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^{1}H AND ^{13}C NMR STUDY OF TAUTOMERISM IN AZOLES—I

PROTON TRANSFER IN THE ABSENCE OF SOLVATION

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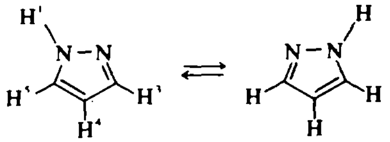
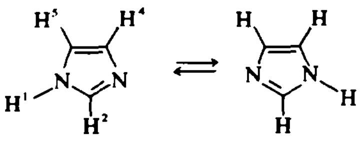
Abstract—^{13}C NMR is used to show that proton transfer in concentrated (1–2 M) imidazole or pyrazole solutions proceeds through self-association of solute via an intermolecular mechanism. The results are described in terms of a hydrogen bond potential with two minima. A tunnel mechanism is assumed to operate alongside the activation mechanism in the elementary step.

Although proton transfer and H-bonding in azoles have been dealt with in numerous papers (see, e.g. Refs. 1–4), tautomeric species have not been identified in solutions of imidazole or pyrazole by NMR methods. The prototropic rearrangement rates are so high that the molecules retain, in ^{1}H NMR terms, their effective C_{2v} symmetry in a very wide temperature range. Positions 4,5 and 3,5 are isochronous in imidazole and pyrazole respectively, hence the A_2X spectra. The ^{13}C NMR technique provides a wider range of the chemical shifts, and has allowed us to study the proton exchange kinetics in the heterocycles under discussion.





To slow down the rearrangements so that they may be followed by NMR, the temperature should not exceed −100°C. We have used ether/tetrahydrofuran 1 and ether-acetone 2 mixtures. To raise the pyrazole self-association to a significant extent, and shorten the accumulation time of ^{13}C NMR experiments, we have chosen concentrations of 1 and 2 M.

^{13}C NMR pyrazole spectra are shown in Fig. 1. The low-temperature spectrum obtained in the mixture 1 at −118°C consists of three well-resolved signals due to the nuclei C-3, C-5, and C-4 (Fig. 1a).†

Increasing the temperature raises the proton exchange rates, to broaden the signals and make them coalesce at −100°C (Fig. 1b). The further heating accelerates the rearrangement and narrows the line to its natural width (at −40°C, Fig. 1d). The C-4 signal width is not affected in the temperature region under study, so contribution of the other relaxation mechanisms is constant therein. Similar effects are observed in imidazole.

The usual technique[5] (an approximation involving equally-populated non-coupled AB states) has given the proton exchange rate constants at various temperatures. In a striking manner, the logarithmic constant vs temperature plot is not of the Arrhenius shape (Fig. 2). The non-linearity may be due to various factors such as variability of the reaction mechanism, a temperature-dependence of the reaction enthalpy, and others. These, however, could hardly play the role in a system where the limiting structures are equivalent while the number of molecular types involved is limited, therefore the non-linearity may be assumed to be due to a tunnel effect operating during the initial proton transfer. The curve may suggest that starting from −105°C the barriered transfer begins giving way to a non-activation tunnel penetration.[6] This agrees with the decrease in E_a^{exptl} (from 4·85 down to 1·65 kcal mole^{-1}) and the negative compensation effect of the frequency factor in Table 1 (the pre-exponent varies in a parallel with the energy of activation).[7]

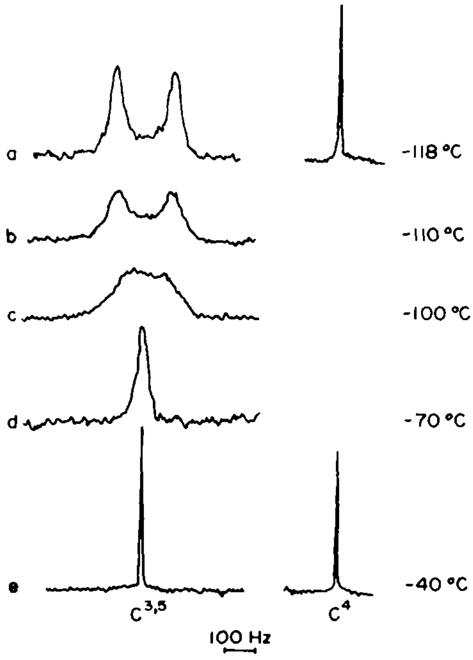


Fig. 1. Temperature dependence of the ^{13}C NMR C-3, C-5 and C-4 signals of pyrazole (operating frequency 22·635 MHz).

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†The C-3 and C-5 assignments are arbitrary.

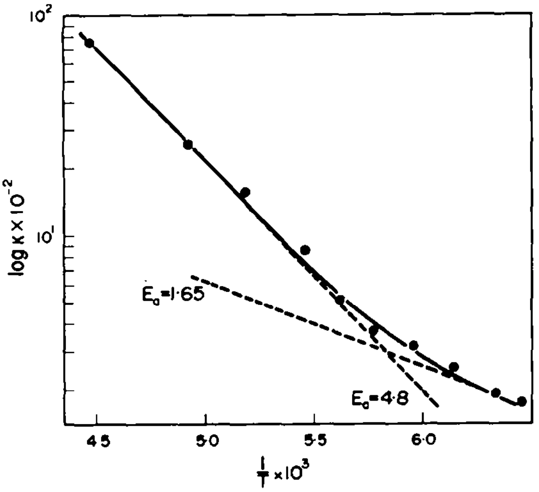

Fig. 2. Arrhenius plot for pyrazole.

Table 1

t (°C)	κ (sec^{-1}) $\left(A \,.\, \exp \frac{E_a}{RT}\right)$	$E_a \left(\frac{\text{kcal}}{\text{mole}}\right)$	A (sec^{-1})
−70	$2{\cdot}55 \times 10^3$	4·8	$3{\cdot}90 \times 10^8$
−95	$5{\cdot}10 \times 10^2$	3·5	$1{\cdot}16 \times 10^7$
−118	$1{\cdot}70 \times 10^2$	1·65	$3{\cdot}55 \times 10^4$

Zimmermann[8] assumed that the tunnel mechanism operated in removing degeneration of the oscillation terms in an almost symmetrical double-well potential of the intermolecular N–H ··· N bond in imidazole. Our data agree both with the double-well potential assumption and with a significant role played by the tunnel effect in the transfer between the minima of this potential.

Consequently, some conclusions on molecular mechanism of the transfer may be made. In imidazole, a proton may be tunnelled only via the intermolecular hydrogen bond N–H ··· H. Intramolecular tunnelling is incompatible with the imidazole geometry. Since the imidazole exchange and activation parameters are close to those of pyrazole the exchange in pyrazole may also be assumed to be mostly intermolecular.

The NH-deshielding shown by the ^{1}H NMR spectra of the heterocycles at lower temperatures also shows that the equilibrium is shifted towards hydrogen-bonded associates (Table 2).

Table 2

t°C	δ_{NH} imidazole	 pyrazole
+50	8·6	11·7
0	9·2	12·2
−30	9·5	12·8
−90	10·5	14·1

Therefore, concentrated solutions of the azoles in 1 or 2 may be described in terms of the self-association model proved for diluted solutions in CCl_4 earlier.[9]† A natural assumption is that proton transfer occurs via a collective mechanism in which pyrazole trimers or imidazole oligomers participate (Scheme 2a and 2b).

Unlike the cyclic pyrazole associates, ionogenic intermediates should be considered to operate in the open-chain imidazole associates (Scheme 2b).

Zundel,[12] however, has already noted that this assumption rather disagrees with the experimental data; there are no protonated imidazole bands in the IR spectra. The hypothesis of disproportionation and the resulting ionic structures may be avoided by assuming that cyclisation does take place by way of interaction of oligomer chains and that the transfer is implemented within the cyclic structures. The cyclisation may be favoured by plane-to-plane interactions.[11]

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†Significant self-association was reported for solutions in high-solvating solvents such as acetone and dioxan.[1,10] A ring-to-ring self-association was observed in dimethyl sulphoxide.[11]

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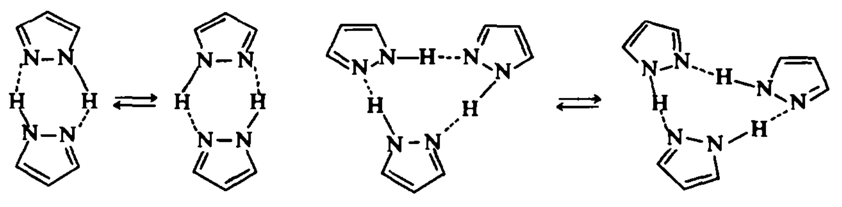
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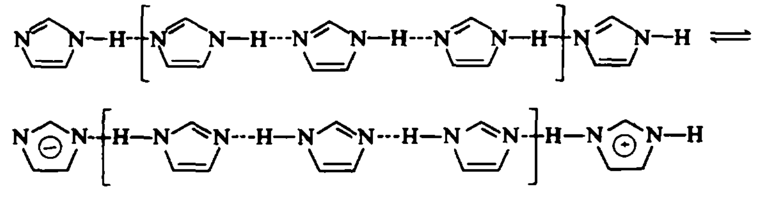
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