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THE PROTON MAGNETIC RESONANCE SPECTRUM OF 1-METHYLPYRAZOLE

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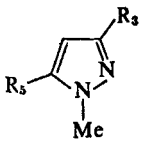
Abstract—5-Deutero-1-methylpyrazole was synthesised and used to assign multiplets in the PMR spectrum of 1-methylpyrazole.

THE PROTON magnetic resonance spectrum of 1-methylpyrazole (**1**) has been reported many times, but authors disagree on the assignment of signals to H-3 and H-5. Elguero and his co-workers,[1] using homo- and hetero-nuclear decoupling provided evidence that, in $CDCl_3$ and CCl_4 solutions, H-5 absorbs at higher field than H-3. Identification of signals using model compounds as criteria has led to the alternative assignment,[2,3] and in one case the two chemical shifts are described as equal.[4] Although there can be little doubt that the first assignment[1] is correct, we thought it advisable to verify these results using a specifically deuterated derivative.

(**1**) $R_3 = H$, $R_5 = H$
(**2**) $R_3 = H$, $R_5 = COOD$
(**3**) $R_3 = COOH$, $R_5 = H$
(**4**) $R_3 = H$, $R_5 = COOH$
(**5**) $R_3 = H$, $R_5 = D$
(**6**) $R_3 = H$, $R_5 = COOMe$
(**7**) $R_3 = COOMe$, $R_5 = H$



Incorporation of deuterium into positions 3 or 5 of (**1**) was troublesome, but decarboxylation of the 5-deutero-carboxylic acid (**2**) led to 50 to 60% labelling at position 5, with apparently no scrambling. The 3- and 5-carboxylic acids, (**3**) and (**4**), were prepared by oxidation[5] of a mixture of 1,3- and 1,5-dimethylpyrazoles[6] and were separated by distillation of the methyl esters. The partial deuteration of C-5 reduces the signal of this proton making possible unambiguous identification of the multiplets from H-3 and H-5 (Fig. 1). Our results for a number of solvents are listed in Table 1 and where applicable confirm the work of Elguero *et al.*[1].

In the neutral molecule, the absorption due to H-3, on the carbon atom adjacent to N-2, is always more broadened and contains less fine structure than that of H-5, an observation which readily distinguishes the two signals. The spectrum of the cation, measured in trifluoroacetic acid, is sharpened, probably due to reduced nitrogen quadrupole coupling caused by removal of the nitrogen lone pair dipole on protonation. The multiplets observed for the ring protons of the deuterated cation (Fig. 1) can be explained in terms of the superimposed spectra of an approximately equimolar mixture of the deuterated and non-deuterated species.

Our results emphasize the hazards of using model compounds to assign multiplets to specific protons in molecules where the respective chemical shifts are small. In this

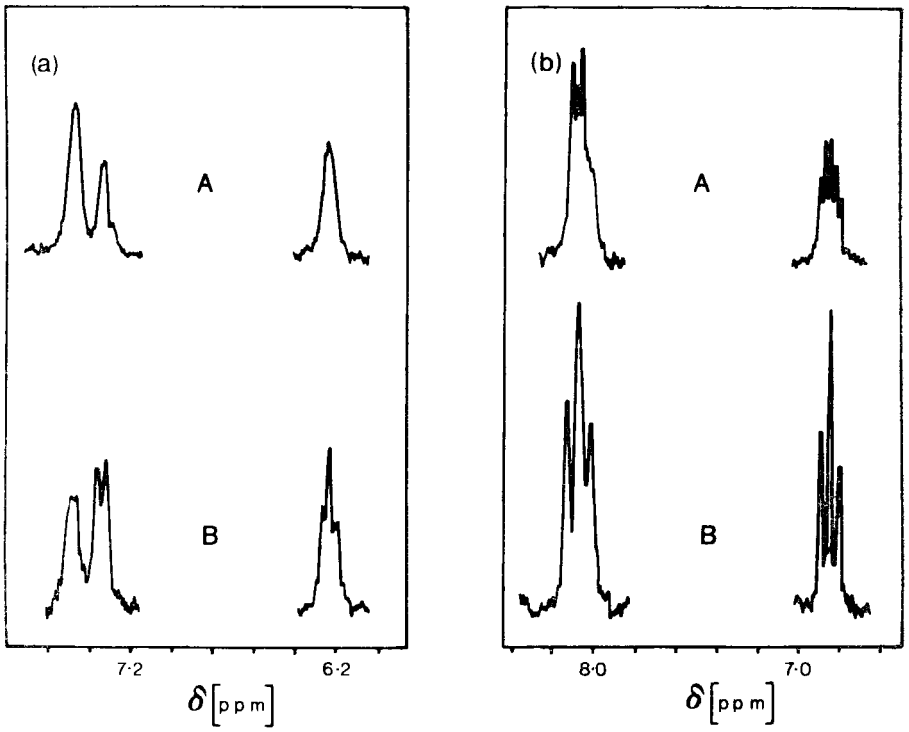


FIG. 1. The PMR spectrum in (a) $CDCl_3$ and (b) TFA of

A. 1-methylpyrazole (**1**). B. 50/50 mixture of (**1**) and its 5-deutero derivative (**5**).

TABLE 1. (a) CHEMICAL SHIFTS (δ) OF THE RING PROTONS OF 1-METHYLPYRAZOLE. VALUES OBTAINED FROM MULTIPLE RESONANCE EXPERIMENTS[1] IN PARENTHESES.

Solvent	H-3	H-4	H-5
CCl_4	7·28 (7·30)	6·10 (6·10)	7·22 (7·22)
$CDCl_3$	7·48 (7·49)	6·23 (6·22)	7·33 (7·35)
TFA	8·08 (8·11)	6·83 (6·83)	8·02 (8·05)
DMSO	7·41 (7·41)	6·20 (6·21)	7·65 (7·66)
Benzene	7·52	6·04	6·74
Pyridine	7·66	6·27	7·47

(b) PMR DATA FOR INTERMEDIATE COMPOUNDS IN THE DEUTERATION OF 1-METHYLPYRAZOLE

Compound	Solvent	δ-3	δ-4	δ-5	δ-NMe	δ-COOMe	J
(**3**)	DMSO	—	6·73	7·84	3·93	—	2·5
(**4**)	DMSO	7·52	6·85	—	4·12	—	2·0
(**6**)	CCl_4	7·38	6·76	—	4·19	3·87	2·5
(**7**)	CCl_4	—	6·68	7·46	3·99	3·87	2·5

case even methyl substituents[2,3,4] can perturb the magnetic environment enough to invert the assignment.

EXPERIMENTAL

1-Methylpyrazole (**1**) was prepared by the method of Jones.[7]

5-Deutero-1-methylpyrazole (**5**). Alkaline permanganate oxidation of a mixture of 1,3- and 1,5-

dimethylpyrazoles,[5] prepared by the method of Burness[6] gave a mixture of 1-methylpyrazole 3- and 5-*carboxylic acids* (**3**), (**4**). Esterification of the mixed acid (2·2 g) was achieved by refluxing for four hours in methanol (10 ml) and concentrated sulphuric acid (1 g). The mixed esters (2·0 g) were separated by distillation: 5-methoxycarbonyl (**6**), b.p. 150 to 5°/7·5 mm; 3-methoxycarbonyl (**7**), b.p. 260 to 3°/7·0 mm. Hydrolysis of the esters (1:1 hydrochloric acid under reflux for four hours) gave the pure acids. 1-Methyl-5-carboxypyrazole (**4**), m.p. 223 to 4° (lit., 222°)[8]. Found C, 47·27; H, 4·91; N, 22·44%. 1-Methyl-3-carboxypyrazole (**3**), m.p. 151 to 2°. Found C, 47·36; H, 4·82; N, 22·30%. Calculated from $C_5H_6N_2O_2$, C, 47·58; H, 4·76; N, 22·20%. The 1-methyl-5-carboxypyrazole was deuterated by exchange with deuterium oxide (4 times) and then decarboxylated in the presence of copper bronze at 130° to give a mixture (60 to 75% yield) of 1-methylpyrazole and its 5-deutero derivative.

The proton magnetic resonance spectra of 4% w/v solutions were recorded in the field sweep mode, on a Perkin–Elmer R10 spectrometer. TMS was used as an internal reference, and chemical shifts (±0·02 ppm) were measured using the side-band technique.

REFERENCES

1. J. Elguero, R. Jacquier and Mme. Hong Cung N. Tien Duc, *Bull. Soc. Chim. France*, 3727 (1966).
2. L. Tensmeyer and C. Ainsworth, *J. Org. Chem.* **31,** 1878 (1966).
3. I. L. Finar and E. F. Mooney, *Spectrochim. Acta*, **20,** 1269 (1964).
4. C. L. Habraken, H. J. Munter, and J. Westgeet, *Rec. Trav. Chim.* **86,** 56 (1967).
5. L. Claisen and P. Roosen, *Liebigs Ann. Chem.* **278,** 278,292 (1894).
6. J. D. Burness, *J. Org. Chem.* **21,** 100 (1956).
7. R. G. Jones, *J. Am. Chem. Soc.* **71,** 3997 (1949).
8. R. Hüttel and M. E. Schön, *Ann. Chem.* **625,** 55 (1959).