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Short Communication

Rescinnamine and reserpine — a comparative study of their ^{13}C NMR spectra

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Abstract: A comparative analysis of the natural-abundance ^{13}C NMR spectra of the Rauwolfia alkaloids rescinnamine and reserpine is reported.

Keywords: *^{13}C NMR; reserpine and rescinnamine.*

Introduction

The indole alkaloids, reserpine and rescinnamine have long attracted interest on account of their pharmacological properties [1, 2]. They have been extensively studied and some properties explained on the basis of their structural characteristics [3]. In fact, their similar behaviour [4] seems to indicate that their structural properties are very similar. The reserpine structure has been corroborated by ^{13}C NMR [5]. However, the reported chemical shifts of C(3), C(5), C(21) and the 17-methoxy group of rescinnamine [6], probably due to the similarity of their values, have been interchanged and then incorrectly assigned [5]. For this reason, this study of the ^{13}C NMR spectra of rescinnamine has been undertaken not only for the correct chemical shift assignment, but also for corroborating by direct analysis of the assumed structural properties of this alkaloid.

Experimental

^{13}C NMR spectra were run at 50.2 MHz on a Varian XL-200 spectrometer using $CDCl_3$ as solvent. Solutions were prepared containing *ca* 100 mg of sample in approximately 2 ml of deuterochloroform. Chemical shifts are reported with respect to tetramethylsilane, using the ^{13}C resonance of the $CDCl_3$ (at 77.0 ppm) as an internal standard.

Rescinnamine was supplied by Boehringer and Sohn and was used as received. 3,4,5-Trimethoxy cinnamic acid was purchased from Sigma.

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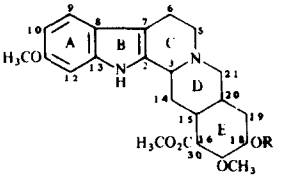
Table 1
^{13}C NMR chemical shifts (ppm) for I, II and reserpine (III)

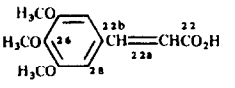
C	2	3	5	6	7	8	9	10	11	12	13	14	15	16
I	130.5	53.7	51.2	16.7	107.8	122.1	118.4	108.8	156.0	95.1	136.3	24.2	32.2	51.8
II														
III	130.2*	53.6*	51.1*	16.7*	107.7*	121.9*	118.2*	108.7*	155.8*	95.0*	136.1*	24.1*	32.2*	51.6*
C	17	18	19	20	21	22	22a	22b	23	24	25	26	33	34
I	77.7	77.7	29.6	33.9	48.9	172.6	117.3	145.1	129.7	105.2	153.4	140.1	56.1	60.9
II						172.5	116.4	146.9	129.4	105.4	153.3	140.3	56.0	60.9
III	77.7*	77.7*	29.6*	33.8*	48.9*	172.5*			124.9	106.7	152.5	141.9	56.0	60.6*

*From reference 5.

Results and Discussion

The signals were tentatively assigned by comparison with the reported ^{13}C NMR data for similar alkaloids [5, 7, 8]. However, as rescinnamine has a complex structure (I), the analysis was accomplished more easily after an initial chemical shift evaluation of a smaller molecule used as a model compound (II).





(II)

(I) R = 3.4.5 $(OCH_3)_3C_6H_2CH{=}CHCO{-}$
(III) R = 3.4.5 $(OCH_3)_3C_6H_2CO{-}$

Due to the gross dissimilarity of the carbon sites within the molecules, the assignments were made with the aid of the chemical shift theory and the Attached Proton Tests (APT) techniques. The chemical shift theory has been used to tentatively assign the carbon chemical shifts of the model compound (II). For a substituent such as methoxy,

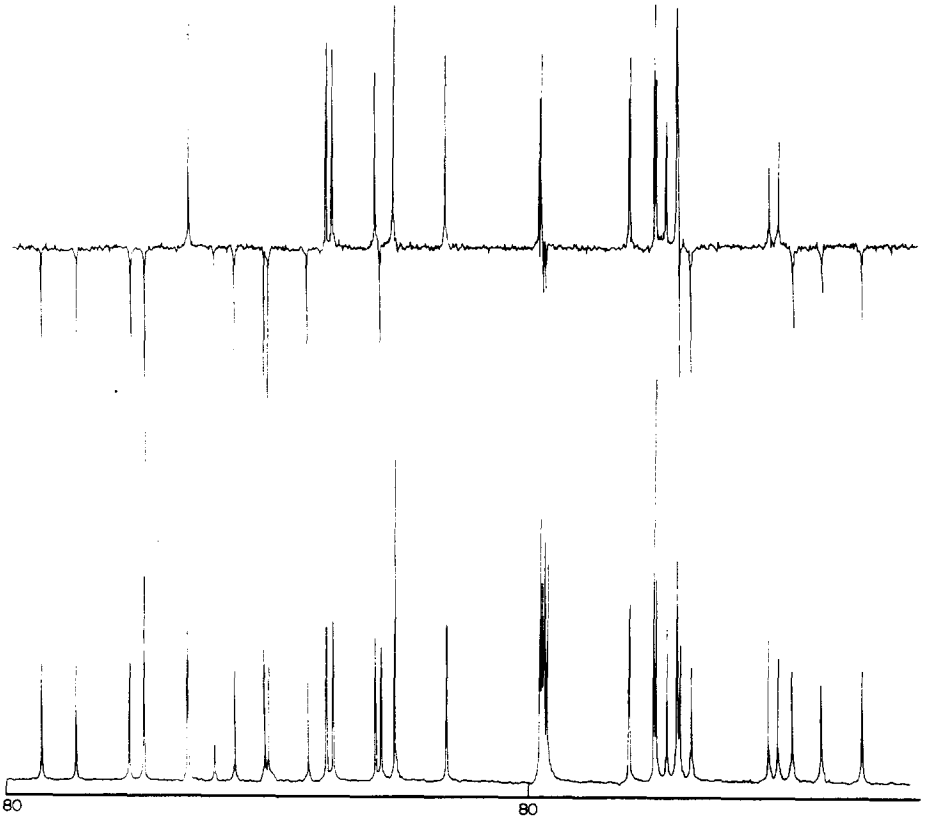


Figure 1
APT and ^{13}C [^{1}H] spectra for rescinnamine.

$-OCH_3$, the ortho and para positions are shielded and the carbon of attachment deshielded, while the meta position does not vary much from benzene [9] (Table 1). On the other hand, the APT technique has been utilized to differentiate [10, 11] the resonances due to the methyl, methylene, methyne or quaternary carbon atoms in the ^{13}C [^1H] spectrum. Applying the standard pulse sequence for an APT experiment, the components of ^{13}C magnetization for a CH group will give a full negative signal while those of a CH_2 group will produce a full positive signal. Methyl signals behave rather like those for CH groups, and quaternary carbons in a similar fashion to CH_2 groups. The result is a clear distinction between CH_3 or CH on one hand and CH_2 or quaternary carbons on the other. Figures 1 and 2 show APT and ^{13}C [^1H] NMR spectra for compounds I and II, respectively.

The use of APT techniques, the carbon shift values for compound II and the data reported in the literature, [5, 7, 8] allowed the interpretation of the alkaloid spectra. The ^{13}C NMR chemical shift values are collected in Table 1.

It is worth at this point to relate chemical shift values with structural characteristics. Reserpine and rescinnamine derive from the 6-methoxy indole nucleus and possess cis fused D and E rings. Also, the hydrogen atom at position 3 lies above the ring plane in the β-equatorial configuration [3].

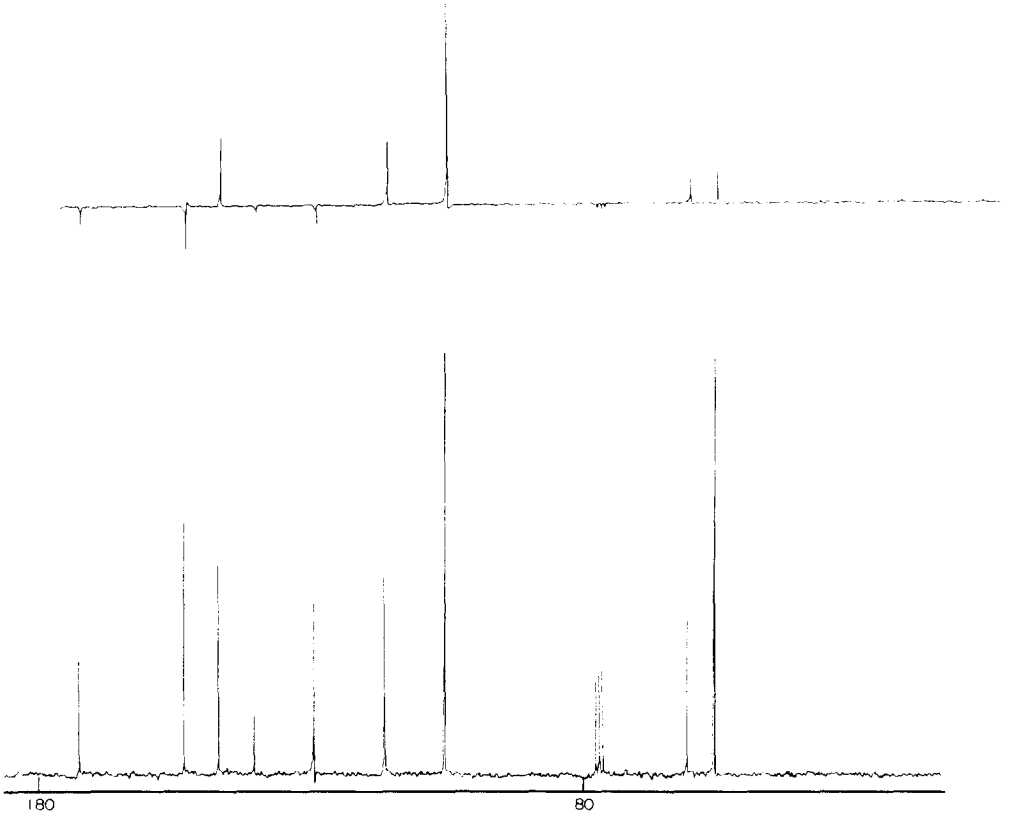


Figure 2
APT and ^{13}C [^1H] spectra for trimethoxy cinnamic acid.

This structure can be corroborated by ^{13}C NMR data. On the basis of the different chemical shift values of the C(3) atom, the possible epimers (α, β) can be distinguished. In fact, if the proton on C(3) is α-axial a value of 60.1 for the chemical shift of the C(3) atom is obtained while if it is β-equatorial this value diminishes to 53.7 [12]. The value of 53.7 observed for this alkaloid indicates that the proton on C(3) is β-equatorial.

On the other hand, the actual conformation state (cis or trans C/D and D/E ring junction) can be inferred from the chemical shift values of the C, D and E ring carbon atoms. A direct comparison with the values of the chemical shifts of some isomers of yohimbine [12] allows the rescinnamine conformation to be established. For example, in the case of cis C/D and D/E ring junction, δC(5) = 50.8, δC(15) = 32.5 and δC(21) = 49.4 ppm while for trans C/D and cis D/E the chemical shifts for the same carbon atom are 53.2, 37.9 and 60.4, respectively. The chemical shift data in Table 1 indicate that rescinnamine as reserpine possess cis C/D and D/E ring junctions.

As it can be concluded, the structural interpretation of the ^{13}C NMR spectra of this alkaloid is in excellent agreement with the established structural properties [3].

Finally, from a survey of Table 1 it is seen that the chemical shifts of the reserpine [5] and rescinnamine carbon atom are the same within the errors limits. The only difference between these alkaloid spectra is the existence of two extra signals [C(22a) and C(22b)] in the case of the rescinnamine spectra. In particular, the signal at 145.1 ppm, C(22b), which is grossly dissimilar to the carbon sites of reserpine, and could be useful to identify the presence of rescinnamine in mixtures of reserpine derivatives.

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