DIFFERENCE IN THE SIGNALS OF THE N—H PROTON IN THE NMR SPECTRA OF THE INDOLE, INDOLINE, AND HYDROXYINDOLE ALKALOIDS

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It is known that the position, the chemical shift (CS), of the signal of the NH proton in NMR spectra, like that of the OH proton, is governed by the nature of the hydrogen bond and depends on the concentration and the temperature.

The presence of a hydrogen bond always shifts a proton signal in the weak-field direction, and a rise in the temperature has the opposite effect [1]. When the temperature and concentration are constant, the CS of the N—H proton can be used to estimate the degree to which inter- and intramolecular hydrogen bonds exist in various alkaloids.

In this paper we give the results of the measurements of the CS of the signal of the N—H proton in the NMR spectra of the Vinca alkaloids [2] (table).

CS of the Signals of the N—H Protons in Various Vinca Alkaloids in $CDCl_3$

Alkaloids	τ ppm	Alkaloids	τ ppm
Vincanine (I)	−0.69	Picrinine (XII)	6.50
2,16, 19, 20-Tetrahydrovincanine (II)	6.50	Vincaricine (XIII)	6.50
Vinervinine (III)	1.17	Reserpinine (XIV)	2.10
Akuammicine (IV)	1.05	Ervine (XV)	2.15
2,16-Dihydroakuammicine (V)	6.00	O-Acetyltombosine (XVI)	1.75
Ervamine (VI)	1.16	O-Acetylininhimbine (XVII)	2.03
Ervinidinine (VII)	1.09	Vinerine (XVIII)	1.05
Dihydroervinidinine (VIII)	5.65	Vineridine (XIX)	0.56
Ervincinine (IX)	1.10	Majdine (XX)	2.18
Copsinine (X)	6.50	Isomajdine (XXI)	1.51
Pseudocopsinine (XI)	5.68	Carapanaubine (XXII)	0.80

All the spectra were obtained on a JNM-4H-100/100 MHz instrument at room temperature (22–24° C) using concentrations of 5–10% in $CDCl_3$ solution with HMDS as internal standard.

The assignment of the signals to the N—H protons was made on the basis of a comparison of the spectra taken at room temperature and at a higher temperature of the sample, and also on the basis of the method of deuterium-exchange with CD_3OD and D_2O.

In view of the fact that the spectra of all the substances were taken at strictly identical concentrations, we checked the concentration dependence of the CS of the NH group in the case of reserpinine (XIV).

When the solution was diluted more than three times (from 15 to 5%) the signal of the NH group in XIV shifted in the stronger-field direction by only 0.15–0.20 ppm. Consequently it may be considered that a change in the concentration of between 5 and 10% has an insignificant effect on the CS of the NH proton.

The figures in the table show that the CS of the signal of the N—H proton in the α-methyleneindoline alkaloids (I, III, IV, VI, VII, and IX) and in the indole alkaloids (XIV–XVII) differ considerably. As a rule, the CS of the NH in the α-methyleneindoline alkaloids appears in a weaker field (−0.69 to −1.20 ppm) than in the indole alkaloids (1.72–2.15 ppm), and the CS of the NH group in the hydroxyindole alkaloids (XVIII–XXII) occupies an intermediate position (0.56–2.18 ppm).

The most characteristic fact is that in the 2,16-dihydro derivatives of the α-methyleneindoline alkaloids (I, IV, VII), as in the alkaloids X–XIII, the signal of the NH proton is shifted markedly in the strong-field direction to τ =

= 5.50–6.50 ppm. Thus, for example, in akuammicine (IV), τ = 1.05 ppm, and in its dihydro derivative (V) τ_{NH} = 6.00 ppm. A similar pattern is observed in the case of ervamine (VI), vincanine (I), ervinidinine (VIII), etc., and also for the alkaloids copsinine (XI), etc.

This important criterion can be used successfully for the recognition and identification of new alkaloids of Vinca and for structural purposes.

Earlier, one of the authors [3] showed that the integral intensities (A) of the N—H bands in the IR spectra of the α-methyleneindoline alkaloids and their 2,16-dihydro derivatives differed substantially (almost threefold). The assumption was also made that a N—H...O=C—H chelate bond was formed in vincanine (I). Such a marked weak-field shift of the NH signal in the NMR spectrum to −0.69 ppm and its independence of the temperature and dilution apparently confirm the conclusion that a chelate bond exists in a vincanine.

Since the main contribution to the shift from the hydrogen bond in the NMR spectra is made by the polarization of the X—H bond [4], it is obvious that the shift in the signal of the NH proton in the strong-field direction and the decrease in the intensity of the IR bands in these alkaloids can be explained by a decrease in the polarity of the N—H bond. Consequently the changes in the parameters in the NMR spectra (τ, NH) and the IR spectra (A and ν_{N-H} are due mainly to the change in the polarity of the N—H bonds, although there is no strict correlation between τ, ν_{NH}, and A.

CONCLUSIONS

On the basis of the results of measurements of the chemical shifts of the signal of the NH proton in Vinca alkaloids, it has been established that the CS of the NH group in the α-methyleneindoline alkaloids and their 2,16-dihydro derivatives differ substantially.

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