INTEGRAL INTENSITIES OF THE ABSORPTION BANDS OF THE SKELETAL VIBRATIONS OF THE HETEROAROMATIC RING IN THE IR SPECTRA OF THE FURANOQUINOLINE ALKALOIDS

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UDC 541.67.944/945

We have shown previously that the integral intensity A of the bands in the 1480-1630-cm^{-1} region of substituted naphthalenes, biphenyls [1], and aporphine alkaloids [2] depends on the nature and positions of the substituents in the aromatic ring. This fact is in harmony with papers [3-7] in which a linear relationship has been shown between the value of A of the antisymmetric stretching vibrations ν_{as} of the aromatic and heteroaromatic rings of substituted benzenes, pyridines, and furans and the Hammett–Taft constants.

To study the substituent–heteroaromatic ring influence, we have measured the integral intensities A of the bands in the 1480-1630-cm^{-1} region of furanoquinoline alkaloids and some model compounds (I-XIV) (Table 1). In pyridine (III) and quinoline (IV), as in benzene, the band of the symmetric skeletal vibrations of the ring ν_s at about 1500 cm^{-1} is practically absent.

However, condensation of a benzene ring with a pyridine ring, i.e., in quinoline (IV), doubles the total integral intensity ΣA of the ν_{as} bands of the skeletal vibrations of the ring in the 1610-1570-cm^{-1} region as compared with benzene (I) and pyridine (III). It is important that the introduction of an $-OCH_3$ group into the γ position of the pyridine nucleus causes the appearance of a strong ν_s band at about 1500 cm^{-1} and the increase in the value of the total integral intensity ($\Sigma A = A_{\nu_s} + A_{\nu_{as}}$) almost 11-fold as compared with pyridine (III), which can be explained by the positive mesomeric effect of the methoxy substituent in the γ position to the nitrogen atom of the pyridine nucleus. A similar pattern is observed in substituted benzenes [8], biphenyls, and the aporphine alkaloids [1, 2].

The intensities of the absorption bands in the region of the spectra of the furanoquinoline alkaloids (I-XIV) that have been studied change in the manner shown in Table 1. On passing from 4-methoxypyridine (V) to dubinidine (VI), there is a further increase in ΣA. This can hardly be due to condensation with the benzene ring and, most probably, here the

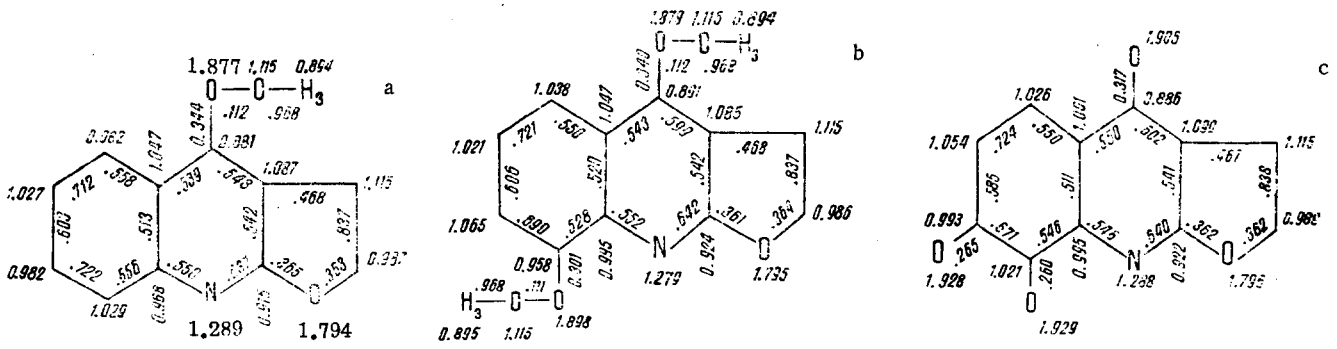

Fig. 1. Molecular diagrams of the molecules of dictamnine (a), γ-fagarine (b), and skimmianine (c).

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 223-227, March-April, 1976. Original article submitted June 17, 1975.

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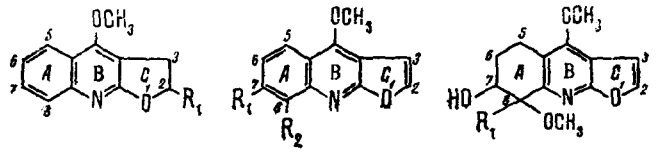
TABLE 1. Integral Intensities of the IR Bands of the Skeletal Vibrations of the Heteroaromatic Ring in the 1630-1480 cm^{-1} Region of the Furanoquinoline Alkaloids



VI VII-XII XIII-XIV

Compound	ν_s, cm^{-1}	$A_s \cdot 10^4$, $mole^{-1} \cdot liter \cdot cm^{-2}$	ν_{as}, cm^{-1}	$A_{as} \cdot 10^4$, $mole^{-1} \cdot liter \cdot cm^{-2}$	$\nu_{as'}$, cm^{-1}	$A_{as'} \cdot 10^4$, $mole^{-1} \cdot liter \cdot cm^{-2}$	$\Sigma A = A_s + A_{as} + A_{as'}$
Benzene (I)	1485	0,36	—	—	—	—	0,36
Anisole (II)	1510	1,30	—	—	1600	1,10	2,40
Pyridine (III)	—	—	1585	*	1600	0,42	0,42
Quinoline (IV)	—	—	1570	*	1595 1620	0,75	0,75
4-Methoxypyridine (V)	1510	1,50	1555	*	1595	3,10	4,60
Dubinidine (VI), R_1 = $HOC(CH_2OH)CH_3$	1510	0,67	1580	3,30	1620	3,40	7,40
Dictamnine (VII), R_1, R_2 = H	1505	0,80	1575	2,75	1620	2,30	5,85
γ-Fagarine (VIII), R_1 = H; R_2 = $-OCH_3$	1505	2,50	1575	1,10	1610	1,30	4,90
Robustine (IX), R_1 = H; R_2 = $-OH$	1505	2,50	1580	0,95	1620	1,40	4,90
Skimmianine (X), R_2, R_1 = $-OCH_3$	1510	1,54	1585	2,30	1610 1620	3,0	6,84
Haplopine acetate (XI), R_1 = $-OCOCH_3$; R_2 = $-OCH_3$	1510	2,70	—	—	1630	2,40	5,10
Evoxine (XII), R_1 = $-OCH_2-CH(OH)-C(CH_3)_2OH$; R_2 = $-OCH_3$	—	—	1580	2,50	1610 1620	3,10	5,60
Perforine (XIII), R_1 = $-CH_2-CH_2-C(CH_3)_2OH$	1530	1,35	1580	*	1605	2,90	4,25
Haplofilidine (XIV), R_1 = $CH_2-CH=C(CH_3)_2$	1530	0,91	1580	*	1600	2,20	3,10

*The value of A_{as} is a component of the value of $A_{as'}$, since the ν_{as} absorption band overlaps $\nu_{as'}$.

electron-donating influence of the oxygen atom of the dihydrofuran ring has an effect. Passage from the dihydrofuran ring to the furan ring in derivatives of dictamnine (VII-XII) is accompanied by a fall in the value of ΣA. Thus, for example, ΣA for dubinidine (VI) is 7.40 and ΔA for dictamnine (VII) is 5.85 practical units. The lower value of ΣA for the dictamnine derivatives (VII-XII) as compared with dubinidine (VI) is probably due to an increase in the delocalization of the unshared electron pair of the oxygen atom of the furan ring into the C_2—C_3 double bond.

The value of ΣA for dictamnine (VII) decreases with the introduction of an $-OCH_3$ effect. stituent into position 8 (VIII) and rises when it is added at position 7 of the benzene ring (X). As can be seen from Table 1, ΣA (VII) = 5.85 and ΣA (VIII) = 4.90, while ΣA (X) = 6.84 practical units. On the basis of the molecular diagrams (a, b, and c) of dictamnine (VII), γ-fagarine (VIII), and skimmianine (X) calculated by the MO method in Hückel's approximation [9], it may be assumed that the 7-OCH_3 group of the benzene nucleus (X) strengthens the interaction of the 4-methoxy group with the pyridine ring and the nitrogen atom, thereby increasing the π-electron density of the quinoline nucleus [10]. On the introduction of an $-OCH_3$ substituent in position 8 of the benzene ring (VIII), a weakening of the above-mentioned interaction takes place.

The replacement of the methoxy substituent in position 7 of the aromatic ring by an $-OCOCH_3$ (XI) or an $-OCH_2-CHOH-C(CH_3)_2OH$ group (XII) causes a decrease in the value of ΣA relative to skimmianine (X). In this case, the electron-accepting influence of the $-OCOCH_3$

group in haplopine acetate (XI) and the ortho effect of $-OCH_2-CHOH-C(CH_3)_2OH$ in evoxine (XII) reduces the electron-donating properties of the benzene ring of skimmianine derivatives [1,2].

In the perforine derivatives (XIII) and (XIV), the value of ΣA is lower than in the other furanoquinoline alkaloids (VI-XII) (see Table 1). This experimental fact shows that in perforine (XIII) and haplofilidine (XIV), with the hydrogenation of the aromatic ring the electron-accepting properties of the furan nucleus are enhanced.

The difference in the values of ΣA for compounds (XIII) and (XIV) can apparently be explained by the influence of the hydrogen bonds of the —OH groups in them.

Thus, on passing from dubinidine (VI) to derivatives of dictamnine (VII-XII) and of perforine (XIII, XIV), i.e., with an increase in the electron-accepting properties of the furan ring, A falls in the following sequence: ΣA (VI) > ΣA (VII-XII) > ΣA (XIII, XIV).

The facts presented show that it is possible to identify a series of compounds (VI-XIV) under investigation from the value of ΣA.

The change in the values of ΣA for dictamnine derivatives (VII-XII) is obviously due to the different natures and positions of the substituents in the benzene ring. It must be mentioned that in compounds (V-XIV), the values of ΣA exceed the values of the intensities of the absorption bonds of the amide and ester carbonyl groups.

EXPERIMENTAL METHOD

The IR spectra were recorded on a UR-20 double-beam infrared spectrophotometer in the 1470-1650-cm^{-1} region (NaCl prism). Chloroform was used as the solvent. The spectral slit width for the range from 1470 to 1650 cm^{-1} was 8 cm^{-1}. The rate of scanning was 32 cm^{-1}/min. Nondismountable standard cells with NaCl windows having thicknesses of the absorbing layer of 0.0176, 0.038, 0.060, and 0.055 cm (0.1 × 0.1 cm), and also quartz cells with a thickness of the absorbing layer of 1 cm, were used.

The integral intensities were measured by the Bourgin method [11]. The errors of measurement of intensities were ±6%.

SUMMARY

1. The integral intensities of the bands of the skeletal vibrations of the heteroaromatic ring in the 1480-1630-cm^{-1} region of eight furanoquinoline alkaloids have been measured.

2. A connection has been found between the values of ΣA and the structures of the furanoquinoline alkaloids and their derivatives which enables such a series of heteroaromatic compounds to be identified: It has been shown that the introduction of an $-OCH_3$ group into the γ position of the pyridine nucleus leads to a marked rise (almost twofold) in the value of ΣA;

In derivatives of dictamnine (VII-XII), the value of ΣA depends on the position of the methoxy group and on the nature of the substituent in position 7 of the benzene ring;

With an increase in the delocalization of the unshared pair of electrons of the oxygen atom of the furan ring, the value of ΣA of the series of alkaloids investigated (VI-XIV) decreases; and

Compounds (V-XIV) have the very high values of ΣA of 5.0-7.0 practical units and they exceed the value of the intensities of the carbonyl bands ν(C=O).

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STRUCTURE OF HERBOXINE

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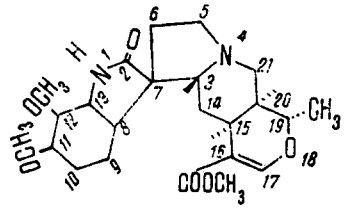
UDC 547.944/1

Continuing an investigation of the alkaloids of *Vinca herbaceae* [1], we have isolated a new base, which we have called herboxine. Herboxine (I), $C_{23}H_{28}N_2O_6$, has mp 179-181°C, $[\alpha]_D$ +40° (c 1.13; methanol). The UV spectrum of (I) — λ_{max} 224 nm (log ε 4.39), inflection at 250 nm — is characteristic for the hydroxyindole alkaloids.

The IR spectrum of (I) has absorption bands at 775 and 800 cm^{-1} (1,2,3,4-tetrasubstituted benzene ring) and 1710 and 1635 cm^{-1} (ester and amide carbonyl groups). The mass spectrum of (I) is characterized by the peaks of ions with m/e 428 (M^+; 100%), 413, 411, 397, 223, 222, 219, 208, 206, 204, 180, and 69. The NMR spectrum of (I) shows signals from the protons of a >CH—CH_3 group (δ 1.18 ppm, 3 H, doublet, J = 6 Hz; and 4.12 ppm, 1 H, quartet, J = 10 Hz), the methoxy of an ester group (3.37 ppm, singlet), two aromatic methoxyls (3.71, 3.78 ppm, singlets), >C=CH—O— (7.32 ppm, 1 H, singlet), NH (8.20 ppm, 1 H, broadened singlet), and two aromatic protons, C_9H (6.70 ppm, 1 H, doublet, J = 8 Hz), and $C_{10}H$ (6.40 ppm, 1 H, doublet, J = 8 Hz).

The similarity of the IR, mass, and NMR spectra of herboxine and those of majdine (II) and isomajdine (III) [2] permitted the assumption that (I) is an isomer of majdine or isomajdine. To answer this question, we performed a comparative investigation of the chemical properties and spectral characteristics of majdine, isomajdine, and the products of their isomerization in acetic acid (IV and V, respectively) [3] with those of herboxine. It was found that herboxine was identical with compound (IV), i.e., (I) differs from majdine by the configuration at C_3 and has the structure



I

EXPERIMENTAL METHOD

The IR spectra were taken on a UR-20 spectrometer (tablets with KBr), the mass spectra on an MKh-1303 instrument with a glass inlet system at 40 eV, and the NMR spectra on a JNM 4H-100/100 Hz instrument with HMDS as internal standard (δ scale). The homogeneity of the substances was checked by chromatography in a thin layer of KSK silica gel in the ethyl acetate—methanol (9:1) system.

Herboxine (I). The material (12 g) from the mother liquor after the isolation of majdine was passed through a column of alumina (activity grade II, 1:10). Elution was per-

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 227-229, March-April, 1976. Original article submitted July 1, 1975.

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