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IR Spectroscopic Study of Substances Containing Iodine Adduct.

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ABSTRACT

This article presents the study results of the structural units of substances containing iodine adducts (R1 and R8) by infrared spectroscopy. It is shown that the substances R1 and R8 are complexes of iodine and zwitterionic aminoacids and lithium cations in the case of R8. The characteristic functional groups, enabling the identification of the studied complexes were established.

Keywords: substance, iodine adducts, IR-spectroscopy, functional group, aminogroup, hydroxyl group, iodine.

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INTRODUCTION

One of the prospective large classes of chemical compounds used in drug development is adducts. Adducts [1] are chemical substances formed by the addition reaction proceeds without formation of side product - pollutants [2]. The original substances containing iodine adduct with antimicrobial properties were obtained in Scientific Center of Anti-Infectious Drugs, Almaty, Republic of Kazakhstan.

Purpose of the study: to study the mechanism of interaction of the reactants in the synthesis reaction of iodine adducts in an aqueous-organic medium, and evaluation of the suitability of the obtained coordination compounds for further pharmaceutical development and preparing a dosage forms based on them. Method of molecular IR spectroscopy was chosen for the study of the complexation process. The complexation is to shift the absorption band which characterized for functional atomic group participating in complexation. Also complexation is the formation of new intermolecular hydrogen bonds, forming bonds at the donor-acceptor mechanism or other bonds between the ligands and the core-complexing agent [3]. To excite free fluctuations of the functional group and a similar group related to the complex requires a different amount of energy [4]. The sensitivity of infrared spectroscopy allows identifying this type of structural changes by the displacement of bands of the characteristic peaks [5]. The IR spectra of the pure starting components and the resulting complex compound allow to establish the functional groups involved in the complex formation and to assume the nature of bond formed [6-9].

EXPERIMENTAL

Iodine coordination compounds with amino acids, code-named R1 and R8 were synthesized, and have different composition and produce technology. The synthesis is based on a reaction of complexation of amino acid (glycine and alanine) and polyiodide ions in aqueous-organic medium. The used solvent is characterized by a polarity index of 4.3 and a dipole moment of 1.7.

Synthesis of R1: 2.598 g (29 mmol) of alanine were dissolved in 18 ml of water by heating (75 ± 5 °C). Simultaneously, 7.402 g (29 mmol) of molecular iodine dissolved in 97 ml of 95% ethanol. Further homogeneous hot alanine solution was slowly poured into a solution of iodine in ethanol. The resulting mixture was heated to 80-90 °C with vigorous stirring for 120 minutes. The complexation process accompanied by a marked increase in the viscosity of the reaction mixture and a precipitate of red-brown color, but viscosity decreased again over time. After stabilization of the viscosity the resulting solution was evaporated to wet residues level (at 20 ± 5 °C in the dark) and the precipitate was separated. The resulting precipitate was dried at room temperature and washed 5 times with 20 ml portions of cyclohexane (until termination cyclohexane staining). The yield was 7.55 g (75.5%).

Synthesis of R8: 2.89 g (22 mmol) of lithium iodide was dissolved in 38 ml of 95% ethanol. To this solution was added 5.49 g (22 mmol) of molecular iodine. The mixture was vigorously stirred until complete dissolution of the solid phase. In parallel, 1.62 g (22 mmol) of glycine dissolved in 3 ml of hot (75 ± 5 °C) water. The hot aqueous solution was slowly added to lithium triiodide alcohol solution under vigorous stirring. The reaction mixture was stirred at 85 ± 5 °C for 3 hours. The mixture was cooled to room temperature in a dark cool place, and evaporated to a state of wet residue. The precipitate was filtered off and dried. The dry precipitate was washed with 20 ml cyclohexane portions until colorless flush water (about 5 times). The yield was 6.34 g (63.4%).

Studies of the mechanism of the reactants interaction during the formation of R1 and R8 iodine adducts conducted by molecular infrared spectroscopy in the frequency range 4000 to 650 cm^{-1} by IR spectrophotometer Nicolet 6700, Thermo Scientific company (USA). Scanning was performed on the Smart Performer console by internal reflection on the ZnSe crystal. The number of scans was 32. The spectral characteristics of the studied complexes are given in Table 1: the wave number of band ν , cm^{-1} , the assignment of bandwidth [6-8].

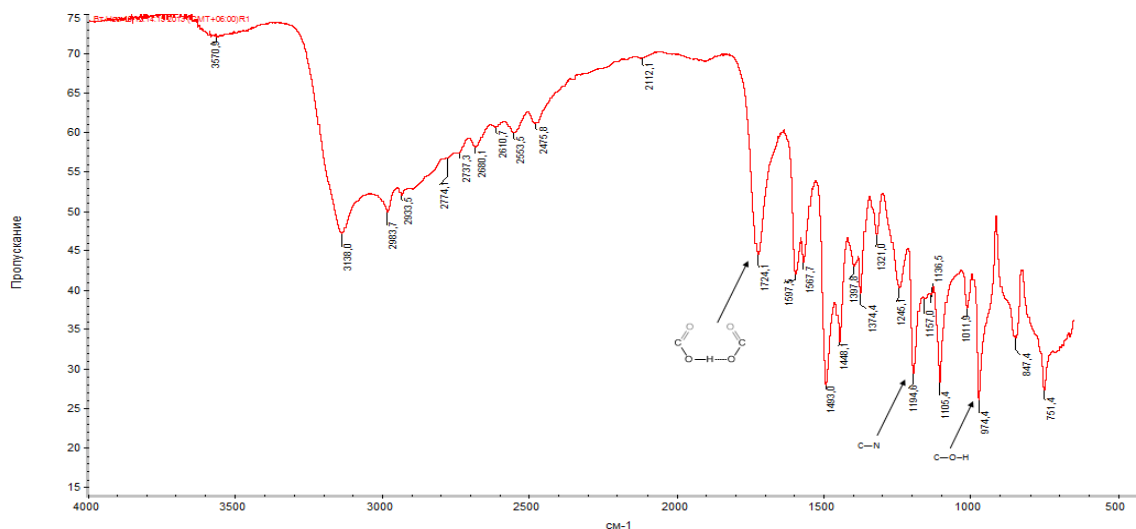


Figure 1 – IR spectrum of the R1 substance

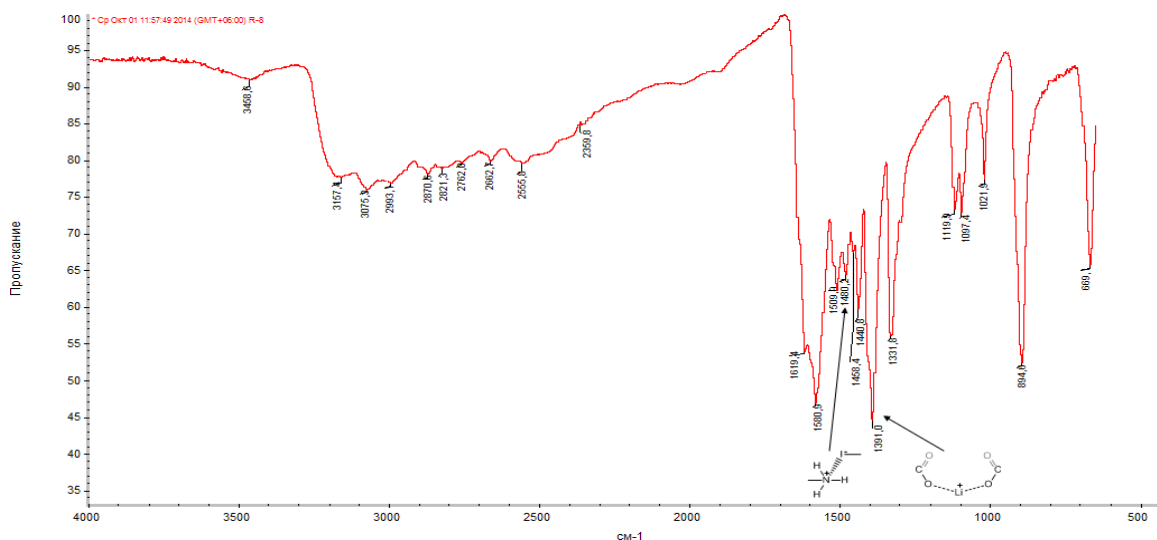


Figure 2 – IR spectrum of the R8 substance

Table 1: The spectral characteristics of the synthesized complex compounds (IR spectra)

№	IR spectra of the starting components			IR spectra of the substances		Interpretation of the absorption bands [5, 6]
	Glycine	Alanine	Lithium iodide	R1	R8	
	2	3	4	5	6	7
1	—	—	—	3570	3459	ν OH,
2	—	—	3373	—	—	ν H—O—H
3	3151	3068	—	3138	3157	ν NH ₂ , NH ₃ ⁺
4	3007	2974	—	2984	3075	ν_s NH ₃ ⁺
5	—	—	—	2934	2993	ν_{as} CH ₂ , δ_{as} CH ₃
6	—	—	—	—	2871	ν_s CH ₂
7	2821	2860	—	—	2821	ν_s —O—H
8	—	2799	—	2737	2762	
9	—	—	—	—	—	
10	2693	2729	—	2680	2663	δ_{as} NH ₂
11	—	—	—	2611	—	ν NH ₃ ⁺
12	2601	2594	—	—	—	ν_s CH ₃
13	—	—	—	2554	2556	δ_s NH ₂
14	2501	2513	—	—	—	ν_s CH ₂

15	—	—	—	2476	—	$\nu \text{NH}_2^+, \text{NH}^+$
16	—	—	—	1724	—	$\nu \text{COOH:OOC}$
17	—	—	—	1619	—	—COO ⁻
18	—	—	—	1598	1581	
19	—	—	1594	—	—	Li-I
20	1582	1586	—	—	—	$\nu \text{C=O}$
21	—	—	—	1568	—	$\nu \text{NH}_2^+ \text{CH}_2\text{COO}^-$
22	1502	1528	—	1493	1510	$\delta \text{NH}_3^+ \text{CH}_2\text{COO}^-$
23	—	—	—	—	1481	$\nu -\text{NH}_3^+ \cdot \text{I}^-$
24	—	—	—	—	1458	δNH_3^+
25	1443	1453	—	1448	1441	δCH
26	1408	1408	—	1398	—	δNH_3^+
27	—	1404	—	—	1391	COO:Li:OOC
28	—	—	—	1374	—	δNH_3^+
29	1332	1352	—	1321	1339	COO ⁻
30	—	1306	—	—	—	$\nu -\text{C}-\text{N}-$
31	—	1238	—	1245	—	$\text{H}_3\text{N}^+-\text{C}-\text{C}-\text{O}-$
	—	—	—	1195	—	$\nu -\text{C}-\text{N}-$
32	1132	1144	—	1189	—	$\nu -\text{C}-\text{N}-$
33	1112	1114	—	1105	1112	
34	—	—	—	—	1097	
35	1034	1015	—	1012	1022	$\nu -\text{C}-\text{OH}, \delta_{s/as} \text{NH}_3^+, \nu \text{C}-\text{N}$
36	—	919	—	974	—	$\nu -\text{C}-\text{OH}$
37	909	—	—	—	894	$\nu -\text{C}-\text{N}-$
38	892	850	—	847	—	
39	—	—	—	751	669	Iodate ion IO_3^-
40	695	—	—	—	—	$\delta \text{C}-\text{H}$

RESULTS AND DISCUSSION

Studies have shown that the spectrum of R1 and R8 are a number of new absorption bands are absent in the spectra of the starting components.

The band at 1724 cm^{-1} , manifested in the R1 product spectrum is narrow, medium intensity, well separated. The contribution of this band to provide neither the initial components, nor an organic solvent. These bands are characteristic to fluctuations of oxygen-containing functional groups. Thus, this band shows the coordination of two molecules of the amino acid by forming hydrogen bonds of the carboxyl groups. This fact confirms the shift of the band that appears on 974 cm^{-1} to 55 cm^{-1} to the red-infrared spectrum with respect to the original amino acid, as well as increasing its intensity. This band is characteristic of planar deformation vibrations of hydroxyl functional groups. The band at 1194 cm^{-1} is a narrow intense and characteristic for valence vibrations amino group (carbon-nitrogen). In this case, this band may indicate the formation of donor-acceptor bond between the iodine molecules and atoms of nitrogen molecules of amino acids. The IR spectrum R1 is presented in Figure 1.

A similar phenomenon is observed in the R8 IR spectrum (Figure 2). The appearance of a narrow weaker (but well distinguishable) band at 1480 cm^{-1} can be attributed to the asymmetric deformation vibrations of the quaternary amine groups linked donor-acceptor bonds with an iodine molecule. In addition, there is a shift of intense narrow band at 1391 cm^{-1} to 13 cm^{-1} in the shorter wavelengths of IR range of the spectrum with respect to the original amino acid. Since recording spectra were in identical conditions, this shift may indicate binding the oxygen atoms of the carboxyl functional groups in amino acids by hydrogen bonds, formed by lithium cation.

According to the method [9.10], the inorganic components of the test substances have absorption bands in the low frequency and in the border with its region of the spectrum. In diatomic molecules of alkali metal halides can be only a single vibration, which is active in the IR spectrum. The calculated basic frequency (wave number) vibrations given in [9] and for potassium iodide is up to 210.6 cm^{-1} .

Molecular iodine (I_2) not polarized, therefore has, as well as all diatomic molecules, one primary vibration at $190 - 215 \text{ cm}^{-1}$, active in the Raman spectrum. In the molecular complexes of iodine (I_2) with amines the valence vibrations I-I go down to $171 - 188 \text{ cm}^{-1}$ and appear the new, donor-acceptor bond N-I in the field of $65 - 146 \text{ cm}^{-1}$, which position depends on the amine. These data indicate that the main frequency of vibrations of molecular iodine, potassium iodide and polyiodide, located in the low region and lowering upon complexation in the IR spectra cannot be detected in this equipment.

The halogen derivatives of organic compounds have strong absorption bands of valence vibrations C-X in an accessible region of the spectrum: the mono-substituted by C-Cl $\nu = 750-700$ and 650 cm^{-1} ; C-I $\nu = 500 \text{ cm}^{-1}$, $\delta = 750 - 720 \text{ cm}^{-1}$.

The characteristic frequencies (ν, cm^{-1}) absorption of various groupings of atoms in these compounds is valence vibrations C-H: $\nu_{as} \text{ CH}_2$ 2940-2915 medium, $\nu_s \text{ CH}_2$ 2870-2845 medium, cyclic groups at 3080-3040 cm^{-1} . Deformation vibrations of C-H: $\delta \text{ CH}_2$ 1480-1440 and $\delta \text{ CH}$ 1340 cm^{-1} . Fluctuations skeleton - (CH₂) - 750-720 and 1020-1000 cm^{-1} .

All the characteristic frequency of the hydroxyl groups are closely related to the formation of hydrogen bonds. In practice, the most important is the valence band $\nu \text{ OH}$ in 3300 cm^{-1} , which position is highly dependent on the concentration and the measurement conditions. The band of the OH group with intermolecular hydrogen bonds is shown at 3500 cm^{-1} and below but intramolecular - at $3600- 3500 \text{ cm}^{-1}$. Band $\nu \text{ C-O}$ $\nu \text{ OH}$ more intense, but in- $1200-1000 \text{ cm}^{-1}$ absorb other groups. Deformation vibrations of free OH group is located at 1200, and the related at $1500-1300 \text{ cm}^{-1}$ (broad, often two lanes).

For aliphatic and cyclic C-O-C group in the infrared spectrum are only active asymmetric valence vibrations in the $1150-1070 \text{ cm}^{-1}$.

Amino acids containing NH_2 group have bands of valency vibrations ν_{as} and $\nu_s \text{ NH}_3^+$ with medium intensity and bands of deformation vibrations $\delta_{as/s} \text{ NH}_3^+$ in $3130-3030$, $1660-1610$ and 1300 cm^{-1} , respectively.

Amino acid I (monocarboxylic α -amino acid) has a band of variable intensity $\delta \text{ NH}_3^+$ at $1550-1485 \text{ cm}^{-1}$. The terminal in the peptide chain NH_2 group has two bands of weak intensity, ν weak $3500-3300$ and band δ medium, strong $1650-1580 \text{ cm}^{-1}$. The valency vibrations of C-N are shown at $1220-1020 \text{ cm}^{-1}$ (weak, medium).

For dicarboxylic α -amino acid (amino acid II) and other amino acids characterized a strong band of valence vibrations $\nu \text{ C=O}$ uncharged carboxyl $1755-1720$ and $1730-1700 \text{ cm}^{-1}$, respectively. The dicarboxylic amino acids have a strong band $1230-1215 \text{ cm}^{-1}$ C-O vibrations. All amino acids contain ionized carboxyl COO^- , strong band of valence vibrations is $\nu = 1630-1560 \text{ cm}^{-1}$. There are two types COO^- group: $\text{NH}_2^+-\text{CH}_2-\text{COO}^-$ ($1630-1620 \text{ cm}^{-1}$) and $\text{NH}-\text{CH}_2-\text{COO}^-$ ($1585-1575 \text{ cm}^{-1}$). In general, the intensity of the two bands is approximately the same and is about three times more the intensity of deionized COO^- group.

Primary free $-\text{CONH}_2$ groups have two bands $\nu \text{ NH}$ 3500 , 3400 cm^{-1} , and associated multiple bands $3050-3200 \text{ cm}^{-1}$. Amide band I $\nu \text{ C=O}$ 1690 and 1650 cm^{-1} , and 1600 and 1640 cm^{-1} - mainly at $\delta \text{ NH}$ to $\delta \text{ NH}$ superimposed $\nu \text{ C N}$.

For dicarboxylic alpha-amino acids (amino acid II) and other amino acids are characterized by non-ionized carboxyl band $1410-1408$ and $1390-1379 \text{ cm}^{-1}$ respectively. The dicarboxylic aminoacids have a strong band at $1230-1215 \text{ cm}^{-1}$ CO vibrations.

According to infrared spectroscopic studies R1 and R8 original drug substances were determined characteristic frequency absorption, which can be used for authentication (identification) of the substances. Substance to be considered authentic if its IR spectrum comprising absorption bands in ranges indicating in Table 2.

Table 2: Identification of the absorption frequency of substances R1 and R8

№	The range of characteristic frequencies, cm ⁻¹	
	R1 substance	R8 substance
1	1719 ÷ 1729	1475 ÷ 1485
2	1369 ÷ 1379	1386 ÷ 1396
3	1189 ÷ 1199	1016 ÷ 1026
4	969 ÷ 979	889 ÷ 899
5	746 ÷ 756	664 ÷ 674

During the study of the spectral characteristics of R1 and R8 of original medicinal substances was identified frequency identification, allow establishing their authenticity.

CONCLUSION

The mechanism of formation of complex compounds, R1 and R8 by IR spectroscopy was studied. Complexes R1 and R8 are coordination compounds of molecular iodine with amino acids and in case with R8 alkali metal.

The study found that the formation of the substance is carried out by:

- in case of R1: formation of intermolecular hydrogen bonds of the carboxyl functional groups of the amino acid molecules, and donor-acceptor bonds of nitrogen atoms and molecular iodine to form a quaternary amine structure;
- in case of R8: coordinating oxygen atoms of the amino acids molecules positively charged around the lithium ion and formation donor-acceptor bonds of nitrogen atoms and molecular iodine, also forming a quaternary amine structure.

The studies results have shown that IR spectroscopy can be used to confirm the authenticity of the substances containing iodine adducts and monitoring of manufacturing dosage forms based on them.

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