A STUDY OF IMIDAZOLE BY THE PROTON MAGNETIC RESONANCE METHOD

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The concentration dependence of the chemical shifts of the protons of imidazole in six polar organic solvents and water has been studied. In aqueous solutions an exchange of the NH protons between the imidazole and the water molecules takes place. In organic solvents, the position and half-width of the NH line of imidazole depend on the concentration. With an increase in the concentration, this line shifts in the downfield direction. The shift Δ (1 ppm for a solution of imidazole in DMSO) may be due to the formation of an ordinary hydrogen bond $(>NH\cdots N\leqslant)$ between the imidazole molecules.

Imidazole and its derivatives have been widely studied by the PMR method. The main attention of the authors of the majority of the relevant papers is devoted to the CH protons of the imidazole nucleus [1-5]. Zimmerman et al. [6-8] have studied the dependence of the position of the line of the NH proton on the concentration of imidazole in acetone and have observed a change in the chemical shift δ over a range of 5 ppm with a variation of the concentration. This change is due to the formation of a hydrogen bond between the NH proton of one imidazole molecule and the nitrogen atom of another. The large shift of the NH line in the downfield direction in concentrated solutions resulting from the formation of such a hydrogen bond, in contrast to the chemical shifts usually observed in such cases, is due to a peculiarity of the hydrogen bond considered. The state of the proton in this hydrogen bond is composed of the states of two limiting structures: $(>NH\cdots N\leqslant)$ and $(>\overset{-}{N}\cdots H\overset{+}{N}\leqslant)$, which are represented with approximately equal weights. In the polar limiting structure $(>\overset{-}{N}\cdots H\overset{+}{N}\leqslant)$, the proton is present in the neighborhood of a nitrogen atom that possesses a deficiency of electrons. In this position the proton must be subject to weak screening, and since this structure takes part to the extent of almost one half in the hydrogen bond, the NH signal must be present in an unusually weak field.

We have studied the dependence of the chemical shifts of the protons of imidazole on the concentration in six polar organic solvents and in water. Figure 1 shows the PMR spectra of imidazole at various concentrations in dimethyl sulfoxide (DMSO). The PMR spectrum of imidazole contains three absorption lines, which relate to the protons present in positions 4(5), 2, and 1. With a decrease in the concentration there is a shift of the line of the NH proton in the upfield direction and a considerable broadening of it; at the same time, the absorption line of protons 4 and 5 does not change its position, and the line of proton 2 shifts in the upfield direction by approximately 0.1 ppm. Figure 2 shows the dependence of the chemical shifts of the protons of imidazole on the concentration for organic solvents. The dependence of the chemical shifts of the CH protons on the concentration is given only for solutions of imidazole in DMSO, since their values are approximately the same for all the solvents considered. The ranges of the change in the chemical shift of the line of the NH proton with a change in the concentration are different for different solvents. For the case of imidazole in acetone, this range is 1.5 ppm and in DMSO it is 1 ppm. The unusual behavior of the line of the NH protons with a change in the concentration for various solvents can be ex-

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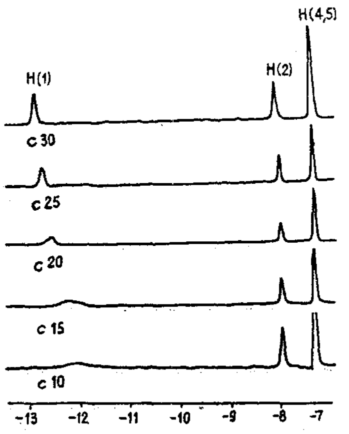

Fig. 1

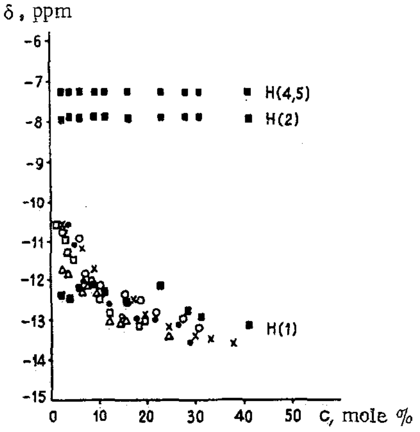

Fig. 2

Fig. 1. PMR spectra of imidazole at various concentrations in DMSO; c represents the concentration of imidazole, mole %.

Fig. 2. Dependence of the chemical shifts of the protons of imidazole on its concentration in various solvents: ×) DMEA; △) acetone; ●) acetonitrile; ○) tetraethylene sulfone; □) nitromethane; ■) DMSO.

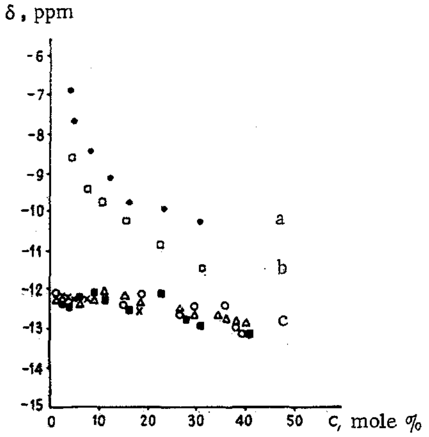

Fig. 3

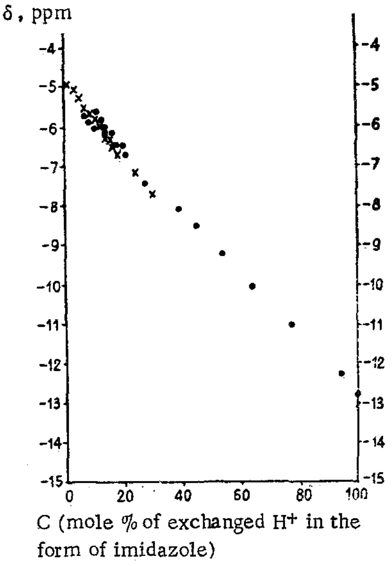

Fig. 4

Fig. 3. Dependence of the chemical shift of the NH proton on the concentration of imidazole in DMSO for solutions purified in different ways. Different symbols denote results obtained in different series of experiments. The samples for the dependences denoted by circles were prepared in a chamber filled with Ar.

Fig. 4. Dependence of the observed chemical shift of the line of the NH proton on the concentration of imidazole in water.

plained by the fact that imidazole forms hydrogen bonds of the type $>NH\cdots X$, where X is a molecule of the solvent. However, it has been noted that the position of the line of the NH proton depends on the conditions under which the sample was prepared. Figure 3 shows the dependence of the chemical shift of the line of the NH protons on the concentration of imidazole in DMSO for the solvent and imidazole purified in different ways. It can be seen from the figure that with a decrease in the amount of impurities in the solution (the amount of impurities decreases from a to c) the line of the NH proton of imidazole shifts in the downfield direction, and the dependence of the chemical shift on the concentration becomes considerably less. In view of this, it may be assumed that the change in the position of the line of the NH proton with a change in the concentration takes place because of foreign impurities present in the solvent and in the imidazole itself. Impurities of the type of RH, which may be responsible for the change in the position of the NH line must contain protons capable of exchange. One of the main RH impurities is water, the influence of which has been studied in the present work.

The PMR spectrum of an aqueous solution of imidazole contains one common line relating to the NH protons and to the protons of the water. Figure 4 shows the dependence of the chemical shift of this line (δ_{obs}) on the concentration of imidazoline in water. The relationship marked by the crosses in the figure relate to solutions of imidazole in water and that marked by dots to a mixture of imidazole and water dissolved in DMSO. If δ_{H_2O} and δ_{NH} denote the chemical shifts for the protons of pure water and the protons of the NH group in imidazole and p_{H_2O} and p_{NH} the fractions of these protons, the relationship shown in Fig. 4 can be written in the form

$$\delta_{obs} = p_{H_2O}\delta_{H_2O} + p_{NH}\delta_{NH}.$$

This equation describes the transition of a proton between two positions: in the water and in the imidazole. On comparing the relationships shown in Figs. 2 and 4, it may be assumed that the value of the chemical shift of the line of the NH proton of imidazole in dilute solutions must lie in the region of -12 ppm. An accurate value of the chemical shift of the line of the NH proton cannot be given because two types of hydrogen bonds may be formed in solution. At low concentrations hydrogen bonds are formed mainly between the imidazole and the solvent ($>$NH····X), and at high concentrations predominantly between the molecules of imidazole ($>$NH····N$\lessdot$). From the results obtained in this work it follows that the change in the position of the NH line over a very wide range (5 ppm) with a change in the concentration, as shown by Zimmerman et al. [6, 7] is due to foreign impurities present in the imidazole solutions.

EXPERIMENTAL

The PMR spectra were obtained on a TsLA spectrometer with a working frequency of 40 MHz at 23°C. The calibration of the spectra was carried out by means of a 3G-11 device. The chemical shifts were measured relative to the line of the CH (4, 5) protons, no change in the position of which was observed with a change in the concentration. TMS was used to determine the position of the line of the CH(4,5) protons as an internal standard. The chemical shift (δ) was determined from the formula

$$\delta = \frac{H_{abs} - H_{st}}{H_{st}} \cdot 10^6 \text{ ppm},$$

and was measured with an accuracy of ±2%. The filling of the tubes was performed in an atmosphere of air, with the exception of the case specially mentioned (Fig. 3). The purification of the imidazole and DMSO for the relationships shown in Fig. 3 was carried out in three ways: a) commercial DMSO and commercial imidazole (99%) were dried in a vacuum desiccator at 60°C; b) the DMSO was distilled in vacuum and the middle fraction was collected, and the imidazole was dried in a vacuum desiccator at 60°C; c) the DMSO was distilled in vacuum and the imidazole was subjected to vacuum distillation. The purification of the other five solvents was carried out by published methods, and the imidazole was previously subjected to vacuum distillation.

The samples for the relationship shown by dots in Fig. 4 were prepared in the following way: first solutions with different ratios of water to DMSO were prepared in amounts of 2 ml each, and then equal amounts of imidazole were dissolved in them so that 5 M solutions were obtained.

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