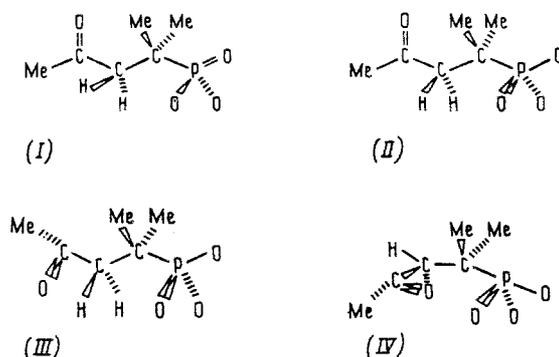


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The drug, dimephosphone, in aqueous media has two most probable conformers. The formation of hydrogen bonds with water and complexes with  $\text{SnCl}_4$  in acetonitrile involves the phosphoryl oxygen atom. Complexation favors some of the dimephosphone conformers.

In a previous communication [1], we examined the structure of the drug, dimephosphone (DMP), using IR and Raman spectroscopy and calculated data derived from the molecular mechanics and dipole moment methods. Conformers (I)-(IV) were shown to be most probable in the liquid phase (Fig. 1).



However, DMP as a drug is used as a 15% aqueous solution. In a polar medium, the more polar conformers (I), (III), and (IV) should achieve a quantitative advantage but the water molecules are capable of a specific interaction with DMP and, a priori, it is difficult to predict the favored form. Thus, we undertook a special IR and Raman spectral study of DMP in aqueous media as well as of DMP solution with complexing agents imitating specific bonding with DMP. These experiments were carried out on a Bruker IFS-113 spectrometer in cells with  $\text{GaF}_2$  windows and KRS-5 and RTI-30 spectrometers with an  $\text{Ar}^+$  laser as the source of excitation of the Raman lines.

Figure 1 gives the IR spectrum of liquid DMP (a) and the difference spectrum of its aqueous solution (b). In the latter case, a strong  $\nu\text{OH}$  signal is found at  $\sim 3450\text{ cm}^{-1}$ . The most likely reason for this finding lies in changes in the spectral indices of water upon contact with DMP. Complete compensation for these changes cannot be achieved by subtraction of the spectrum of pure water. The same factor complicates analysis of the spectrum at  $1630\text{-}1660\text{ cm}^{-1}$ , in which the water deformation bands appear. The  $\nu\text{C}=\text{O}$  band is virtually unchanged. On the other hand, very strong changes in the  $\nu\text{P}=\text{O}$  are clearly seen with a shift from  $1245$  to  $1203\text{ cm}^{-1}$ . This shift indicates hydrogen bonding of water molecules with the phosphoryl oxygen atom [Scheme 1, (IIa)].

Another feature of the spectrum of the aqueous solution of DMP is the appearance of a weak diffuse band at  $\sim 2600\text{ cm}^{-1}$  (Fig. 1b).

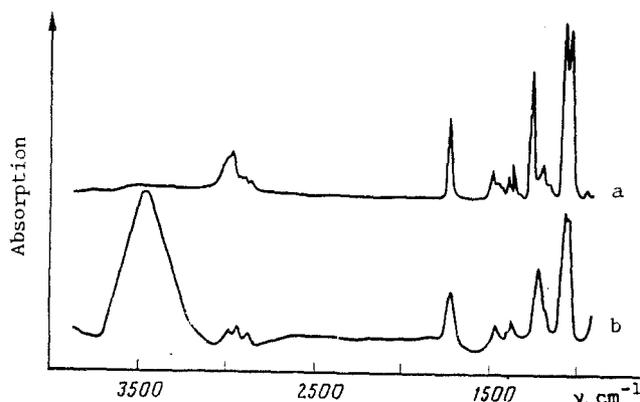
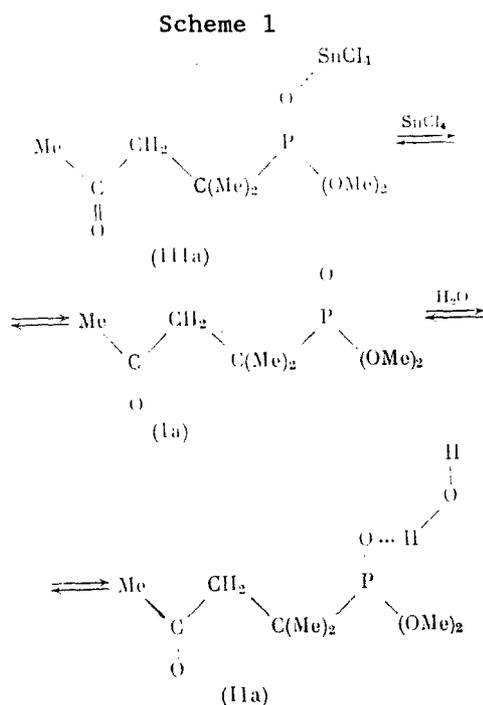


Fig. 1. IR spectrum of liquid DMP (a) and difference spectrum of its aqueous solution (b).



As noted above, there were no signs of an interaction of DMP with water at the carbonyl group. Probably, the carbonyl group cannot disrupt the network of the hydrogen bonds of water due to its reduced proton-acceptor capacity. On the other hand, there is a change in the ratio of the intensities of the components comprising the  $\nu_{C=O}$  band upon the dissolution of DMP [1]. This finding indicates that the interaction of water molecules with the P=O bond leads to changes in the conformational composition of DMP. Indeed, in our previous work [1], we showed that the  $\nu_{C=O}$  frequencies in conformers (I) and (II), which are identical (calculated frequency  $1728\text{ cm}^{-1}$ , Table 1), differ from the corresponding values for (III) ( $1721\text{ cm}^{-1}$ ) and (IV) ( $1717\text{ cm}^{-1}$ ). Thus, the changes in the occupancies of the conformers should lead to changes in the ratio of the intensities of the components of the  $\nu_{C=O}$  band [1]. Figure 2a gives the change in the Raman  $\nu_{C=O}$  line relative to the dilution by water. A decrease in the intensity of the high-frequency component occurs with decreasing DMP concentration, indicating a decrease in the fraction of forms (I) and (II). An analogous conclusion follows from an analysis of the spectrum at  $800\text{-}600\text{ cm}^{-1}$  (Fig. 2b). Here, we encounter the stretching ( $\nu_{P-C}\ 700\text{ cm}^{-1}$ ) and deformation vibrations ( $\delta_{OCC}\ 600\text{ cm}^{-1}$ ) of the conformers examined [1]. The fraction of conformers (I) and (II) markedly decreases with increasing dilution as seen in Fig. 2b, which gives the change in the corresponding Raman lines of DMP depending on its concentration. In our previous work [1], we proposed that the biological activity of DMP may be related to its capacity for complexation. Conformer (IV) may act as a bidentate ligand, while (I)-(III) may

TABLE 1

Conformer (I)	$\nu_{C=O}$		$\nu_{C-C}$			
(I)	1728		833		794	
(II)	1728		833		794	
(III)		1724			812	778
(IV)		1717		823		785
*	1720	1711	842 sh	825	796	774
**	1720	1711	842	825 sh	792	763

\* Solution of DMP in  $\text{CH}_3\text{CN}$ .

\*\* Solution of DMP in  $\text{CH}_3\text{CN}$  with  $\text{SnCl}_4$ .

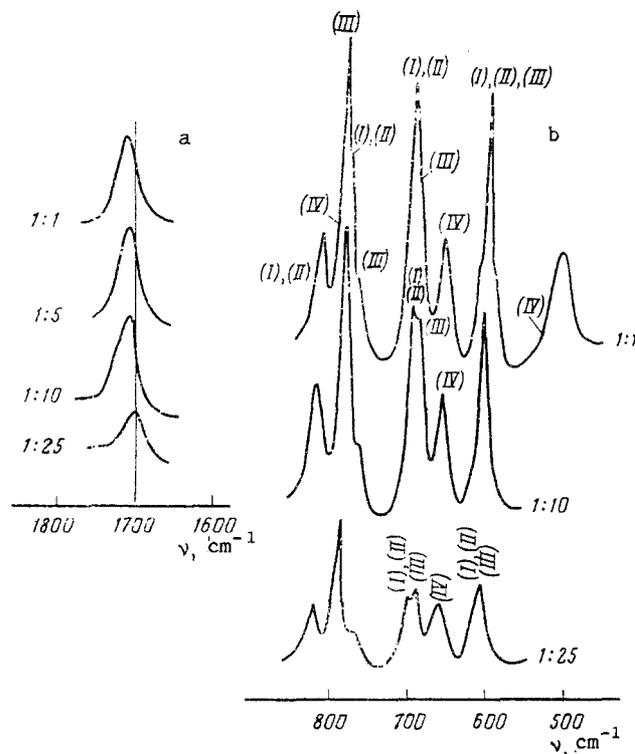


Fig. 2. Change in the Raman lines upon the dilution of DMP by water. The vibrations were assigned to conformers (I)-(IV) according to our previous data [1].

act as monodentate ligands. Thus, these experiments indicate that an aqueous medium stabilizes two conformers: (IV), which is disposed to bidentate, apparently selective bonding with target molecules, and (III), which tends to monodentate bonding.

In order to explain the participation of the functional groups of DMP in complexation processes, we studied the reaction of DMP and  $\text{SnCl}_4$ , which was previously dissolved in acetonitrile. Thus, the DMP molecules in these experiments are also in a polar environment (it proved impossible to dissolve  $\text{SnCl}_4$  in aqueous solution due to their chemical reaction). As in the case of the aqueous solution, a shift of the phosphoryl  $\nu_{P=O}$  band toward lower frequencies to  $1192\text{ cm}^{-1}$  ( $\Delta\nu = 50\text{ cm}^{-1}$ ) is observed upon the addition of  $\text{SnCl}_4$  to an acetonitrile solution of DMP (Fig. 3). This finding indicated the participation of the phosphoryl group in complexation in this case as well. The  $\nu_{C=O}$  band is not shifted, i.e., the  $C=O$  group does not take part in the complexation with  $\text{SnCl}_4$  by analogy to the case with water. However, Fig. 4 shows that the low-frequency component of the  $\nu_{C=O}$  doublet at  $1711\text{ cm}^{-1}$  decreases in intensity upon the addition of the complexing agent. As previously, this finding may be related to a shift in the conformational equilibrium. In this case, the complexation process, taking place at the phosphoryl oxygen atom, leads to an increase in the content of conformers (I) and (II), which contribute to the high-frequency  $\nu_{C=O}$  component. Thus, this situation differs from that

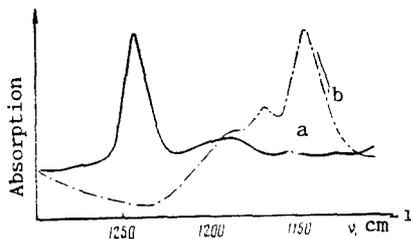


Fig. 3

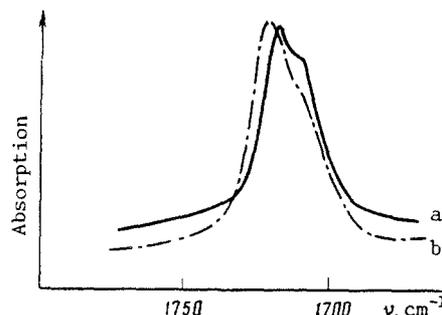


Fig. 4

Fig. 3. IR spectra in the vicinity of  $\nu$ P=O: a) DMP, b) solution of DMP in acetonitrile with  $\text{SnCl}_4$ .

Fig. 4. Change in the  $\nu$ C=O band: a) DMP, b) DMP complexed with  $\text{SnCl}_4$ .

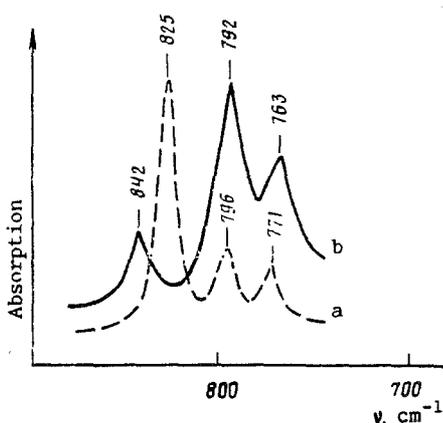


Fig. 5. IR spectra: a) DMP, b) DMP complexed with  $\text{SnCl}_4$ .

found in aqueous solution, in which forms (III) and (IV) are stabilized. Additional information on the equilibrium may be obtained by studying the  $\nu$ C-C band at 850-760  $\text{cm}^{-1}$ , which displays conformational sensitivity [1] (Fig. 5). Here, on addition of  $\text{SnCl}_4$  the band at 825  $\text{cm}^{-1}$  virtually disappears. Table 1 shows this band should be assigned to conformer (IV). Hence, a monodentate complex of DMP and  $\text{SnCl}_4$  in conformations (I), (II), and, possibly, (III) is the most probable type of complexation.

Thus, the phosphoryl groups of DMP groups are primarily involved in specific interactions in both aqueous and polar media. This may indicate a separation of the function of the P=O and C=O bonds in the treated organism. The C=O groups are predominantly free for the target objects. The P=O groups, which are blocked, for example, by water molecules, may interact only with competitive sites.

#### LITERATURE CITED

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