Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. Gelsemine[1]

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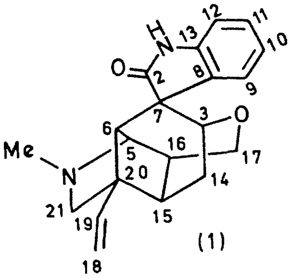
Summary A ^{13}C n.m.r. spectrum of the alkaloid gelsemine has been recorded and the signals of all carbons assigned.

WHILE at the present, early stage of development of natural abundance ^{13}C n.m.r. spectroscopy enough techniques have been discovered to allow full analyses of even complex organic natural products,[1,2] the majority of structure determinations by this new method have required the use of large numbers of model compounds. ^{13}C n.m.r. analysis by chemical-shift theory alone or, at worst, with the use of a minimum amount of models can be envisaged as becoming feasible for natural substances whose complexity of structure is so extreme as to optimize the environmental dissimilarity of their carbon centres. A representative example of such compounds is the alkaloid gelsemine (**1**).[3]



(1)

A noise-resonance-decoupled spectrum of gelsemine (**1**) (Figure) reveals signals for all of its twenty carbons. Application of chemical-shift theory[4] and single-frequency decoupling[1,2] differentiates the substitution pattern of the individual carbon sites and permits direct assignment of the chemical shifts of carbons 2, 7, 8, 13, 14, 18, and 20 and the *N*-methyl group (Table). The ^{13}C n.m.r. spectrum of 18,19-dihydrogelsemine (**2**) exhibits an upfield shift of one of the remaining saturated methylene groups and similar shifts of two upfield, saturated methines. Saturation of the vinyl group would be expected to affect neighbouring C-21, C-6, and C-15 much more strongly than C-17 and C-16. This argument leads to signal assignment of carbons 16, 17, and 21. The ^{13}C n.m.r. spectrum of 2-deoxo-2,2,18,19-tetrahydrogelsemine (**3**) shows downfield shifts of one downfield and one upfield signal of the remaining saturated methines with respect to their positions in the spectrum of 18,19-dihydrogelsemine (**2**). Removal of the oxindole carbonyl group would be expected to affect vicinal C-3 and C-6 to a much greater extent than C-5 and C-15. This conclusion and the above-noted difference of the methine signals of the spectra of gelsemine (**1**) and its dihydro-derivative (**2**) allow assignment of the chemical-shift values of all remaining saturated carbon centres. The absence of gelsemine's 53·9 p.p.m. signal in the ^{13}C n.m.r. spectrum of oxindole (**4**) reveals it to be associated with C-19 of the alkaloid. Finally, the chemical shifts of the unsubstituted aromatic carbons were assigned by analogy with those of aniline[5] and its derivatives.[6] The $o > p > m$ order (with respect to the nitrogenous substituent) of chemical shifts of these substances was maintained by gelsemine (**1**) as well as oxindole (**4**).

^{13}C *Chemical shifts*[a]

	C-2	C-3	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20	C-21	N-Me
(**1**)	13·1	123·1	120·5	151·9	138·2	60·7	64·7	71·0	64·7	83·5	51·9	169·4	154·2	156·6	131·0	80·4	53·9	138·2	126·5	141·9
(**2**)[b]		123·2	121·5	153·9	138·0							169·8[d]	155·3	156·6	131·0	183·0	171·0[d]	140·3	129·1	142·9
(**3**)	136·2	121·7	121·7	152·8	140·1	74·5	64·9	83·5	64·9	93·8	42·0	169·1[d]	155·9	156·2	130·9	182·6	170·3[d]	140·1	129·5	139·0
(**4**)[c]	13·9				156·2	67·2	68·1	70·4	64·7	82·7	49·8									

[a] The spectra were taken in chloroform solution and are recorded in p.p.m. from carbon disulphide [$\delta(CS_2) = \delta(CHCl_3) + 115{\cdot}2$].
[b] The chemical shifts of none of the trigonal carbons were determined.
[c] For ease of comparison the carbons of oxindole (**4**) are numbered identically with their counterparts in the oxindolyl moiety of gelsemine(**1**).
[d] These figures may be reversed.

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It is noteworthy that the oxymethylene and oxymethine functions normally expected downfield of aminomethylene and aminomethine groups, respectively,[4] show chemical shifts upfield instead. While the exact reason for this effect is still obscure, it probably is associated with the specific stereochemistry of the highly fused ring systems. Similar observations have been made in the field of tropane alkaloids.[6] Another unexpected result is the shift of the *N*-methyl carbon of gelsemine (**1**) on saturation of its vinyl or carbonyl groups. Finally, comparison of the spectra of gelsemine (**1**) and oxindole (**4**) reveals a striking downfield shift of the C-9 signal by the C-7 substituents and/or by the non-bonded interaction of C-9 with C-5 and C-17.

The above spectral determination constitutes the first ^{13}C n.m.r. analysis of an alkaloid.

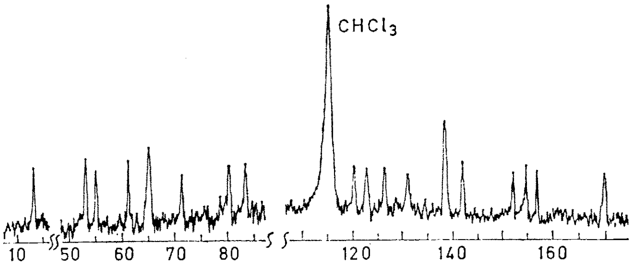

FIGURE. *Noise-resonance-decoupled natural-abundance* ^{13}C *n.m.r. spectrum of a* ca. 10 *mole* % *solution of gelsemine* (**1**) *in chloroform after* 120 *scans.*

(*Received, May* 29*th*, 1970; *Com.* 827.)

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