Short Communications

A 400 MHz ^{1}H NMR Study of Five Aspidospermane-type Alkaloids

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To obtain useful ^{1}H NMR data for the structure determinations of new aspidospermane-type alkaloids, we undertook a 400 MHz ^{1}H NMR study of 11-methoxytabersonine *1*, vandrikidine *2*, hazuntinine *3* and vandrikine *4*, isolated from the leaves or the stem bark of the Madagascan plants *Craspidospermum verticillatum* Boj. (Apocynaceae) and *Hazunta velutina* Pichon (Apocynaceae).[1-3] In connection with this study we were also able to show that the new *Aspidosperma* alkaloid (product M, m.p. 214 °C, $[\alpha]_D^{20}$ −388° (c, 1, $CHCl_3$), M^+ at *m/e* 398 ($C_{22}H_{26}N_2O_5$)) isolated from the root bark of *Craspidospermum verticillatum*,[1] is 19-hydroxyvandrikine *5*, and that vandrikidine *2* has a 19*R* configuration.

The application of consecutive double resonance experiments permitted all the protons in compounds *1*−*5* to be assigned. The chemical shifts and the coupling constants determined are presented in Tables 1 and 2.

Of the 26 protons of 11-methoxytabersonine *1*, the identification of 17 is straightforward: CH_3- (δ 0.63), H_R-19* (δ 1.00), H_S-19* (δ 0.86), CH_3O-** (δ 3.75), $-CO_2CH_3$** (δ 3.76), H−15 (δ 5.70), H−14 (δ 5.78), H−10 (δ 6.38), H−12 (δ 6.41), H−9 (δ 7.10) and NH (δ 8.96).

Irradiation of H−14 allowed the identification of both H−3's (δ 3.44 and δ 3.16). The distinction between these protons was mainly based on the coupling constants (Table 1).***

The signals at δ 2.42 and 2.54 were assigned to H_R-17 and H_S-17, respectively. These protons could be distinguished on the basis of the long-

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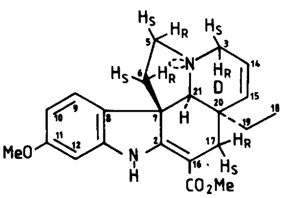
*, ** Assignments may be interchanged.

*** It is supposed that the D ring in compounds *1*, *2* and *3* exists in a slightly modified half chair form and in compounds *4* and *5* in a chair form. The present ^{1}H NMR results seem to be in good agreement with these suppositions.



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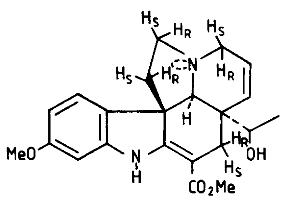

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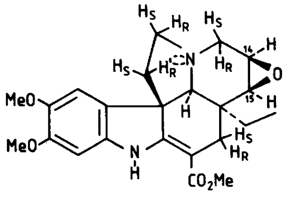

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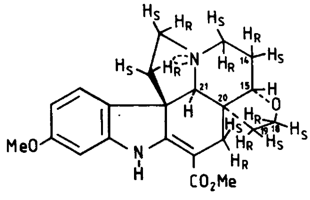

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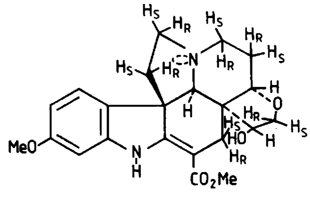

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Table 1. ^1H NMR data of 11-methoxytabersonine *1*, vandrikidine *2* and hazuntinine *3*. Spectra were run in $CDCl_3$ at 400 MHz. Values are in δ (TMS = 0), s, singlet, d, doublet, t, triplet, q, quartet, m, multiplet, br, broad. The coupling constants between the aromatic protons are not included. The Hanson prochirality nomenclature system[4] is applied to distinguish between the H-atoms of different -CH_2- groups. It should be noted that the priority sequence at C-17 in compounds *1* and *2* is different from that in compound *3*. The signal due to the OH-group of vandrikidine *2* is omitted.

H-atoms	*1*	*2*	*3*
Chemical shifts (δ)			
H_R-3	3.16 br d	3.28 br d	2.93 br d
H_S-3	3.44 ddd	3.44 ddd	3.58 dd
H_R-5	3.02 br dd	3.03 br dd	3.05 br dd
H_S-5	2.67 ddd	2.76 ddd	2.72 ddd
H_R-6	2.04 ddd	2.06 ddd	2.10 ddd
H_S-6	1.76 br dd	1.82 ddd	1.70 br dd
H-9	7.10	7.18	6.80
H-10	6.38	6.40	–
H-12	6.41	6.42	6.49
H-14	5.78 ddd	6.06 ddd	3.26 dd
H-15	5.70 br d	5.73 br d	3.07 d
H_R-17	2.42 d	2.48 d	2.70 dd
H_S-17	2.54 dd	2.62 dd	2.54 d
H-18	0.63 t	1.00 d	0.74 t
H_R-19	1.00[a] dq	–	0.99[d] br q
H_S-19	0.86[a] dq	3.25 q	0.97[d] br q
H-21	2.63 d	3.30 d	2.43 d
CO_2Me	3.76[b] s	3.76[c] s	3.78 s
OMe	3.75[b] s	3.75[c] s	3.86 s
OMe	–	–	3.86 s
NH	8.96 br s	8.92 br s	8.88 br s

Coupling constants (Hz)

1: $J_{3R,3S}=15$; $J_{3R,14}\approx2$; $J_{3S,14}=5$; $J_{3S,15}\approx2$; $J_{5R,5S}=12$; $J_{5R,6R}=7$; $J_{5R,6S}\approx1$; $J_{5S,6R}=10$; $J_{5S,6S}=5$; $J_{6R,6S}=14$; $J_{14,15}=10$; $J_{17R,17S}=15$; $J_{17S,21}\approx2$; $J_{18,19R}=7$; $J_{18,19S}=7$; $J_{19R,19S}=15$.

2: $J_{3R,3S}=15$; $J_{3R,14}\approx2$; $J_{3S,14}=5$; $J_{3S,15}\approx2$; $J_{5R,5S}=12$; $J_{5R,6R}=7$; $J_{5R,6S}\approx1$; $J_{5S,6R}=10$; $J_{5S,6S}=5$; $J_{6R,6S}=14$; $J_{14,15}=10$; $J_{17R,17S}=15$; $J_{17S,21}\approx2$; $J_{18,19}=7$.

3: $J_{3R,3S}=14$; $J_{3R,14}\approx0.5$; $J_{3S,14}\approx1.5$; $J_{5R,5S}=12$; $J_{5R,6R}=7$; $J_{5R,6S}\approx1$; $J_{5S,6R}=10$; $J_{5S,6S}=5$; $J_{6R,6S}=14$; $J_{14,15}=4.5$; $J_{17R,17S}=15$; $J_{17R,21}\approx2$; $J_{18,19R}=7$; $J_{18,19S}=7$; $J_{19R,19S}=15$.

[a,b,c,d] Assignments may be interchanged.

Table 2. ^1H NMR data of vandrikine *4* and 19-hydroxyvandrikine *5*. Spectra were run in $CDCl_3$ at 400 MHz. Values are in δ (TMS = 0), s, singlet, d, doublet, t, triplet, q, quartet, m, multiplet, br, broad. The coupling constants between the aromatic protons are not included. The Hanson prochirality nomenclature system[4] is applied to distinguish between the H-atoms of different −CH_2− groups. The signal due to the OH-group of 19-hydroxyvandrikine *5* is omitted.

H-atoms	*4*	*5*
Chemical shifts (δ)		
H_R-3	2.94 br dd	2.98 br dd
H_S-3	2.71 br d	2.76 br d
H_R-5	2.93 br d	2.96 br d
H_S-5	2.64 ddd	2.82 ddd
H_R-6	2.00 ddd	2.00 ddd
H_S-6	1.72 br dd	1.81 br dd
H-9	7.10	7.15
H-10	6.39	6.42
H-12	6.40	6.40
H_R-14	1.95[a] m	1.95[e] m
H_S-14	1.92[a] m	1.90[e] m
H-15	3.65 t	3.73 t
H_R-17	2.28 br d	2.37 br d
H_S-17	2.72 d	2.78 d
H_R-18	3.80[b] m	3.93[f] dd
H_S-18	3.72[b] m	3.56[f] dd
H_R-19	1.42[c] ddd	–
H_S-19	1.30[c] ddd	4.07 dd
H-21	2.77 br s	3.21 br s
CO_2Me	3.76[d] s	3.77[g] s
OMe	3.75[d] s	3.76[g] s
NH	8.86 br s	8.92 br s

Coupling constants (Hz)

4: $J_{3R,3S}=10$; $J_{3R,14R}=7.5$; $J_{3R,14S}\approx2$; $J_{3S,14R}\approx4$; $J_{3S,14S}\approx4$; $J_{5R,5S}=12$; $J_{5R,6R}=7$; $J_{5R,6S}\approx1$; $J_{5S,6R}=10$; $J_{5S,6S}=5$; $J_{6R,6S}=14$; $J_{14R,15}=3$; $J_{14S,15}=3$; $J_{17R,17S}=15$; $J_{17R,21}\approx1$; $J_{18R,18S}\approx10$; $J_{18R,19R}=9$; $J_{18R,19S}=5$; $J_{18S,19R}=7$; $J_{18S,19S}=7.5$; $J_{19R,19S}=12$.

5: $J_{3R,3S}=10$; $J_{3R,14R}=7.5$; $J_{3R,14S}\approx2$; $J_{3S,14R}\approx4$; $J_{3S,14S}\approx4$; $J_{5R,5S}=12$; $J_{5R,6R}=7$; $J_{5R,6S}\approx1$; $J_{5S,6R}=10$; $J_{5S,6S}=5$; $J_{6R,6S}=14$; $J_{14R,15}=3$; $J_{14S,15}=3$; $J_{17R,17S}=15$; $J_{17R,21}\approx1$; $J_{18R,18S}=10$; $J_{18R,19}=5$; $J_{18S,19}=7.5$.

[a,d,e,g] Assignments may be interchanged. [b,c,f] Tentative assignments.

range coupling ($\approx$2 Hz; W-configuration) of H_S-17 with H-21. This coupling also confirmed the correct assignment of the signal at δ 2.63 to H-21.

The remaining 4 protons represent the C(5)−C(6) ethylene bridge and form a separate system, which could be easily resolved by consecutive irradiations.

The assignment of the signals of vandrikidine *2*, hazuntinine *3* (Table 1), vandrikine *4* and 19-hydroxyvandrikine *5* (Table 2) followed a procedure similar to that described for 11-methoxytabersonine *1*. A comparison of the ^{1}H NMR data of vandrikidine *2* (Table 1) with those of 19*R*-hydroxytabersonine and 19*S*-hydroxytabersonine [5] indicates a 19*R* configuration for vandrikidine *2*. The coupling constants ($J_{3_R,14}\approx0.5$ Hz; $J_{3_S,14}\approx1.5$ Hz) found for hazuntinine *3*, support the presence of a 14β,15β-epoxy group. The spectra of vandrikine *4* and 19-hydroxyvandrikine *5* are very similar. The coupling constants ($J_{14_R,15}=3$ Hz; $J_{14_S,15}=3$ Hz) indicate that H-15 bisects H-14's. The chemical shifts and the coupling constants found for the three proton system of the C(18)−C(19) ethylene bridge of 19-hydroxyvandrikine *5*, compared with those of the corresponding four proton system of vandrikine *4*, clearly support the proposed 19-OH structure. This structure is further supported by the strong influence of the OH-group on the chemical shift of H-21.

Experimental. The NMR spectra were recorded on a laboratory-built 400 MHz ^{1}H high resolution spectrometer (I.E.F. 400) [6] and obtained by collecting 8 to 16 free-induction decay signals for a $\approx$0.01 M solution of the samples in 450 μl of $CDCl_3$.

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