INTEGRAL INTENSITIES OF THE IR BANDS OF THE STRETCHING VIBRATIONS OF THE NH, C=O, AND C=C GROUPS IN THE *VINCA* ALKALOIDS

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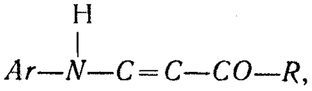
Yunusov and Yuldashev and their co-workers have isolated a series of alkaloids from plants of the genus *Vinca* [1-10].

We have previously studied the frequencies in the IR spectra of vincanine and its derivatives [11]. With the object of a more detailed investigation of the structure of the alkaloids, we have measured the integral intensities of their IR bands for the stretching vibrations of the NH, C=O, and C=C groups.

Integral intensities of the IR bands of the stretching vibrations of the NH groups. The alkaloids vincanine, vinervine akuammicine, and ervamine contain the grouping



$Ar{-}\overset{H}{\overset{|}{N}}{-}C{=}C{-}CO{-}R$,

which can evidently form so-called chelate hydrogen bonds in these alkaloids [12].

The NH stretching vibrations in such systems with π-electrons are displaced towards the low-frequency region of the spectrum by only 50-200 cm^{-1}, while chelation with the participation of O-H and other acceptor groups leads to considerable displacement of ν_{max} OH to 1000 cm^{-1} [12].

It can be seen from the table that the frequencies and integral intensities of the bands of the NH stretching vibrations differ substantially in the indole and the indoline alkaloids. The maximum absorption of the NH band in indole (I)* is 3490 cm^{-1}, with an intensity of 1.75×10^4 units. The intensity of the NH band in norharman (II) is somewhat higher than in indole because of the condensation of the heterocyclic pyridine nucleus with the indole. At the same time, in harman (III) the intensity of the band studied decreases, which is apparently due to the influence of the electron-donating substituent CH_3. The frequency of the NH bands in indole, harman, and norharman is fairly high (3480-3490 cm^{-1}) and corresponds to the stretching vibrations of a NH group not bound by a hydrogen bond.

Reserpinine (XVII) absorbs at ν_{max} = 3475 cm^{-1}, A = $1.6_0 \times 10^4$ units, and O-acetyltombozine (XIV) has ν_{max} = = 3475 cm^{-1}, A = $1.9_3 \times 10^4$ units.

The high values of the intensities of the NH bands in indole and the indole alkaloids are due to the influence of conjugation on the nitrogen atom of the heterocycle with the nucleus, which leads to the appearance of an induced dipole moment of the NH bond along its coordinate, i.e., $\frac{\partial \mu_{NH}}{\partial q_{NH}}$, rises, and, in its turn, this leads to an increase in the integral intensity of the NH bond.

In the indoline alkaloids [vincanine (IV), dihydrovincanine (V), akuammicine (X), dihydroakuammicine (XII), and the O-methyl ether of vinervine (XI)] the frequency of the NH stretching vibrations is low in comparison with that of the indole alkaloids. This decrease in ν_{max} NH is evidently connected with the formation of various types of hydrogen bonds. To gain an idea of the types of hydrogen bonds from the NH frequencies is difficult, since all the indoline alkaloids (IV), (V), (VIII)-(XII) absorb in a narrow range of frequencies from 3410 to 3325 cm^{-1}.

It can be seen from the structure of vincanine (IV), dihydrovincanine (V), akuammicine (X), the O-methyl ether of vinervine (XI), and ervamine (XV) that in these compounds the formation of a chelate bond between the C=O and NH groups is possible. The presence of such a bond should naturally cause an increase in the integral intensity of the NH band as compared with those compounds in which the chelate bond is excluded. In actual fact, the values of the integral intensities of the bands of the NH stretching vibrations in akuammicine (X) and vinervine O-methyl ether (XI) are almost three times higher than the intensity of the dihydro derivatives (XII) and (XIII) corresponding to them. Thus, for example, the intensity of the NH band in akuammicine (X) is 1.75×10^4 units, while for dihydroakuammicine (XII), where chelation is impossible because of the absence of a double bond, it is 0.60×10^4 units, although the change in their frequencies at the maximum of the NH absorption is only 16 cm^{-1}.

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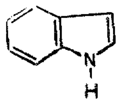
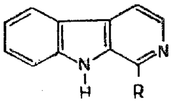
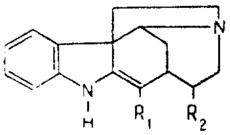
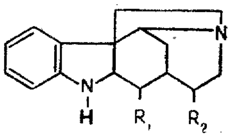
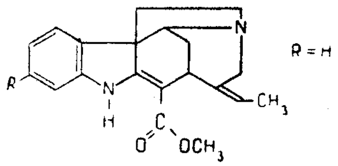
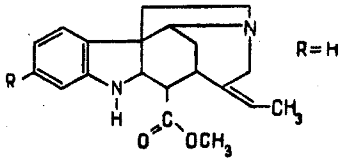
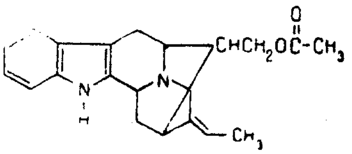
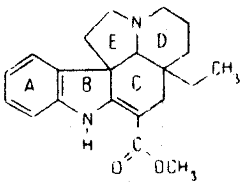
* Here and below, the numbering of the substances is as given in the table.

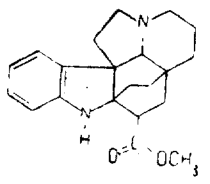
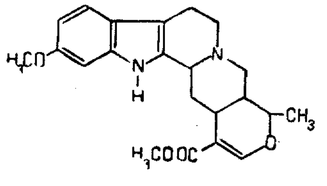
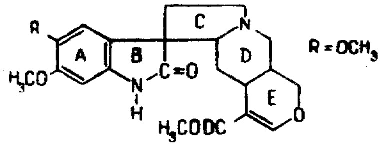
Frequencies and Integral Intensities of the Bands of the Stretching Vibrations of the NH, C=O, and C=C Bonds in $CHCl_3$

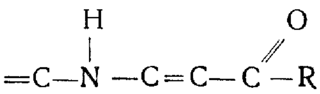
No.	Substance	ν_{max}, cm^{-1}	$A \cdot 10^{-4}$, $cm^{-2} l \cdot m^{-1}$
I		3490 1623 1588	1.7_5 0.24
II	 R = H	3473 1629 1568 1500	1.9_3 0.80 0.25 0.45
III	$R = CH_3$	3480 1630 1577 1503	1.2_0 1.0_0 0.45 0.60
IV	 $R_1 = CHO$ $R_2 = {=}CH-CH_3$	3340 1667 1615 1552	1.3_6 2.30 1.3_6 7.5_0
V	$R_1 = CHO$ $R_2 = CH_2-CH_3$	3325 1640 1609 1551	1.4_0 2.0_0 1.1_0 6.5_0
VI	$R_1 = C \equiv N$ $R_2 = {=}CH-CH_3$	3418 3300 1643 1615	1.0_0 2.0_0 3.2_0 2.2_0
VII	 $R_1 = CH_2OH$ $R_2 = {=}CH-CH_3$	1662 1603	1.2_5

[Table continued from previous page]

No.	Substance	ν_{max}, cm^{-1}	$A \cdot 10^{-4}$, $cm^{-2}\,l \cdot m^{-1}$
VIII	$R_1 = CH_3$ $R_2 = = CH - CH_3$	3410	0.50
		1610	0.80
IX	$R_1 = CH_3$ $R_2 = CH_2 - CH_3$	3410	0.50
		1610	0.75
X		3382	1.7_5
		1667	9.0_0
		1603	6.0_0
XI	$R = OCH_3$	3398	0.60
		1730	3.0_0
		1608	0.90
XII		3390	1.7_5
		1667	9.0_0
		1600	6.0_0
		1495	1.2_0
XIII	$R = OCH_3$	3390	
		1734	0.6_0
		1619	3.2_0
		1595	1.1_0
XIV		3475	1.9_3
		1730	4.6_0
XV		3380	1.4_0
		1673	6.2_0
		1610	4.5_0

[Table concluded]

No.	Substance	ν_{max}, cm^{-1}	$A \cdot 10^{-4}$, cm^{-2} $l \cdot m^{-1}$
XVI		3380 1726 1608	0.7_0 3.5_0 1.3_0
XVII		3475 1695 1630 1503	1.6_0 4.3_0 3.5_0 0.60
XVIII		3345 1725 1628 1507	1.3_6 9.8_0 6.0_0 1.2_5
XIX	R = H	3382 1722 1630 1508	1.3_0 9.8_0 6.2_0 1.4_5
XX	R = H	3442 3180 1710 1628 1605 1508	1.0_0 3.5_0 10.0 6.8_0 1.4_0
XXI	R = H	3440 3180 1710 1690 1630 1504	2.0_0 3.5_0 10.5 6.5_0 1.3_0



In the compounds of the vincanine type and those related to it containing the grouping $=C-\overset{H}{\overset{|}{N}}-C=C-\overset{O}{\overset{/\!/}{C}}-R$ with π-electrons, the appearance of a quasi-aromatic six-membered ring with a hydrogen bond is assumed [13, 14].

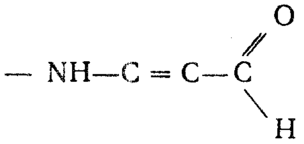
In the hydroxyindole alkaloids (XVII)-(XXI), the frequencies and integral intensities of the bands of the NH stretching vibrations are close to those of the indoline alkaloids with a chelate bond. Thus, the spectral characteristics of maidine (XVIII) practically coincide with the characteristics of vincanine (IV). The increase in the value of the integral intensities of the NH bands in the hydroxyindole alkaloids as compared with dihydroindoline alkaloids can be explained, on the one hand, by an increase in the polarity of the NH bond as a result of the attraction of the unshared pair of electrons of the nitrogen atom of the amino group to the oxygen atom of the carbonyl group and, on the other hand, by the possibility of the formation of intermolecular hydrogen bonds.

In the IR spectrum of the hydroxyindole alkaloid vineridine (XX) and its synthetic analog hydroxyindolereserpinine (XXI), two bands with maxima at 3180 and 3440 (3442) cm^{-1} appear in the 3100–3500 cm^{-1} region. The first of the bands in the compound mentioned is extremely broad (diffuse). This gives grounds for assuming that it arises from intermolecular hydrogen bonds. In actual fact, in the IR spectra of these two compounds in highly dilute solutions and with correspondingly thick absorption layers, the broad band with a maximum at 3180 cm^{-1} disappears completely, and only a high-frequency NH band at 3440 cm^{-1} remains. The latter evidently relates to the free vibrations of the NH bond.

When vineridine (XX) is acetylated and re-formed, it is transformed from a less labile form into one which is more stable and is identical with vinerine (XIX) [9]. The spectroscopic results indicate that vinerine (XIX) has one NH band with a maximum at 3382 cm^{-1} ($A = 1.30 \times 10^4$ units). However, in the spectrum of vineridine (XX), as has been mentioned, in addition to a high-frequency band (3442 cm^{-1}), a broad band (3180 cm^{-1}) appears which is due to intermolecular hydrogen bonds. On the basis of chemical results, this difference in the IR spectrum in the region mentioned can be explained by the assumption that vinerine and vineridine differ by the conformation of the C and D rings (see table, substance XVIII).

Integral intensities of the IR bands of the stretching vibrations of the C=O and C=C bonds. In the alkaloids, a series of bands, whose assignment causes difficulties, appears in the 1500–1700 cm^{-1} region (see table). These difficulties are evidently connected with the fact that the structure of the molecules of these alkaloids is extremely complex and contains a grouping consisting of C=C bonds of an aromatic and an aliphatic nature, C=O, and NH, while various types of H bonds can also be formed.

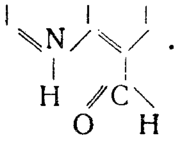
In the compounds indole (I), norharman (II), and harman (III), from two to three bands appear in the 1500–1700 cm^{-1} region through the vibrations of the aromatic and heteroaromatic rings. The intensity of these bands is low. In vincanine (IV) three bands appear in the region under investigation. We previously assigned the high-frequency band with a maximum at 1667 cm^{-1} to the stretching vibrations of the C=C of an ethylidene group [11]. However, the intensity of this band is fairly high (2.30×10^4 units), while the intensity of the band with a maximum at 1615 cm^{-1} is $1.3_6 \times 10^4$ units, i.e., approximately equal to the intensity of the high-frequency band in harman (III). This band with a maximum at 1615 cm^{-1} in vincanine relates to the vibrations of the aromatic and heteroaromatic nuclei. So far as concerns the 1667 cm^{-1} band of vincanine, it is apparently due to complex vibrations of the grouping



$-\mathrm{NH}-\mathrm{C}=\mathrm{C}-\mathrm{C}(=\mathrm{O})\mathrm{H}$

since in dihydrovincanine (V), where the ethylenic bond is lacking, a band with a maximum at 1640 cm^{-1} whose intensity is 2.0×10^4 units also appears.

Furthermore, it can be seen from the table that vincanine (IV) and dihydrovincanine (V) each have a band at 1552 cm^{-1}, the intensities of these bands being 7.5×10^4 and 6.5×10^4 units respectively.

Such high values of the intensity of this band show that powerful conjugation and a strong hydrogen bond are present here in the system  . This leads to a considerable polarization of the C=O bond of the aldehyde.

The band at 1552 cm^{-1} in vincanine (IV) and dihydrovincanine (V) relates to the C=O stretching vibrations of the aldehyde, since in the nitrile derivative of vincanine (VI) they disappear completely.

When the intensities of the bands of the vibrations of the double bonds (ring and side-chain) in dihydrovincanine (VII), deoxydihydrovincanine (VIII), and deoxyhexahydrovincanine (IX) are compared, it can be seen that the intensity of the band of the ethylenic double bond is evidently low in view of the fact that its contribution has practically no effect on the over-all total intensity of the band at about 1600 cm^{-1}.

The table also shows that in compounds in which there is an ester group as well as an aldehyde group [akuammicine (X), vinervine O-methyl ester (XI)], bands appear at about 1667 and 1600 cm^{-1} whose integral intensity is markedly increased. It is known that the integral intensities of the C=O bands of esters have values of from $2.7-3.5 \times \times 10^4$ units (in $CHCl_3$) [15]. In our case, the intensity of the high-frequency band at 1667 cm^{-1} is 9.0×10^4 units, and the intensity of the band at about 1600 cm^{-1} is 6.0×10^4 units. This sharp rise in the intensity of the bands mentioned is apparently the result of the strong conjugation of the C=O of the ester group with the double bond of the ring and the influence of the intramolecular hydrogen bond in consequence of which an increase in the polarities of both the C=O and the C=C bonds takes place. In actual fact, in the dihydro derivatives of these two compounds, i.e., in compounds (XII) and (XIII), the frequencies and integral intensities of the C=O and C=C bands have the normal values.

Thus, for example, in dihydroakuammicine (XII) the C=O band absorbs at 1730 cm^{-1}, and its intensity is 3.0×10^4 units, while the band of the vibrations of the double bonds of the rings has a value of 1608 cm^{-1} and $A = 0.90 \times 10^4$ units.

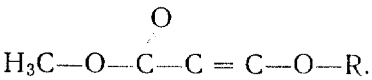
In ervamine (XV) the value of A for the C=O group is somewhat lower than the same values in compounds (X) and (XI). Probably, although the ester group in ervamine (XV) is also conjugated with a double bond, as in the case of compounds (X) and (XI), the different conformations of rings D and E in ervamine exert a considerable influence. It remains to elucidate the question of why in compounds (X), (XI), and (XV) there is no band at 1552 cm^{-1} as is observed in vincaninine (IV), and dihydrovincanine (V).

This is possibly connected with the fact that the proton of the aldehyde group in (IV) and (V) is replaced by the heavier OCH_3 radical in compounds (X), (XI), and (XV), and therefore the vibrations of the grouping

$-C=C-\overset{O}{C}-OCH_3$

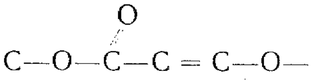
become more complex. These results additionally confirm the fact that in such complex groupings the C=O and C=C vibrations are uncharacteristic and are difficult to interpret.

In resperpine (XVII) and in the hydroxyindole alkaloids (XVIII)–(XXI), three or four bands of different intensities appear in the 1500–1700 cm^{-1} region. The molecules of these compounds contain the grouping



$H_3C-O-\overset{O}{C}-C=C-O-R.$

The bands at 1700 and 1630 cm^{-1} were previously assigned to the complex vibrations of the whole grouping



$C-O-\overset{O}{C}-C=C-O-$

[16,17]. The intensities of these bands have a normal value in reserpinine.

In the hydroxyindole alkaloids, the intensities of all the bands in the region of the spectrum investigated increase sharply. This rise in the intensities of the bands cannot be due to the presence in these compounds of an additional amide carbonyl group $-N-C=O$, since this should lead to an increase in the intensity of only one of the bands, probably the low-frequency band at 1630 cm^{-1}. However, as the table shows, in these compounds the intensities of both bands increase markedly.

The values of the integral intensities of the bands in the 1600–1700 cm^{-1} region of the alkaloids (XIX)–(XXI) show that the structures of these alkaloids are similar to one another.

In conclusion, we may mention that we have also measured the intensities of the bands in the 1500-cm^{-1} region arising from the vibrations of the rings. However, these results cannot serve as a reliable criterion of any particular changes taking place in the molecules of complex compounds.

Experimental

The IR spectra of 20 different derivatives and synthetic substances were recorded on a UR-10 double-beam spectrophotometer (Zeiss) in the 3100-3600 cm^{-1} region (LiF prism) and the 1500–1800 cm^{-1} region (NaCl prism) in chloroform solutions. The spectral slit widths in the regions mentioned (slit program 4) were 4 and 8 cm^{-1} respectively. The rates of scanning of the spectra were 12 and 32 cm^{-1} per min.

The work was carried out with nondismountable standard cells with NaCl windows and thicknesses of the absorbing layer of 0.101, 0.621, 0.0386, 0.0168, and 0.0106 cm. The integral intensities of the bands were calculated by Wilson and Wells's extrapolation method [18], with corrections for the edges of the bands. In individual cases of the measurement of the intensities of the broad diffuse bands arising through the formation of intermolecular hydrogen bonds, the edge correction could not be taken into account. The errors in the measurement of the integral intensities of the bands amounted to ± 7%.

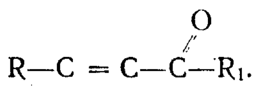
Summary

1. The frequencies and integral intensities of the bands of the stretching vibrations of the NH, C=O, and C=C groups in some indoline, indole, and hydroxyindole alkaloids and certain other compounds have been investigated.

2. From the changes in the intensities of the NH bands in vincanine, akuammicine, vinervine O-methyl ether, and their dihydro derivatives, it has been concluded that the first-mentioned compounds contain chelate bonds.

3. On the basis of the results of the measurements of the intensities for vincanine and dihydrovincanine, the bands in the 1500–1700 cm^{-1} region have been identified.

4. The bands in the 1600–1700 cm^{-1} region of a number of natural alkaloids are due to the complex vibrations of the whole grouping



$R-C=C-\overset{O}{\overset{/\!/}{C}}-R_1$.

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