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

PROTON TRANSFER IN KETONE SOLVENTS

A. N. NESMEYANOV, E. B. ZAVELOVICH,* V. N. BABIN,
N. S. KOCHETKOVA and E. I. FEDIN
Institute of Organo-Element Compounds of the Academy of Sciences of the U.S.S.R., Moscow B-312, U.S.S.R.

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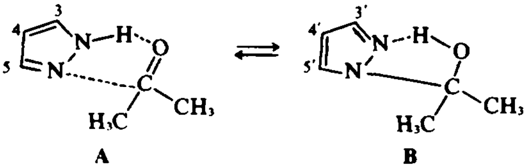
Abstract—Prototropic tautomerism in azoles solvated by ketone solvents has been studied by ^{1}H and ^{13}C NMR. Spectral changes due to addition of the heterocycle NH to the ketones are independent of changes due to the degenerate prototropic rearrangement occurring in the solute. The solvent effect causes lowering of the fraction of self-associated molecules.

Fast proton transfer in ketone solvents such as acetone or methyl ethyl ketone is accompanied with a slow reversible addition of the azole NH group to the carbonyl group of the solvent. An example for pyrazole has been reported.[1]



The equilibrium scheme is based on ^{1}H NMR spectra of some azoles in acetone. However, the spectral diagrams were reported[1] only for the pyrazole site of the adducts (carbinols of the type B).

We wanted to investigate whether the solvent affects the prototropic rearrangement mechanism, and to identify structures of the adducts. We have studied the temperature dependence of ^{1}H and ^{13}C NMR spectra of pyrazole in solvent systems such as diethyl ether/acetone **1** and diethyl ether/methyl ethyl ketone **2**. Fig. 1 presents the temperature dependence of the ^{13}C NMR spectrum of pyrazole dissolved in **1**. Even at −30°C, there are measurable signals associated with 2-(1-pyrazolyl)propan-2-ol equilibrated with pyrazole. The signals at 108·4 and 95·8 ppm belong to the nuclei C-3′ and C-5′ which become diastereotopic after the aliphatic substituent has added to the nitrogen. The nuclei C-4 and C-4′ are shielded identically. The singlet at −56·7 ppm is not split when the proton-decoupling field is switched off. Consequently, it belongs to the central carbon of the aliphatic substituent in the pyrazole ring of the adduct B. The carbonyl carbon signal of acetone lies at much lower fields, 176·2 ppm. The methyl signal of B arises near the acetone methyl signals (0·9 ppm). In a proton undecoupled spectrum, the ring carbon signals of pyrazole and 2-(1-pyrazolyl)-propan-2-ol are split by the adjacent protons and give doublets; the methyl carbons of the adduct and of acetone give quadruplets.

A decrease in the temperature makes the spectrum of pyrazole A undergo the same transformations as with the THF/ether mixture.[2] Signals of the isochronous C-3 and C-5 nuclei start broadening. The coalescence temperature (−115°) is, however, lower than it is in the mixture **1**. The difference may be assigned to traces of water present in acetone. Even at as low as 10^{-6} M admixtures of water are known[3] to accelerate exchange processes considerably. Below −115°, the C-3, C-5 signals is split, at −138° the spectrum consists of two well-resolved singlets. (Fig. 2). They are distanced by 220 Hz, the same distance was observed in the ether/THF mixture. Alongside with the

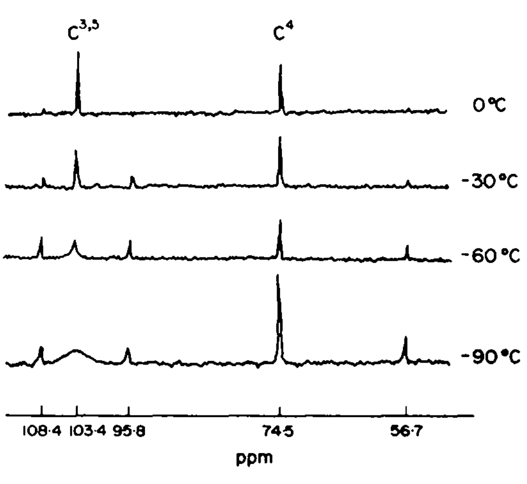


Fig. 1. The temperature dependence of ^{13}C-NMR spectra of the pyrazole in mixture diethyl ether/acetone (operating frequency 22·635 MHz).

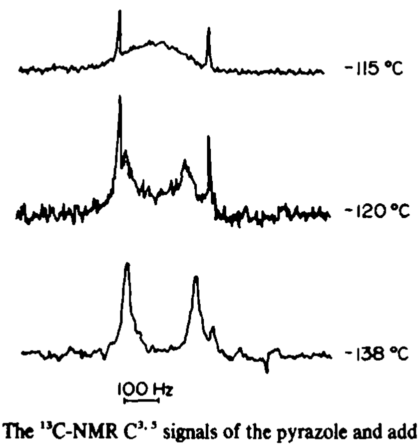


Fig. 2. The ^{13}C-NMR $C^{3,5}$ signals of the pyrazole and adduct B at low temperature (operating frequency 22·635 MHz).

thermal alterations, amplitudes of the adduct B signals rise, the C-3′ and C-5′ signal widths being constant at any of the temperatures studied. This proves once more that the C-3, C-5 signal broadenings are caused by an exchange process.

Consequently, spectral changes caused by addition of pyrazole to the carbonyl group of acetone do not depend on the changes caused by kinetics of the prototropic tautomeric rearrangement. The addition reaction affects the proton exchange in associates by just lowering the fraction of self-associated molecules.

Thermodynamical parameters of the reaction have been measured by studying temperature dependences of ^{1}H NMR spectra of pyrazole in acetone (Figs. 3 and 4). The spectra contain not only the pyrazole signals but also signals of methyl groups of the aliphatic substituent in the adduct **B**. The pyrazole/2-(1-pyrazolyl)propan-2-ol intensities ratio found for the respective signals has given us the equilibrium constant for the reaction at various temperatures (Fig. 5). The resulting enthalpy is 2·48 kcal/mole. The signal at 7·1 ppm (obtained at −60°C, Fig. 3) has been assigned to the hydroxyl proton. The assignment agrees with the ^{13}C NMR data obtained for the central atom in **B**. A noticeable OH proton deshielding observed at lower temperatures suggests that the proton participates in the formation of not only intra- but also intermolecular bonds. Protons involved in intramolecular O–H-bonding are known to absorb at considerably lower fields,[4] therefore contribution of intramolecular bonds of the O–H···N type may be assumed to be not so high. The fact that OH and pyrazole NH proton signals can be observed simultaneously in the spectrum demonstrates that the slow addition of pyrazole to the acetone carbonyl is not accompanied by a fast proton exchange between the non-equivalent positions.

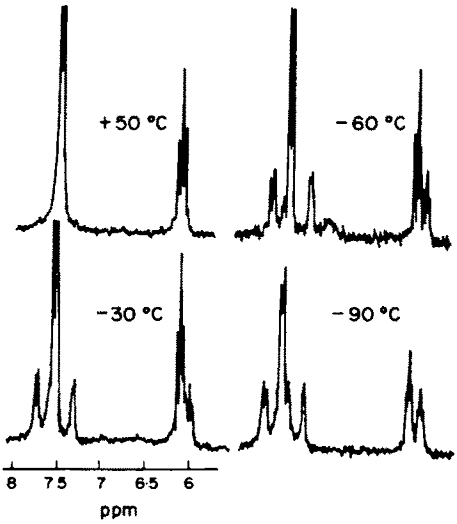


Fig. 3. The temperature dependence of ^{1}H NMR spectra of the pyrazole in acetone.

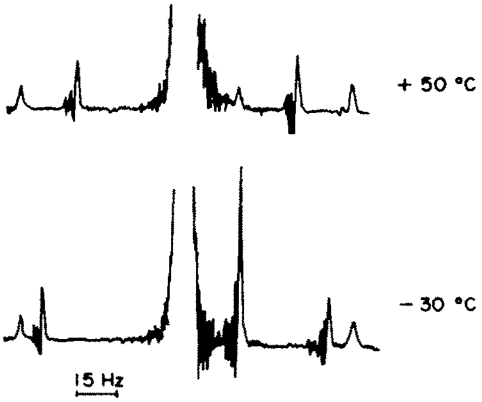


Fig. 4. ^{1}H NMR signals of the methyl groups of the acetone and adduct B.

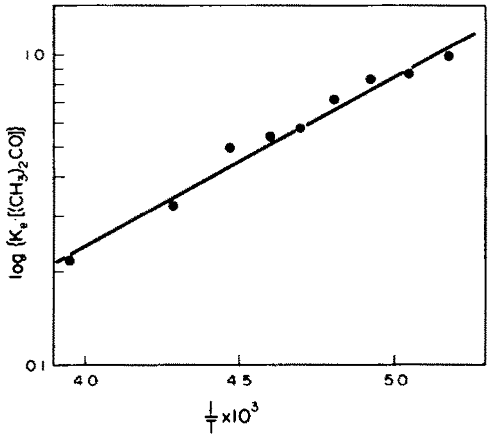


Fig. 5. Equilibrium constant for acetone-pyrazole association at various temperature.

A similar addition has been observed for methyl ethyl ketone.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a NMR-2305 spectrometer (60 MHz), ^{13}C NMR spectra on a Brucker HX-90 instrument. The NMR probe temperature was kept constant within ±1°. PMR chemical shifts are from TMS, ^{13}C NMR chemical shifts from the acetone methyl signal.

Commercial imidazole and pyrazole ("pure for analysis" purity grade) were used. Ether and tetrahydrofuran were purified by chromatography through alumina and distilling over lithium aluminium hydride in an argon atmosphere. The ampoules were filled in an argon atmosphere. Acetone was of the "spectral pure" grade, methyl ethyl ketone of the "chemically pure" grade. These solvents were chromatographed on alumina and distilled in an argon atmosphere.

A similar experimental procedure was applied in Part 1 (Ref. 2) of this work.

REFERENCES

[1] M. L. Roumestant, P. Viallefont, J. Elguero and R. Jacquier, *Tetrahedron Letters* 495 (1969).

[2] A. N. Nesmeyanov, E. B. Zavelovich, V. N. Babin, N. S. Kochetkova and E. I. Fedin, *Tetrahedron* **31**, 1461 (1975).

[3] V. Gutmann, *Coordination Chemistry in Non-Aqueous Solutions*, Moscow (1971).

[4] A. I. Kol'tsov and G. M. Kheifets, *Uspekhi Khim.* **41**, 877 (1972).