shift similarity to C(16) and C(20). However, the former are distinguished by the large β-effect (11-13 ppm) on N_b-methiodide formation and by application of SFSD technique on the 17,21-diacetates, advantage being taken from the insignificant acetylation shifts. Although a distinction between C(3) and C(5) is not necessary in (2) and (4), in all derivatives the former is slightly upfield to the latter.

A criterion for the differentiation of C(16) from C(20) was the observation that C(16) should exhibit sharp one-bond components in SFORD spectra due to few long-range interactions and no se-

cond order couplings in contrast to C(20).

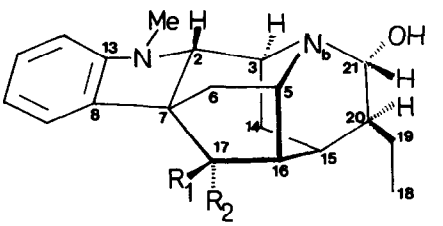
As regards the methylene signals, C(19) is recognized by its invariance on methiodide formation and C(6) is differentiated from C(14) on shift grounds.

A comparison of the spectra of the four isomers reveals that the configurational changes at C(17) C(20) and C(21) is accompanied by significant and diagnostically useful shifts. In particular, the C(17) inversion causes a moderate shift of C(17) itself, a scarse movement of C(7) and a remarkable downfield effect on C(16). On the other hand, concomitant inversion at C(20) and C(21) merely deshields C(3) and C(16) and shields C(5) and C(14), due to the loss and presence of γ-steric interactions, and leaves C(19) invariant as a consequence of the replacement of the γ-effect exerted by C(16) by one of comparable magnitude by C(14).

TABLE

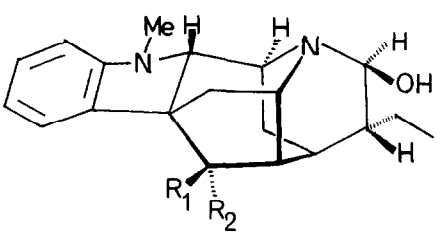
CMR shifts of (1),(2),(3) and (4) 22.5 MHz, $CDCl_3$

carbon	(1)	(2)	(3)	(4)
2	79.3	78.7	75.7	76.3
3	43.0	47.5	44.8	48.1
5	52.8	48.0	53.0	48.6
6	34.8	34.1	34.9	53.1
7	56.1	55.6	54.0	54.5
8	133.3	133.7	131.8	131.8
9	122.8	123.1	120.2	119.6
10	119.0	118.5	118.7	118.8
11	127.1	126.5	127.1	127.3
12	109.5	108.6	109.7	109.5
13	153.6	153.4	153.3	153.9
14	31.4	22.3	31.0	22.3
15	28.3	29.1	27.2	28.2
16	45.2	53.0	34.4	43.4
17	77.3	75.9	70.8	72.3
18	12.2	12.3	12.1	12.4
19	25.4	25.6	25.0	25.8
20	48.0	54.2	48.7	45.6
21	88.1	87.5	88.1	88.1
NCH_3	34.0	34.0	34.4	34.5



(1) R_1:OH;R_2:H

(3) R_1:H;R_2:OH



(2) R_1:OH;R_2:H

(4) R_1:H;R_2:OH

Notes and references

[1] It has been shown by X-ray analysis that N_b-n-propylisoajmalinium bromide has the unnatural configuration at C(21) and is therefore N_b-n-propyl-21-epi-isoajmalinium bromide [R.Prewo and J.J. Stezowski, Acta Cryst., B34, 454(1978)]

[2] The CMR spectrum of (1) was reported without explanation in connection with the structure determination of the related alkaloids rauflexine and reflexine. C(20) was misassigned and C(3),C(5) and C(16) were left indifferentiated [A.Chatterjee, M.Chakrabarty, A.Kumar Ghosh, E.W.Hagaman and E.Wenkert, Tetrahedron Lett., 3879(1978)]. More recently, the above data have been utilized for a discussion of the spectrum of (2). For this compound, C(2), C(14),C(17),C(19) and C(21) were misassigned and C(16) was left indifferentiated with respect to C(3) and C(5) [F.Libot, N.Kunesch and J.Poisson, Phytochemistry, 989(1980)].

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