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STRUCTURAL ANALYSIS BY ^{13}C NMR SPECTROSCOPY OF PLEIOCORINE, A NEW BISINDOLE ALKALOID FROM ALSTONIA DEPLANCHEI van HEURCK et MUELL. ARG.[1,2].

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We wish to report here a successful application of ^{13}C NMR spectroscopy toward the determination of the structure of pleiocorine, a new bisindole alkaloid isolated from the stems and leaves of Alstonia deplanchei van Heurck et Muell. Arg. (Apocynaceae), a species endemic to New Caledonia.

Pleiocorine, $[\alpha]_D^{22}$ +142° (c, 1.04 ; $CHCl_3$), decomposes slowly above 300°C without melting and showed λ_{max}^{EtOH} 244, 297(sh), 344 nm (ε 17.200, 4.600, 8.700) in its uv spectrum. The ir spectrum lacked NH or OH absorption, but showed ester double band (1760, 1738 cm^{-1}) and indoline band (1610 cm^{-1}). The mass spectrum exhibited an intense molecular ion peak at m/e 674 corresponding to the formula $C_{41}H_{46}N_4O_5$. Surprisingly, except for a prominent peak at m/e 615 corresponding to loss of a carbomethoxy grouping, the remainder of the spectrum proved uncharacteristic and contained no peak of significant intensity to provide further structural information.

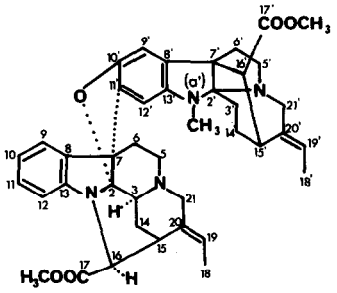
The 240 MHz ^1H NMR spectrum[3] of pleiocorine revealed the presence of two carbomethoxy functions [δ 3.65 (3H) ; 3.72 (3H)], two vinylic methyl groups of ethylidene side chains [δ 1.46 and 1.60 (d, J = 7 Hz)], one N-methyl group [δ 2.72 (3H)], two olefinic [δ 5.4(m)] and six aromatic protons [(δ 6.25 - δ 7.40)] of which two appeared as singlets [(δ 6.36 and 6.72)] indicating an aromatic C-10, C-11 disubstituted indole moiety. It also showed several overlapping multiplets and a well-resolved signal [δ 4.66 (d, J = 4 Hz)] integrating for one proton. The splitting pattern and chemical shift of this latter signal as well as of the signals observed in the aromatic region are reminiscent of those belonging to 2,7-dihydropleiocarpamine unit of villalstonine[4] 2. Correlation of pleiocorine with the known bisindole alkaloid villalstonine 2 was therefore sought principally through a study of their ^{13}C NMR spectra.

Unambiguous carbon signal assignment of the 2,7-dihydropleiocarpamine moiety of villalstonine 2 thus became a necessity. This was acheived (see Table I) by a comparative study of the ^{13}C NMR spectra[5] of villalstonine 2 and macralstonidine[6] 3 - a choice made in consideration of the occurrence of a common macroline - like moeity in these two alkaloids. This common fragment of the two "dimers" exhibited carbon signals identical both from the point of view of chemical shift and single frequency decoupled multiplicity. Also, in view of the presence of an $N_{(a)}$-methyl sarpagine moiety in macralstonidine 3,

a comparison with the ^{13}C NMR spectrum of sarpagine[7] was made leading to results supporting the carbon assignments of the macroline moiety. Thus, by a substractive process, the signals representing the 2,7-dihydropleiocarpamine part of villalstonine 2 could be easily deduced and their appropriate assignments made (Table I) according to chemical shift rules[8].

Noise and single frequency decoupled ^{13}C NMR spectra of pleiocorine exhibited below 60 ppm : two nonprotonated carbons, five methines, nine methylenes and five methyl groups. Above 95 ppm twelve quaternary and eight methine carbons were observed in agreement with the presence of 46 hydrogens in the molecule and suggesting that both indole nitrogens of the new alkaloid are substituted.

Comparison of the ^{13}C NMR data of villalstonine 2 and pleiocorine 1 afforded evidence (Table I) for the occurrence of a 2,7-dihydropleiocarpamine unit in the new alkaloid substituted as in 2 at C-2 and C-7 by an oxygen and by a carbon atom, respectively.



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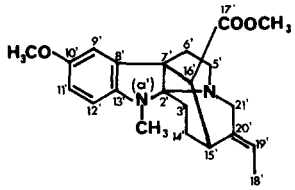

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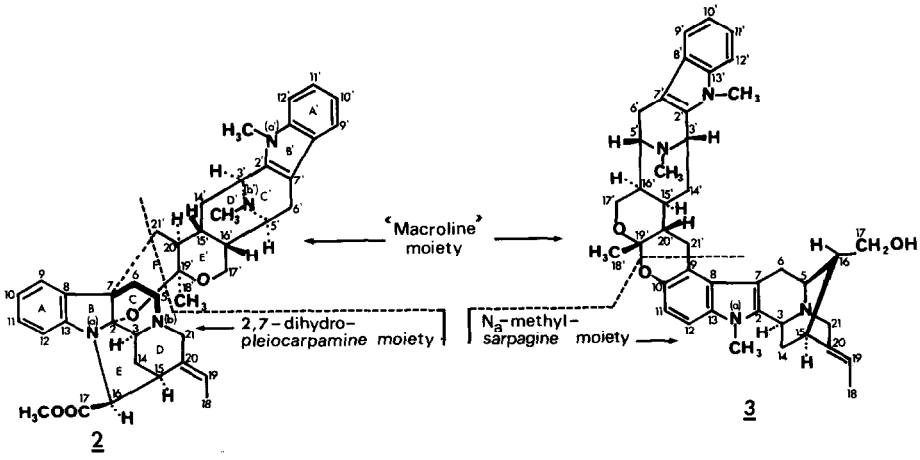

2 3

TABLE I

^{13}C NMR chemical shifts of pleiocorine 1, villalstonine 2, macralstonidine 3 and vincorine 4

	C-2	C-3	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	
1	103.2	51.3	52.0[a]	24.6	54.0	134.4	121.6	119.2[b]	126.3	108.9	144.4	
2	92.2	51.5	53.1[c]	28.6[d]	44.2	132.9	120.9	118.1[e]	126.5	109.3	147.0	
3	133.4[f]	49.5	55.2	26.8	103.3	125.0	111.3	147.6	112.4	107.6	139.8	

	C-14	C-15	C-16	C-17	C-18	C-19	C-20	C-21	$COO\underline{C}H_3$	N_a-CH_3	
1	28.1	32.2	58.1	169.3	12.3	119.5[b]	136.1	48.2[a]	50.6		
2	28.9[d]	31.9	57.8	170.8	12.2	118.4[e]	136.4	47.5[c]	51.9		
3	26.8	30.5	44.4[g]	62.3	12.8	116.5	132.4[f]	56.2		29.1[h]	

	C-2'	C-3'	C-5'	C-6'	C-7'	C-8'	C-9'	C-10'	C-11'	C-12'	C-13'	
1	97.5	40.6	55.0[i]	20.2	56.9	134.8	106.1	151.1	127.4	100.1	143.6	
2	135.9	54.5[j]	53.4[j]	22.9	106.6	126.5	118.1	120.9	118.9	108.7	137.1	
3	136.0	54.4[k]	54.1[k]	22.7	106.9	126.5	118.0	120.7	118.8	108.6	137.1	
4	97.9	40.6	56.1[l]	20.4	57.3	138.2	105.5	152.3	111.7[m]	112.1[m]	143.6	

	C-14'	C-15'	C-16'	C-17'	C-18'	C-19'	C-20'	C-21'	$COO\underline{C}H_3$	N_a,CH_3	N_b,CH_3	OCH_3
1	26.3	34.7	50.9	173.1	13.4	122.5	138.8	58.1[i]	51.6	28.1		
2	32.5	36.8[n]	41.8[n]	65.6	26.5	98.5	37.9[n]	31.4		30.7	27.5	
3	33.1	37.2[o]	41.7[o]	64.9	25.5	98.8	43.5[g]	29.3		29.6[h]	27.6	
4	26.3	34.8	50.7	173.5	13.6	123.2	138.2	58.2[l]	51.7	28.3		54.9

a,b,c,d,e,f,g,h,i,j,k,l,m,n,o : these assignments may be reversed although those given here are preferred.

The nature of the second monomeric indole moiety of pleiocorine could be elaborated by an interpretation of the remaining signals after assignments of the 2,7-dihydropleiocarpamine carbons. The exceptionally low field saturated nonprotonated signal at 97.5 ppm must represent a quaternary carbon attached to two nitrogen atoms since no extra oxygen remains to be accounted for. This observation along with the presence of only two saturated methines led us to consider a vincorine-type[9] skeleton for this moiety. The chemical shifts of the remaining saturated carbons were in perfect agreement (Table I) with the ^{13}C NMR spectrum of vincorine 4 also isolated from A. deplanchei.

Since the second half of pleiocorine should be a C-10', C-11' di-substituted dihydroindole (singlets due to C-9' and C-12' protons in the ^{1}H NMR spectrum) two possibilities had to be considered for the linkage between the two monomeric units. In view of the lowest and highest field aromatic carbon signals at 151.1 and 100.1 ppm assigned to C-10' and C-12' respectively, agreement with the previous results[10] could be reached only with the linkage shown in 1. The stereochemistry of this cis-linkage could not be ascertained from NMR spectroscopy but has been put forward by analogy with all other related bisindole alkaloids having 2,7-dihydropleiocarpamine as a constituent part[11]. Based on the arguments presented here, structure 1 is proposed for pleiocorine.

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REFERENCES

1. Résonance Magnétique Nucléaire du ^{13}C de Produits Naturels et Apparentés XIX ; for paper XVIII see K. Tori, T. Komeno, M. Sangaré, B. Septe, B. Delpech, A. Ahond and G. Lukacs, Tetrahedron Letters, 1157 (1974).
2. Part XXXII in the series "Plantes de Nouvelle-Calédonie" ; for Part XXXI see N. Préaux, M. Koch and M. Plat, Phytochemistry, 13,0000 (1974).
3. We are grateful to Drs S.K. Kan and G. Massiot for 240 MHz ^{1}H NMR spectra.
4. M. Hesse, H. Hurzeler, C.W. Gemenden, B.S. Joshi, W.I. Taylor and H. Schmid, ibid., 49, 1173 (1966).
5. Spectra were recorded in $CDCl_3$ solution at 22.63 MHz on a Bruker HX 90E Fourier transform spectrometer using TMS as internal standard. Chemical shifts in the Table I are with respect to TMS = 0.
6. E.E. Waldner, M. Hesse, W.I. Taylor and H. Schmid, Helv. Chim. Acta, 50 1926 (1967).
7. J. Le Men and G. Lukacs, unpublished results.
8. J.B. Stothers, Carbon-13 NMR Spectroscopy, Academic Press, New-York (1972).
9. H.K. Schnoes, Ph.D. thesis, M.I.T., Cambridge, Mass, USA (1965).
10. E. Wenkert, D.W. Cochran; E.W. Hagaman, F.M. Schell, N. Neuss, A.S. Katner, P. Potier, C. Kan, M. Plat, M. Koch, H. Mehri, J. Poisson, N. Kunesch and Y. Rolland, J. Amer. Chem. Soc., 95, 4990 (1973).
R.H. Levin, J.Y. Lallemand and J.D. Roberts, J. Org. Chem. 38, 1983 (1973).
11. Specialist Periodical Reports, The Alkaloids - Vol. I, the Chemical Society, London (1971).