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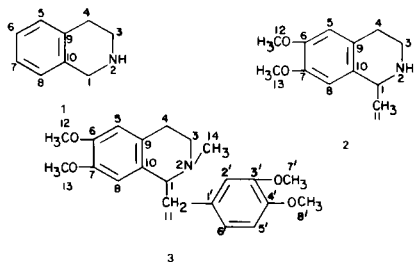
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The ^{13}C nmr chemical shifts of 1,2,3,4-tetrahydroisoquinoline, salsolidine and laudanose are reported. The various carbon resonances have been assigned on the basis of chemical shift theory, intensity of the signals, multiplicities generated in SFORD spectra and the comparison with model compounds.

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Numerous reports in the literature have provided ^{13}C nmr spectra of various classes of alkaloids (1-9). Surprisingly assignments of the chemical shifts of the carbon resonances of an important group, isoquinoline alkaloids have not been reported although their structure and stereochemistry have been well characterized (10). In the present study the assignments of various carbon resonances of 1,2,3,4-tetrahydroisoquinoline (**1**), salsolidine (**2**) and laudanose (**3**) in their ^{13}C nmr spectra are reported. The ^{13}C nmr spectra of isoquinoline alkaloids are theoretically important and could prove useful in the assignment of the structure of other unknown alkaloids of this group.

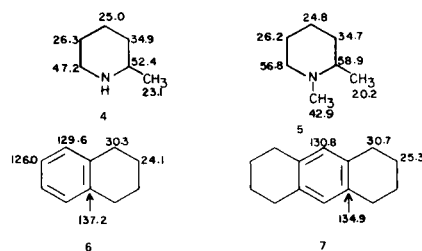
The natural abundance ^{13}C nmr spectra of **1**, **2** and **3** were obtained in deuteriochloroform as an internal lock and solvent and tetramethylsilane as a reference. A proton-noise decoupled and single-frequency off-resonance decoupled (SFORD) spectra of **1**, **2** and **3** were recorded on JEOL FX-60 spectrometer. The proton-noise decoupled spectra gave the chemical shifts of various carbon resonances while the SFORD spectra differentiated the methyl, methylene, methine and quaternary carbons present in these compounds. The assignments of the signals in the ^{13}C nmr spectra of **1-3** were made on the basis of the chemical shift theory, multiplicity obtained from SFORD spectra and comparison with the chemical shifts of the structurally related compounds.



1,2,3,4-Tetrahydroisoquinoline (**1**).

The chemical shift of various carbon resonances of **1** obtained from its ^{13}C nmr spectrum (Figure 1) are recorded in Table I. The five signals in the lowerfield region and three signals in the higher field region accounted for all the nine carbon resonances of **1**. The SFORD spectrum of **1** showed two singlets, three doublets and three triplets. Retcofsky and Friedel (11) while studying

several sets of hydrocarbons, in which one or two benzene rings were fused with one or more cyclohexyl rings, observed that the combined effect of the benzene ring was more or less independent of the skeleton involved. Since a benzene ring is fused with a piperidine ring in **1**, the carbons of benzene ring will experience the effect of nitrogen atom of the fused piperidine ring. The singlets at 135.0 ppm and 133.7 ppm are thus assigned to C-10 and C-9 based on the 3 and 4 carbon signals of **4** (12) and **5** (3), respectively, which, however, could be interchanged. The doublet centered at 128.1 ppm is attributed to the carbon resonances of C-5 and C-8 by comparing the chemical shift of corresponding carbons of **6** and **7** (11).



The remaining signals in the lowerfield region at 124.7 ppm and 124.4 ppm are represented by the resonances of C-6 and C-7, respectively, which, also could be interchanged. These are comparable with the assignments of **6** and **7** (11).

The nitrogen atom in an aliphatic chain produces about 20 ppm and 2 ppm downfield shift to its α and β carbons, respectively (12). Grant and Paul (13) reported that α and β carbons in paraffins cause about 9 ppm downfield shift, and this phenomenon is also useful to some extent for alicyclic compounds. In **1**, C-1 and C-3 are α to nitrogen while C-4 is at the β position to nitrogen. Therefore, C-1 and C-3 will be observed at lowerfield in comparison to C-4 in the ^{13}C nmr spectrum. On the basis of these observations, the triplet centered at 28.0 ppm is assigned to C-4. The distinction between C-1 and C-3 can be made easily since C-3 has one α carbon which causes about 9 ppm downfield shift (13). Thus the triplets centered at 47.3 ppm and 42.8 ppm are assigned to C-3 and C-1, respectively.

Salsolidine (**2**).

The natural abundance carbon-13 signals in the ^{13}C

nmr spectrum of **2** are illustrated in Figure 2. The chemical shift and the nature of multiplicity of these signals are recorded in Table II. As is evident from Figure 2, there are eleven separate signals for the twelve carbons of **2**. The SFORD spectrum of **2** revealed four singlets and two doublets in the lowerfield and one doublet, two triplet and two quartet in the higher field region. A methoxy group attached to the benzene ring has been

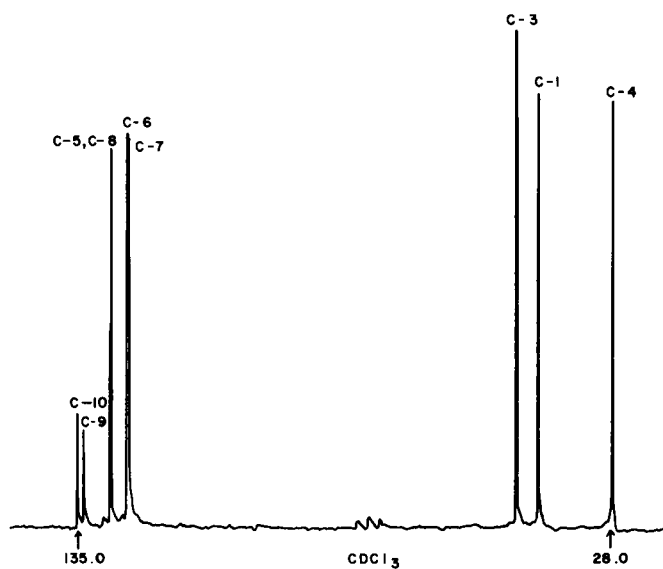


Figure 1. The proton noise decoupled ^{13}C nmr spectrum of 1,2,3,4-tetrahydroisoquinoline.

shown to cause 31.4 ppm and 1.0 ppm downfield shift at *ipso* and *meta* carbons, respectively, while *ortho* and *para* carbons were reported to experience a shielding ef-

fect of 14.4 ppm and 7.7 ppm, respectively (12). The C-8 could possibly interact sterically with the methyl group present at position 1 of **2**. On the basis of these observations, the doublet centered at 111.1 ppm and 108.5 ppm are assigned to C-5 and C-8, respectively. The four singlets are, therefore, due to the carbon resonances of C-6, C-7, C-9 and C-10. The signals at 148.4 ppm and 148.0 ppm are due to the carbon resonances of C-6 and C-7 since C-6 and C-7 are directly attached to a methoxy group and are at *ortho* position to a methoxy group and this assignment, however, may be interchanged. The singlets at 124.8 ppm and 123.0 ppm are attributed to C-10 and C-9, respectively, by comparison to the *meta* and *para* effect of methoxy groups at C-9 and C-10 and the assignments of **1**, and these assignments may be interchanged.

The carbon resonances of both C-12 and C-13 are represented by the signal observed at 55.6 ppm in the ^{13}C nmr spectrum of **2**. The other quartet centered at 19.7 ppm is assigned to C-11. These assignments were made on the basis of chemical shift theory and are comparable with the assignments of **4** (12) and **8** (14). The carbon resonance of C-1 is represented at 50.2 ppm chemical shift due to its multiplicity in SFORD spectrum of **2** and further supported by chemical shift of the corresponding carbon of **4** (12). The C-4 is at β position and C-3 is at α position to the nitrogen atom which is known to produce more downfield shift at α position as compared to β position (12). Therefore, the triplets centered at 38.4 ppm and 24.8 ppm are assigned to C-3 and C-4, respectively.

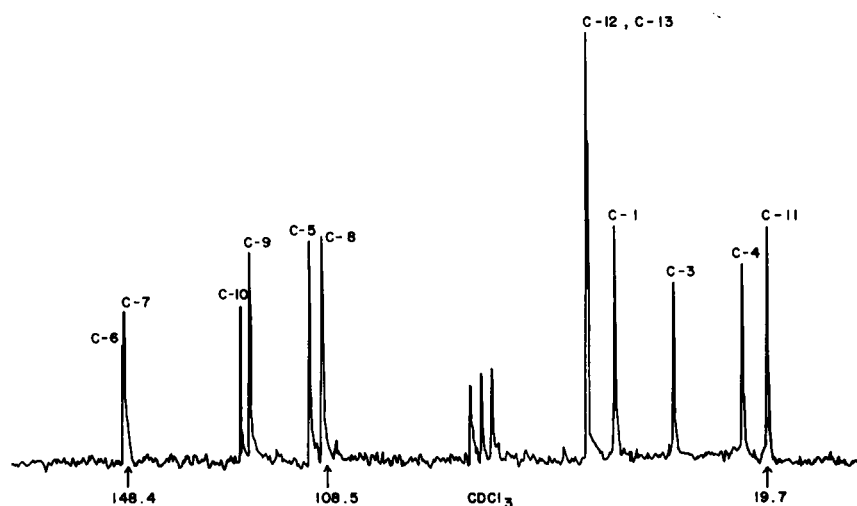
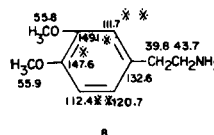


Figure 2. The proton noise decoupled ^{13}C nmr spectrum of salsolidine.

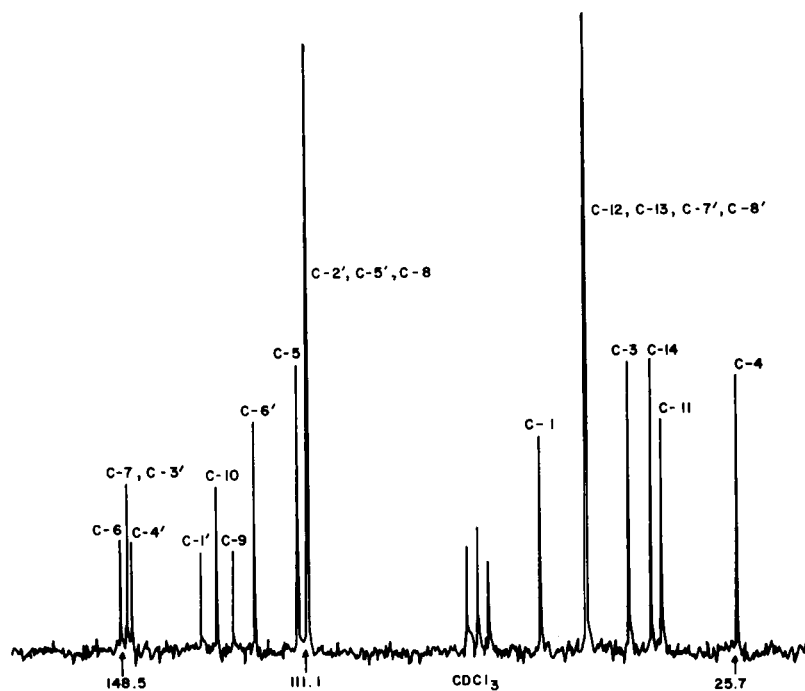


Figure 3. The proton noise decoupled ^{13}C nmr spectrum of laudanosine.

Laudanosine (3).

The ^{13}C nmr spectrum of **3** is illustrated in Figure 3 and the chemical shift of carbon resonances are recorded in Table III. The assignments of its aromatic carbon resonances are complicated, yet efforts have been made to assign all the carbon resonances on the basis of chemical shift theory, multiplicity generated in SFORD spectrum, intensity of the signals and comparison with the chemical shift of the model compounds. There are six singlets and three doublets in the lowerfield region of the SFORD spectrum of **3** which accounted all the twelve

aromatic carbon signals. The C-6, C-7, C-3' and C-4' are directly bonded with a methoxy group and are at an *ortho* position to a methoxy group. The methoxy group attached to a benzene ring is known to cause 31.4 ppm downfield shift to its *ipso* carbon and 14.4 ppm upfield shift to its *ortho* carbon (12). On this basis and comparing the chemical shift of **2** and **8** (14), the singlets at 148.5, 147.2 and 146.3 ppm are assigned to C-6, C-7, C-3' and C-4', which, however, could be interchanged. A methyl group attached to benzene nucleus has been reported to produce 8.9 ppm downfield shift to its *ipso* carbon (12). Since C-1' is bonded to a methylene group and is at

Table I

^{13}C Nmr Spectral Data of Tetrahydroisoquinoline (a)

Assignment (b)	Multiplicity (a)	Chemical Shift
*C-10	s	135.0
*C-9	s	133.7
C-5, C-8	d	128.1
**C-6	d	124.7
**C-7	d	124.4
C-3	t	47.3
C-1	t	42.8
C-4	t	28.0

(a) The chemical shifts are expressed in ppm with respect to tetramethylsilane. (b) Numbering of carbons are shown in structure **1**. (c) Multiplicity obtained from SFORD spectrum; s = singlet, d = doublet, t = triplet and q = quartet; * and ** may be interchanged.

Table II

^{13}C Nmr Spectral Data of Salsolidine (a)

Assignment (b)	Multiplicity (c)	Chemical Shift
*C-6	s	148.4
*C-7	s	148.0
**C-10	s	124.8
**C-9	s	123.0
C-5	d	111.1
C-8	d	108.5
C-12, C-13	q	55.6
C-1	d	50.2
C-3	t	38.4
C-4	t	24.8
C-11	q	19.7

(a,c) See footnote in Table I. (b) Numbering of carbons are shown in structure **2**; * and ** may be interchanged.

Table III

¹³C Nmr Spectral Data of Laudanosine (a)

Assignment (b)	Multiplicity (c)	Chemical Shift
*C-6	s	148.5
*C-7, C-3'	s	147.2
*C-4'	s	146.3
C-1'	s	132.5
**C-10	s	129.5
**C-9	s	126.0
C-6'	d	121.8
***C-5	d	113.1
***C-2', C-5', C-8	d	111.1
C-1	d	64.9
C-12, C-13, C-7', C-8'	q	55.7
C-3	t	47.1
C-14	q	42.7
C-11	t	40.7
C-4	t	25.7

(a,c) See footnote in Table I. (b) Numbering of carbons are shown in structure **3**; *, ** and *** may be interchanged.

meta and *para* positions to the methoxy groups which exhibits 1.0 ppm downfield shift and 7.7 ppm upfield shift to its *meta* and *para* carbons, respectively (12), the singlet at 132.5 ppm is best assigned to C-1'. This assignment is further supported by the chemical shift of the corresponding carbon of **8** (14). The remaining two singlets at 126.0 ppm and 129.3 ppm are attributed to C-9 and C-10, respectively, and these assignments may be interchanged. The C-5, C-8, C-2' and C-5' are at *ortho* and *meta* to the methoxy groups, while C-6' is *meta* and *para* to the methoxy groups. Furthermore, a methyl group has been shown to have no significant influence at its *ortho* and *meta* position in the benzene nucleus (12). Therefore, the signal due to C-6' must be observed at lower field as compared to C-5, C-8, C-2' and C-5'. Thus the doublet centered at 121.8 ppm is represented to C-6' and comparable with the assignments of **8** (14). The signal intensity observed in the proton-noise decoupled spectrum of **3** has revealed that C-5, C-8 and C-2' are represented at 111.1 ppm and C-5' at 113.1 ppm and these assignments, however, may be interchanged.

In the higher field region, the quartet centered at 55.7 ppm is assigned to C-12, C-13, C-7' and C-8' on the basis of chemical shift theory and comparison with the chemical shift of **2** and **8** (14). The other quartet centered at 42.7 ppm is represented to C-14 and is in agreement with the chemical shift of **5** (3). The signal at 64.9 ppm is attributed to C-1 on the basis of multiplicity and comparison with the chemical shift of **5** (3). The three triplets are due to C-3, C-4 and C-11. By comparing the chemical shift of **2**, **4**, **5** and **8** the triplets centered at 47.1, 40.7

and 25.7 ppm are assigned to C-3, C-11 and C-4, respectively.

EXPERIMENTAL

The ¹³C nmr spectra of **1**, **2** and **3** were obtained on a JEOL FX-60 spectrometer operating at 15.00 MHz. The samples were run in 10 mm tubes using deuteriochloroform (30% w/v) as an internal lock and solvent and tetramethylsilane as reference. The spectra were recorded under following conditions: spectral width, 4000 Hz, pulse width 18 μ sec (90°), repetition rate 5.0 sec, data points 4k.

All three compounds, 1,2,3,4-tetrahydroisoquinoline **1**, salsolidine hydrochloride dihydrate **2** and laudanosine **3** were purchased from Aldrich Chemical Co., Milwaukee, Wisconsin.

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