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INTERACTION OF L-CYSTEINE WITH DIMETHYL SULFOXIDE IN MILD CONDITIONS

Z. Kh. PAPANYAN *

Chair of Physical and Colloid Chemistry YSU, Armenia

Interaction of L-cysteine with DMSO in aqueous solutions was studied by FTIR spectroscopy. It is found that the processes involved are not limited by the solvation processes only, but a further oxidative conversion of L-cysteine to L-cystine takes place in mild conditions, separating dimethyl sulfide and water being other products of reaction.

***Keywords*:** L-cysteine, L-cystine, FTIR spectroscopy.

Introduction. Cysteine is the one of the sulfur containing non-essential amino acids along with methionine, which are found naturally in many proteins such as α and β-ceratins, and in free state. The ability of cysteine residues to form disulfide bridges plays an important role on secondary structure and folding of proteins. Another prominent quality is that sulfur can be found in different oxidation states in living systems, which is a key for various biological functions. More about the role and importance of sulfur containing amino acids as well as redox chemistry of cysteine residues in enzymes is summarized in [1, 2].

Few factors determine the importance of the investigation of interactions between L-cysteine and dimethyl sulfoxide (DMSO). Besides being a polar aprotic solvent DMSO is widely used in biology and medicine for drug delivery and as a cryoprotective agent [3, 4]. It is also known, that in some reactions DMSO can serve as an oxidizer by giving it's oxygen atom [5]. However, reports in literature about the possible interactions of L-cysteine with DMSO are scarce and provide various, sometimes contradicting information on the resulting products. According to [6], the interactions in the ternary system L-cysteine–H_2O–organic solvent (including DMSO) are limited to the solvation processes at room temperature, while in [7] a disulfide formation is stated in similar conditions. Similarly an analytical procedure for cysteine determination is described [8], where the reaction in hot acidified solutions yields mainly cysteic acid, whereas in [9] a general procedure for various organic disulfide preparations is given from starting thiols and DMSO.

* E-mail: z.papanyan@ysu.am

Thus, data so far provided in literature are not conclusive about the possibility of the reaction between L-cysteine and DMSO and/or the products formation. In the present work this reaction is studied by FTIR spectroscopy in aqueous medium and under mild experimental conditions (room temperature, without acid addition).

Experimental Part. Reagents DMSO (>99.5%) and L-cysteine (>98.5%) were obtained from "Sigma-Aldrich Co" and used without further purification. Infrared spectra were recorded using Nicolet/NEXUS FTIR spectrometer with spectral resolution of 4 cm^{-1}, the scan number set 32, in the frequency range of 4000–400 cm^{-1}.

In order to prepare L-cysteine solutions double distilled water was added to a weighed amount of amino acid and the mixture was shaken until complete dissolution. All the ratios were prepared gravimetrically. Thus, for the FTIR investigation of the reaction the quantities of reagents (including water) were taken, so that the molar ratio established after mixing reagents were DMSO:L-cysteine = 1:2 and the mass fraction of DMSO was 2.5%. A multibeam ATR cuvette made of Ge served as a reaction vessel during the spectra collection.

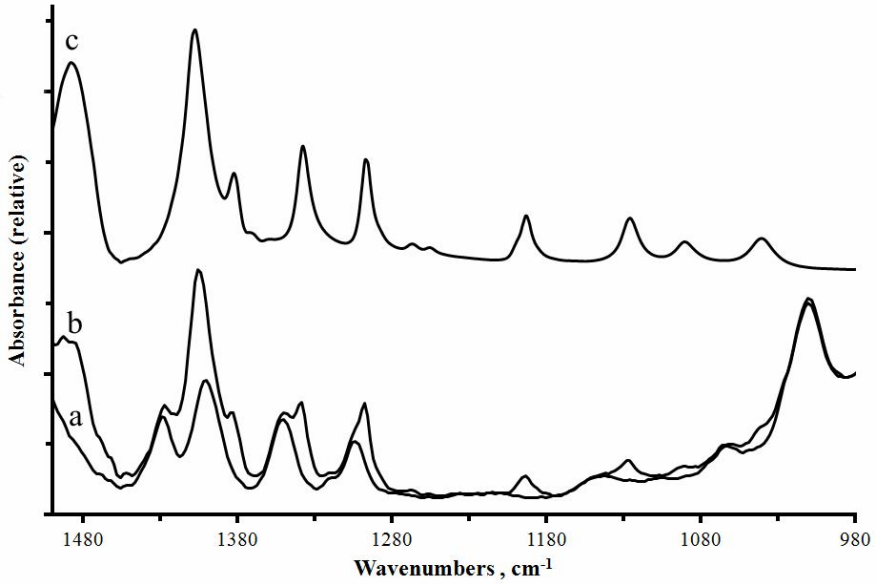
For identification purposes the reaction product of L-cysteine with DMSO was prepared separately by adding of an excess amount of DMSO to 10% L-cysteine solution in water. A turbidity is observed within few minutes indicating the proceeding reaction and formation of insoluble precipitate. The mixture was allowed to stand 24 *h* at room temperature, after which the precipitate was collected by filtration, washed with distilled water and dried to obtain powder. The IR spectra of solid reaction product was obtained from vaseline oil suspension between two KBr windows. For polycrystalline L-cysteine spectra KBr pellet technique was used, for which the mixture of L-cysteine powder with KBr was ground in mortar and pressed into pellets.

Results and Discussion. The infrared spectra were collected in the course of the reaction in the spectral range of 4000–400 cm^{-1}. The vibrational analysis of crystalline L- and LD-cysteine is given in [10] and is in good agreement with the current work. For aqueous solutions of 20 amino acids the interpretation of spectra can be found in [11], however, the given assignments are tentative and in the cases when there is a mismatch with [10] for L-cysteine, theoretical investigation [12] is also taken into consideration. Such an example is the absorption band observable at 941 cm^{-1} that is assigned to δ(SH) vibration in [10] for the polycrystalline sample, whereas in [11] the band at 937 cm^{-1} is thought to belong to β(HNC) for aqueous solutions of L-cysteine. Most likely both represent the same vibration of δ(SH), which agrees with [12].

The spectra obtained during the reaction and the spectrum of the isolated product for comparison are shown in Figure.

It can be seen, that the initial spectrum of reactants' mixture changes significantly in the course of time, several new absorption peaks appear and grow in intensity, exactly under the same frequencies as are for isolated reaction product. The latter is found to be pure L-cystine, the IR spectrum being identical to data given in [13]. A more thorough look reveals a decrease in the relative intensities of δ (SH) 935 cm^{-1} peak for L-cysteine and ν (S=O) 1010 cm^{-1} for DMSO,

simultaneous growth of produced L-cystine bands and few new absorptions under 2917, 2838, 1492 cm^{-1} are also detected, which can be ascribed to the most intense absorptions in dimethyl sulfide spectrum in accordance with [14]. Thus, formation and accumulation of L-cystine and dimethyl sulfide, as well as the consumption of the reagents during the reaction were observed by the virtue of FTIR technique.



IR spectra recorded in the course of the reaction of L-cysteine with DMSO after (a) 0 *min*; (b) 2 *h*; (c) of the isolated product.

On the ground of these observations a scheme of the reaction can be proposed, where the interactions include the thiol groups from cysteine and the oxygen present in DMSO.

$$(CH_3)_2S{=}O + 2\ R-SH \rightarrow R-S-S-R + (CH_3)_2S + H_2O$$

The scheme predicts the formation of DMSO and water along with L-cystine, which was evidenced above. It must be noted, that these results are in agreement with [7], but contrast with [8], where cysteic acid formation from cysteine or cystine is discussed. This discrepancy most likely can be explained by the differing conditions, under which the same reaction is conducted. At harsher conditions, described in [8], the medium was acidified with 6 *N* HCl and brought to constant boiling for 22 *h* at 110^0C, while in the current study the reaction took place at room temperature and without addition of acid, which yielded only L-cystine.

Conclusions. The investigation of the interaction of L-cysteine with DMSO by FTIR spectroscopy showed, that an oxidative formation of L-cystine takes place in mild conditions, dimethyl sulfide and water being the other products of reaction. Also conditions of the reaction appear to be determining on the depth of oxidation and final products formation.

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