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^{13}C N.M.R. SPECTRUM OF NARCICLASINE TETRAACETATE

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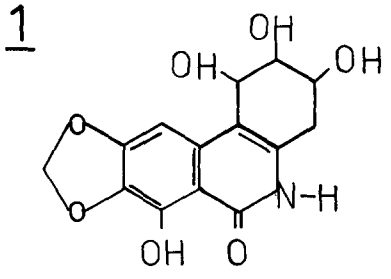
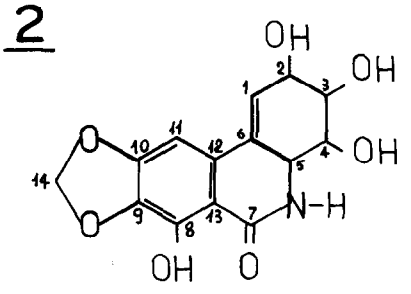
The antimitotic agent narciclasine [1] has recently received wide structural interest.

The formerly [2] proposed structural formula 1 has been revised to 2 mainly





on the basis of synthetic work [3 a,b,c,d] in the field of its aromatization products, and subsequently the p.m.r. spectrum has been reinterpreted accordingly [4]. Moreover, structure 2 has recently received biosynthetic confirmation [5]. We report here the ^{13}C n.m.r. spectrum of narciclasine tetraacetate in natural abundance as an example of the power of this spectroscopic technique in solving structural problems. In particular it will be shown how this method excludes directly the first proposed structure.

The spectrum has been recorded in proton noise decoupling conditions with a Bruker HFX-90 spectrometer. Both the continuous wave (stabilisation on C_6F_6; 1024 scans) and the pulse Fourier spectrum (stabilisation on $CDCl_3$; 4000 scans) have been recorded, the solvent was deuterochloroform, concentration: 100 mg/ml.

Incidently it is interesting to note that beside the enhanced resolution and sensitivity of the Fourier method one has to carefully consider changes in signal intensity with respect to those observed in the continuous wave accumulated spectrum. Therefore it is safer to regard the two spectra as complementary and check with one the results of the other. Besides the noise decoupled spectrum we have also recorded the off-resonance decoupled spectrum in order to observe peak multiplicities. Inspection of Fig. 1 shows that the 22 carbon atoms of the molecule give rise to 19 well resolved signals whose assignments, collected in Tab. 1, were obtained as described in the following discussion. For simplicity the entire spectrum can be divided in three regions, i.e. the carbonyl range at low-field, the saturated carbons range at high field and the unsaturated carbons range in the middle.

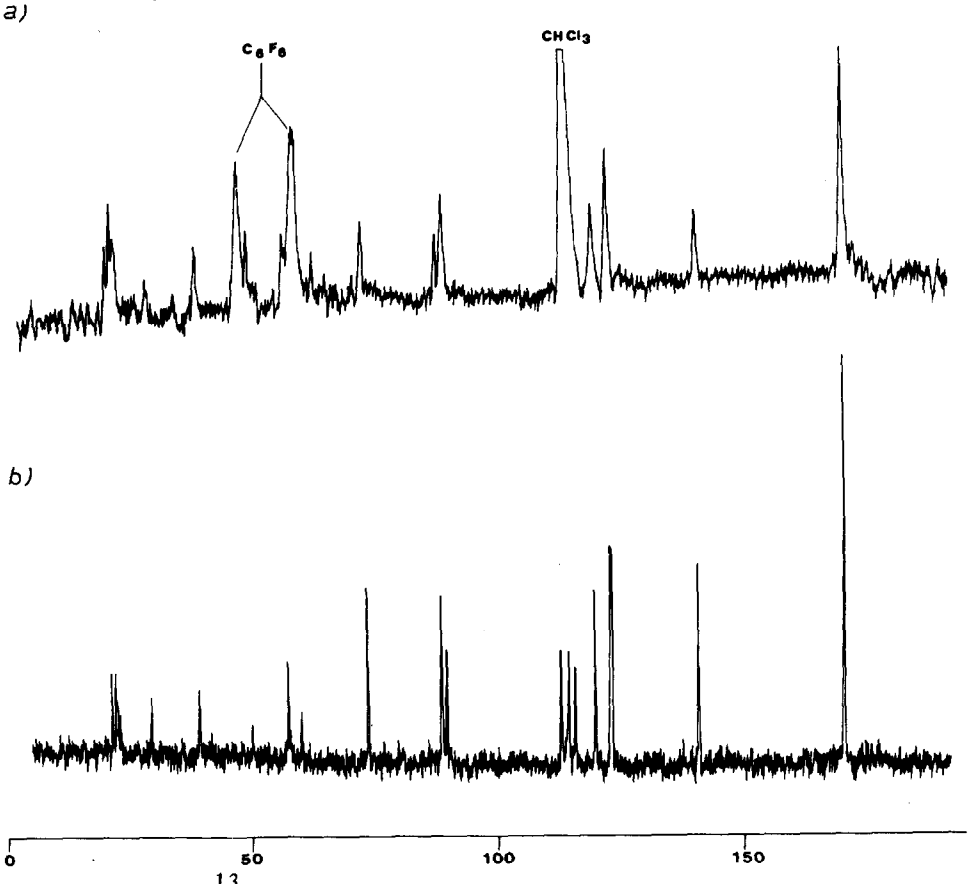


Fig. 1 Proton decoupled ^{13}C n.m.r. spectrum of narciclasine tetraacetate
a) continuous wave, b) Fourier transform.

TABLE 1

Chemical Shift*	Multiplicity	Assignment
20.6	S	O-CO
21.5	S	O-CO
21.7	S	O-CO
22.2	S	O-CO
28.7	S	N-CO
38.3	S	C_6
49.5	S	
56.7	S	C_8,C_9,C_{10},C_{12}
57.2	S	
59.3	S	
72.8	D	C_1
88.0	T	C_{14}
89.1	D	C_{11}
89.2	S	C_{13}
119.6	D	C_2
122.8	D	C_3,C_4
123.0	D	
140.7	D	C_5
170.3	Q	Me

* in ppm upfield from CS_2

The carbonyl absorption of the four acetyl groups occurs in the narrow interval between 20.6 and 22.2 ppm. The subtle structural differences of the acetyl groups account for the small separation still detectable in their carbonyl group resonances, although they are no more effective in differentiating methyl carbon absorptions. The peak at 28.7 ppm is attributed by elimination to the carbonyl of the amide group.

Turning the attention to the central part of the spectrum we note that in the undecoupled mode it is possible to count one triplet, two doublets and six singlets. The triplet centered at 88.0 ppm is without ambiguity due to the only

methylene group present in the molecule i.e. the OCH_2O, the assignment being checked by the characteristic shift observed in related compounds such as the amarillidacee alkaloids[6].

Of the two doublets that centered at 72.8 ppm can be attributed to C_1, because it is in the range of an olefinic CH- group of a trisubstituted double bond as that of the cyclohexene ring in alkaloids such as galantine licorenine and montanine[6]. The doublet at 89.1 ppm is consequently assigned to the aromatic methine C_{11}.

The olefinic carbon C_6 is distinguished from the aromatic carbons on the basis of its shift (38.8 ppm) which compares very well with that of a similar situation in the alkaloid montanine[6]. The chemical shift of the singlet at 89.2 ppm is in the range of an aromatic carbon linked to a carbonyl group as already observed in sterigmatocystine[7] and therefore is identified as due to C_{13}. The four peaks between 49.5 and 59.3 ppm are thus due to the remaining aromatic carbons C_8,C_9,C_{10} and C_{12} without any preferential detailed assignment.

Among the absorptions in the aliphatic region the strong signal at 170.3 ppm is easily recognized because of the multiplicity (quartet) and by its much greater intensity as due to the four methyl groups. The peak at 140.7 ppm, wich is a doublet in the undecoupled mode, is attributable to C_5 by virtue of its shift, which differs remarkably from that of the remaining doublets at 119.6, 122.8 and 123.0 ppm. These latter signals are in the typical region of the CH-O group for which an excellent source of data is available in the literature[8] and therefore it is safe to assign them to C_2,C_3 and C_4. Observing that C_2 is placed in a rather different environment one can tentatively assign it to the signal at 119.6 ppm.

The results of this work show that structure 1 of narciclasine does not agree with its ^{13}C spectrum, only one CH_2 triplet being observable, whereas structure 2 corresponds satisfactorily to the number of signals and their multiplicity.

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