INFRARED ABSORPTION SPECTRA OF SOME DERIVATIVES OF 1,2,3,4-TETRAHYDRO-β-CARBOLINE

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The IR absorption spectra in 3800-1400 cm^{-1} region of 1-propyl-, 1-carboxy-, 1-carboxy-1-methyl-, and 1-benzyl-1-carboxy-6-hydroxy-1,2,3,4-tetrahydro-β-carbolines, their O-methyl derivatives, and their hydrochlorides are discussed. An assignment of the bands due to the stretching vibrations of NH, NH_2^+, OH, COO^-, and COOH groups is proposed. The hypothesis has been put forward that strong intermolecular and intramolecular hydrogen bonds exist in the substances studied.

The synthesis of the amino acids 1-carboxy-6-hydroxy-1,2,3,4-tetrahydro-β-carboline (I) and its 1-methyl and 1-benzyl derivatives (II, III) has been described previously [1].

The present paper discusses the IR absorption spectra of these compounds in the 3800-1400 cm^{-1} region and the spectra of their O-methyl derivatives (IV, V, and VI, respectively) and those of the hydrochlorides of all these substances (Ia-VIa, respectively), and also of the model structures 6-hydroxy-1-propyl- and 6-methoxy-1-propyl-1,2,3,4-tetrahydro-β-carbolines (VII and VIII) and their hydrochlorides (VIIa and VIIIa). The main bands in the IR spectrum of 1-carboxy-1,2,3,4-tetrahydro-β-carboline (IX) have been given in the literature [2] without their assignment. Our figures for the IR spectra of derivatives of 6-hydroxy-1,2,3,4-tetrahydro-β-carboline are given in Table 1 and in Figs. 1 and 2. It can be seen from Fig. 1 that the narrow strong band at 3300-3450 cm^{-1} observed in the spectra of compounds VII, VIIa, VIII, and VIIIa can be assigned to the stretching vibrations of the NH bond of the indole ring. The somewhat lower value of ν_{NH} of these compounds as compared with the figures characteristic for nonbound NH groups of the indole ring [3] show the participation of this group in hydrogen bonds.

On comparing the spectra of the hydroxy derivatives (VII and VIIa) with the spectra of the methoxy derivatives (VIII and VIIIa), and the spectra of the free tetrahydro-β-carbolines with the spectra of their hydrochlorides, it may be concluded that the broad strong bands at 3280, 2750, and 2630 cm^{-1} in the spectrum of VII correspond to the vibrations of OH and NY groups bound by hydrogen bonds, and the band at 3175 cm^{-1} in the spectrum of VIII to the vibrations of the NH of the piperidine ring. In the spectrum of VIIa, the band at 3110 cm^{-1} obviously corresponds to the stretching vibrations of the phenolic hydroxyl. The NH_2^+ group of the hydrochlorides is characterized by a series of six bands of medium or weak intensities located in the 2800-2200 cm^{-1} region (spectra of VIIa and VIIIa). In addition to the bands mentioned, a strong band at about 1600 cm^{-1} and a medium-intensity band close to 1630 cm^{-1} are characteristic for compounds VII, VIIa, VIII, and VIIIa, apparently being connected with vibrations of the indole ring. The interpretation of the spectra of the 1-carboxy derivatives of the tetrahydro-β-carbolines is somewhat more complex. The frequencies found in the spectra of these substances and also literature information are given in Table 1. In the spectra of the 1-carboxy derivatives of tetrahydro-β-carbolines, as in the spectra of the 1-propyl derivatives, ν_{NH} of the indole ring can be identified fairly easily: it is the strong narrow band in the 3420-3300 cm^{-1} region that is present both in the spectra of the amino acids (I-III) and their

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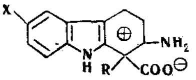
TABLE 1. IR Spectra of Derivatives of 1,2,3,4-Tetrahydro-β-Carbinoline (I-VI, IX)



Compound	NH_2		ν, cm^{-1}			Hydrochloride	ν, cm^{-1}			
	X	*R*	$\bar{COO}_{asym}$	NH	OH		CO	NH	OH	COOH
I	HO	H	1645	3435	3080	Ia	1758	3330	3270	3468
II	HO	CH_3	1623	3300	3145	IIa	1755	3340	3170	—
III	HO	$PhCH_2$	1631	3405	3120	IIIa	1725	3315	3270	3560
IV	CH_3O	H	1658	3340	—	IVa	1758	3320	—	3530
V	CH_3O	CH_3	1625	3402	—	Va	1752	3478	—	—
VI	CH_3O	$PhCH_2$	1638	3408	—	VIa	1738	3260	—	3500
IX²	H	H	1661	3320	—	—	—	—	—	—
	5-Hydroxytryptophan		1593	3418	3264		1740	3460	3100	—

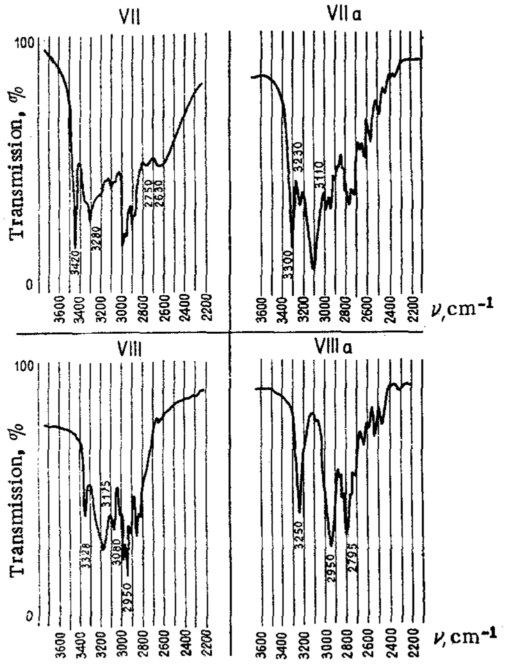


Fig. 1

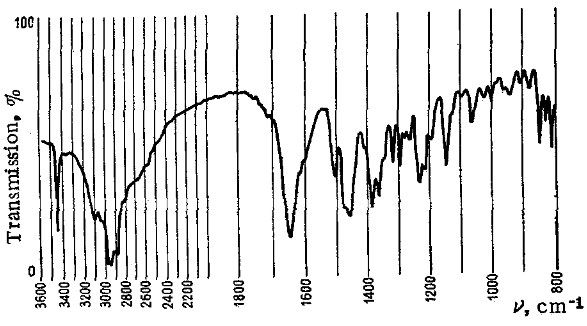


Fig. 2

Fig. 1. IR spectra (mulls in hexachlorobutadiene): 6-hydroxy-1-propyl-1,2,3,4-tetrahydro-β-carboline (VII) and its hydrochloride (VIIa); 6-methoxy-1-propyl-1,2,3,4-tetrahydro-β-carboline (VIII) and its hydrochloride (VIIIa).

Fig. 2. IR absorption spectrum of 1-carboxy-6-hydroxy-1,2,3,4-tetrahydro-β-carboline (I) (mull in paraffin oil).

O-methyl derivatives (IV-VI) themselves and also in the spectra of the corresponding hydrochlorides. The lowered value of ν_{NH} of indole again shows that the NH group participates in the formation of hydrogen bonds. In the spectra of compounds I-III, which contain phenolic hydroxy groups in the indole rings, there is in each case a medium-intensity band in the 3300-3100 cm^{-1} region which is broader than the ν_{NH} band of indole. This band is not found for the O-methyl derivatives (IV-VI) and may be ascribed unambiguously to the stretching vibrations of a hydroxy group participating in a hydrogen bond. In the spectra of the 1-carboxy derivatives of the tetrahydro-β-carbolines and their hydrochlorides there are no bands

TABLE 2. 6-Alkoxy-1,2,3,4-tetrahydro-β-carbolines

Compound	Mp, °C (decomp.)	Empirical formula	Found, %			Calculated, %			R^*_f		Yield, %
			C	H	N	C	H	N	A	B	
IV	218	$C_{13}H_{14}N_2O_3$	63,4	5,7	11,6	63,4	5,7	11,4	0,62	0,70	70,0
V	220	$C_{14}H_{16}N_2O_3$	63,9	6,4	10,4	64,6	6,2	10,8	0,75	0,79	68,0
VI	248	$C_{20}H_{20}N_2O_3$	70,9	6,2	8,6	71,4	6,0	8,3	0,87	0,90	88,0

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* A) In the n-butanol–acetic acid–water (4:1:5) system; B) in the n-butanol–acetic acid–phosphate buffer solution, pH 6.0 (4:1:5) system.

relating to the NH stretching vibrations of the piperidine ring, but in the 2900-2400 cm^{-1} region there are six to eight weak bands characterizing the NH_2^+ group and showing that the amino acids under investigation, like other amino acids described, exist in the solid state in the form of zwitterions. However, while the amino acid zwitterions described in the literature have the band of the asymmetric stretching vibrations of the COO^- group in the 1610-1580 cm^{-1} region [4-6], frequencies of 1645-1625 cm^{-1}, somewhat exceeding the usual values of ν_{COO^-}, are characteristic for the compounds given in Table 1. Several cases are reported in the literature where increased values of ν_{COO^-}, reaching 1650-1700 cm^{-1}, have been observed for individual compounds. Such a rise is generally connected with the possibility of the formation of intramolecular hydrogen bonds of the type of COO^- ..... HOOC [5] or COO^- ..... H–N [8]. We assume that the increased ν_{COO^-} frequencies in the compounds that we are considering are due to the fact that the close spatial position of the carboxy group and N–H bond of the indole ring create conditions for the appearance of an intramolecular hydrogen bond, and it is known from the literature [7, 8] that the inclusion of a COO^- group in intramolecular hydrogen bonds is accompanied by a rise in ν_{COO^-} by 20-30 cm^{-1}. The spectra of the amino acids that we have studied also exhibit the band of the symmetric stretching vibrations of the COO^- group at about 1380 cm^{-1} (Fig. 2). This band is not present in the spectra of the hydrochlorides. The carboxy groups of the hydrochlorides of the amino acids and of their O-methyl derivatives are represented in each case by a band in the 1740-1760 cm^{-1} region. According to x-ray structural data [9], no intramolecular hydrogen bonds exist in amino acids between the ionized carboxyl group and a NH_3^+ group in the α position to the latter. Both these groups take part in strong intermolecular hydrogen bonds. By analogy, it may be assumed that in the amino acids of the tetrahydro-β-carboline group that we have considered the NH_2^+ and COO^- groups are connected with one another only by intermolecular hydrogen bonds.

EXPERIMENTAL

The IR absorption spectra of the substances studied were obtained on a UR-10 instrument. The samples were prepared in the form of mulls in paraffin oil or hexachlorobutadiene. 1-Carboxy-6-methoxy-1,2,3,4-tetrahydro-β-carboline (IV), 1-carboxy-6-methoxy-1-methyl-1,2,3,4-tetrahydro-β-carboline (V), and 1-benzyl-1-carboxy-6-methoxy-1,2,3,4-tetrahydro-β-carboline (VI) were synthesized from 5-methoxytryptamine and, respectively, glyoxylic, pyruvic, and phenylpyruvic acid as described previously [1]. Their chromatographic behavior on paper was studied by the descending methods in the n-butanol–acetic acid–water (4:1:5) and n-butanol–acetic acid–phosphate buffer, pH 6.0 (4:1:5) system. The chromatograms were treated with ethanolic solutions of ninhydrin; the compounds synthesized gave a yellow-orange coloration, on treatment with an alkaline solution of potassium permanganate a yellow coloration on a violet background, and in ultraviolet light a blue fluorescence which was intensified when the chromatograms were heated at 90°C for 10-15 min. The analytical results, yields, and melting points, and the R_f values in paper chromatography of the compounds synthesized are given in Table 2. All the elementary analyses were carried out under the direction of A. D. Shinaeva. The inadequate solubility of the substances in ordinary solvents prevented our studying their IR absorption spectra in solutions.

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