

APPLICATION OF PARAMAGNETIC ADDITIONS TO THE STRUCTURE DETERMINATION OF SOME PYRAZOLES BY NMR.

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When assigning NMR lines of complex organic compounds there often occur some difficulties. The inclusion of an organic molecule in the first coordination sphere of a paramagnetic ion results in considerable changes in its NMR spectrum. These changes are due to additional local magnetic fields generated by the unpaired electrons of the central ion. Eaton (1) took advantage of NMR spectra peculiarities of paramagnetic complexes to measure spin-spin coupling constants in condensed aromatic and polyenic hydrocarbons, which were introduced as substituents to nitrogen atoms of Ni(II) aminotroponimineate. At the same time many organic substances (heterocyclic compounds, amines, alcohols, ethers etc.) are capable of forming complexes with paramagnetic salts directly. Kluiber and Horrocks (2,3) made use of this to assign lines in the NMR spectra of pyridine - and quinoline-N-oxides. For this purpose they studied the dependence of line positions on the amount of Ni(II) or Co(II) acetylacetonates, added to the solutions. A simple method based on complex formation for the determination of organic compound structures and for the assignment of lines in their NMR spectra is proposed here.

On the condition that molecule exchange between the first coordination sphere of the ion and the bulk medium is sufficiently fast the observed spectrum is the average of the paramagnetic and diamagnetic environments:

$$\delta = \delta_p \times p + \delta_d \times d$$

where δ , δ_p and δ_d are the shifts in the averaged spectrum, in the spectrum of complex and that of the diamagnetic compound respectively; X_p and X_d

-being the mole fractions of the substance in complex and in solution. Under these conditions the line width is given by a similar equation (4):

$$\Delta\nu = \Delta\nu_p X_p + \Delta\nu_d X_d$$

where $\Delta\nu$, $\Delta\nu_p$ and $\Delta\nu_d$ are line widths in the averaged spectrum, in the spectrum of complex and that of the diamagnetic compound respectively. As a rule, the line width in a complex is much greater than in a diamagnetic compound. If the electronic relaxation time of an ion is very short (Ni^{2+}) $\Delta\nu_p$ is given by

$$\Delta\nu_p = A r^{-6} + B (\Delta\delta)^2$$

Here r is the distance between the resonating proton and the paramagnetic ion, $\Delta\delta = \delta_p - \delta_d$ - the proton contact shift, A and B are constants for the particular complex at a constant temperature.

In accordance with the equations given above one can easily and unambiguously assign NMR lines by measuring the additional line shifts and broadenings and by estimating the distances r , if the structure of a paramagnetic complex remains unchanged at different ligand concentrations.

This method has been applied to assign NMR lines and to determine the structures of some substituted pyrazoles. To avoid pseudocontact contributions in the observed additional shifts, $NiBr_2 \cdot 3H_2O$ was chosen as a complexing agent (3) (the anhydrous salt does not give any complexes). The mole fraction of the salt in the solutions under investigation did not exceed 5×10^{-3} with regard to pyrazole. NMR spectra were recorded on the JNM-4H-100 spectrometer at room temperature with TMS as an internal reference. CCl_4 and $CHCl_3$ were used as solvents

The spectra of 1,3,5-trimethylpyrazole solutions without (a) and with $NiBr_2 \cdot 3H_2O$ (b) are shown in Fig.1. Here the main difficulty is to assign the proton line of the methyl groups in the positions 3 and 5, the shifts being different by 0.03 ppm (CCl_4). As is seen from Fig.1b, the complex formation leads to the displacement of these lines in opposite directions and to their

showing different broadenings. The comparison of the contact shifts, the line widths and the distances from the central ion for the protons of 3- and 5-CH₃ and 4-H shows that the broadening of the CH₃ lines is determined by dipole-dipole interaction. Therefore it is obvious that the most narrow line in the spectrum corresponds to the remotest 5-CH₃ group. Thus, in the diamagnetic compound the 3-CH₃ resonates in a higher field than the 5-CH₃.

In a similar way the lines at 7.46 and 7.24 ppm (in CHCl₃) in the spectrum of 1-methylpyrazole were referred to 3- and 5-H respectively. Indeed, the complex formation results in a smaller additional shift and in a greater enlargement of the line at 7.46 ppm and hence it should be referred to 3-H.

It is known, that the structure determination of unsymmetrically substituted pyrazoles involves great difficulties even for NMR spectroscopy (5). We have checked on the efficiency of the proposed method by the NMR identification of the following isomers: 1,3- and 1,5-dimethylpyrazole, 1-methyl-3-ethynyl- and 1-methyl-5-ethynylpyrazole. The spectra of dimethylpyrazoles are shown in Fig.2 and Fig.3. The additional shift of the 4H proton is practically equal or slightly greater than that of another pyrazole ring proton and hence the contact contribution in the line width for the 4-H is equal or more than the same contribution for the 3- or 5-H. In the spectrum of one of the isomers (Fig.2) the line broadening for the 4-H is much smaller than that for the other proton. This is only realized in the 1,5-isomer, for which $r_{3H}^6 < r_{4H}^6$. Similar considerations for the methyl groups lead to the same conclusion independently. Thus, our results confirm that the low-boiling isomer (b.p.138°C) is actually the 1,3-isomer (6).

Unfortunately not all of the pyrazole derivatives form complexes with NiBr₂. Of the two isomers 1-methyl-3-ethynylpyrazole and 1-methyl-5-ethynylpyrazole (b.p.50-51°C/13 mm; 88-89°C/13 mm), synthesized by us, only the low-boiling isomer formed the complex, and could be identified as the 1-methyl-5-ethynylpyrazole. We found that the chemical shifts of the acetylenic protons in the positions 3 and 5 differed noticeably and had the values 3.07 and 3.57 ppm (in CHCl₃) respectively. On this basis we could assign the lines of the acetylenic

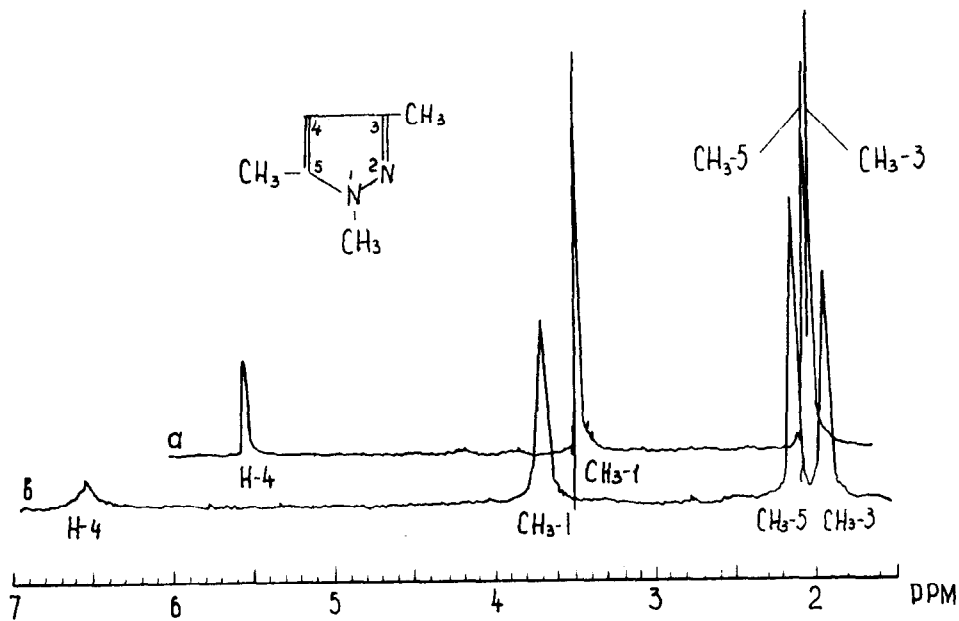


FIG. 1

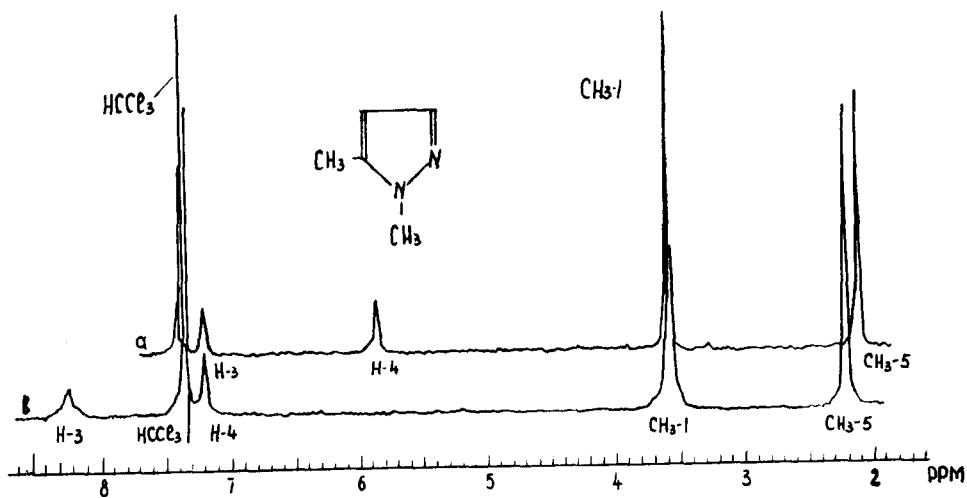


FIG. 2

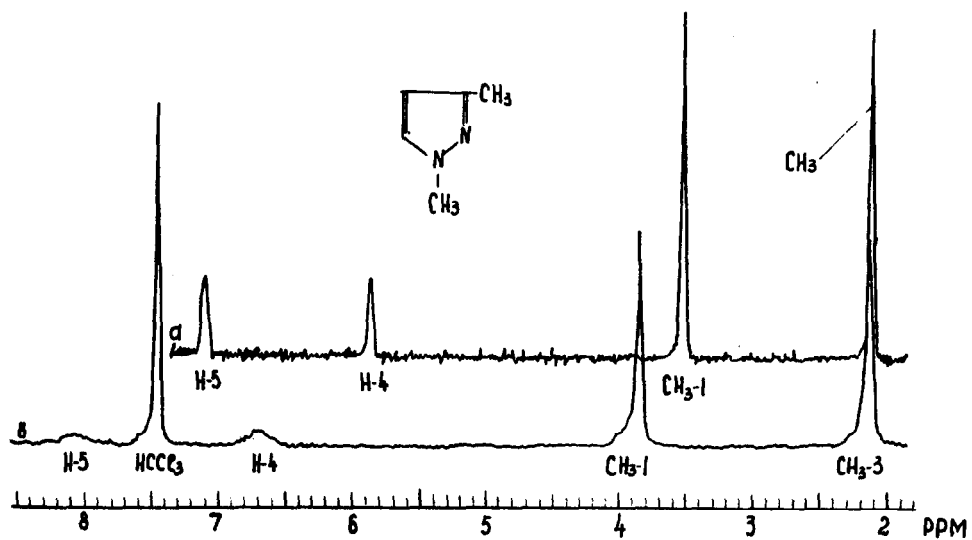


FIG.3

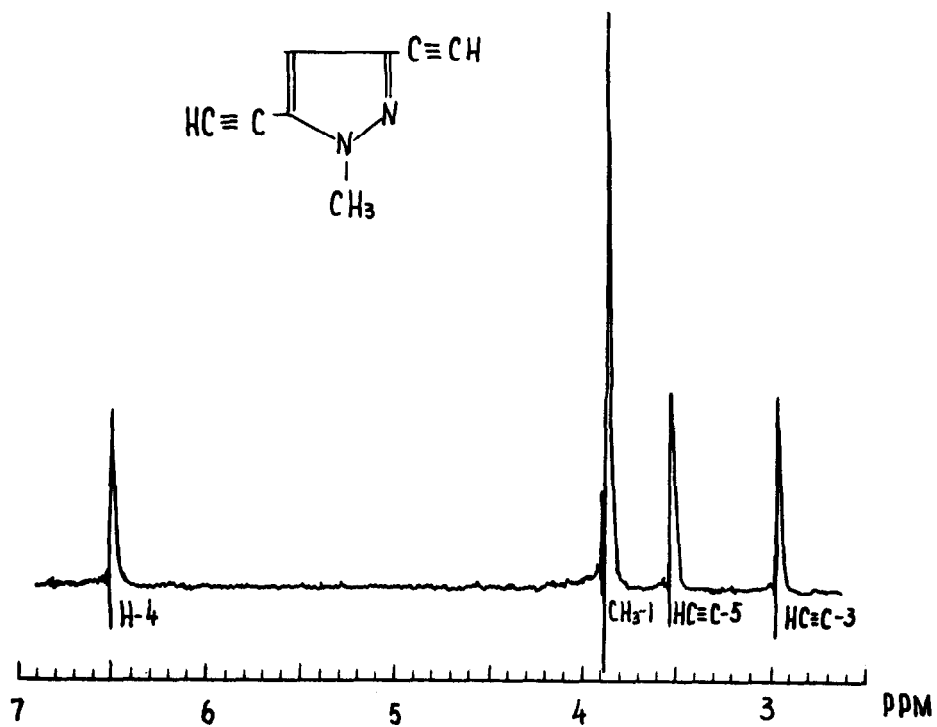


FIG.4

protons in 1-methyl-3,5-diethynylpyrazole (Fig.4).

The methyl derivatives of pyrazole were obtained by methods described in the literature. The pyrazolylacetylene syntheses will be described in another paper. The isomeric purity was controlled by means of gas-liquid chromatography.

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